

# World Journal of *Orthopedics*

*World J Orthop* 2018 January 18; 9(1): 1-6





**ORIGINAL ARTICLE**

**Prospective Study**

- 1 Dutch version of the Victorian Institute of Sports Assessment-Achilles questionnaire for Achilles tendinopathy: Reliability, validity and applicability to non-athletes

*Sierevelt I, van Sterkenburg M, Tol H, van Dalen B, van Dijk N, Haverkamp D*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Qianjun Cui, MD, Professor, Surgeon, Vice Chair for Research, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, 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 Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central and Scopus.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Li-Jun Cui*  
**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**  
**Qianjun (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, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com>

[www.wjgnet.com/2218-5836/editorialboard.htm](http://www.wjgnet.com/2218-5836/editorialboard.htm)

**EDITORIAL OFFICE**  
 Xiu-Xia Song, Director  
*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.fjpublishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.fjpublishing.com/helpdesk>  
<http://www.wjgnet.com>

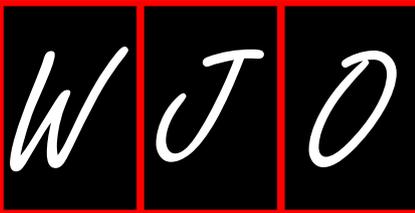
**PUBLICATION DATE**  
 January 18, 2018

**COPYRIGHT**  
 © 2018 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.fjpublishing.com>



Prospective Study

## Dutch version of the Victorian Institute of Sports Assessment-Achilles questionnaire for Achilles tendinopathy: Reliability, validity and applicability to non-athletes

Inger Sierevelt, Maayke van Sterkenburg, Hans Tol, Bella van Dalen, Niek van Dijk, Daniel Haverkamp

Inger Sierevelt, Daniel Haverkamp, Department of Orthopaedic Surgery, Slotervaart Hospital, Amsterdam 1066 EC, The Netherlands

Maayke van Sterkenburg, Niek van Dijk, Department of Orthopedic Surgery, Academic Medical Center, Amsterdam 1105 AZ, The Netherlands

Hans Tol, Academic Center for Evidence Based Sports Medicine, Academic Medical Center Amsterdam, Amsterdam 1105 AZ, The Netherlands

Bella van Dalen, Bergmanclinics te Naarden, Naarden 1411 GE, The Netherlands

**Author contributions:** All the authors contributed to this manuscript.

**Institutional review board statement:** The local accredited ethics committee (Dutch acronym: METC) reviewed this study in an expedited manner and determined, based on the Dutch Medical Research Involving Human Subjects Act (Dutch acronym: WMO), that the research activities described meet the requirements for exemption from METC review under the WMO.

**Informed consent statement:** All patients received a patient information brochure.

**Conflict-of-interest statement:** The authors do not report a conflict of interest.

**Data sharing statement:** None.

**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: Daniel Haverkamp, MD, PhD, Department of Orthopaedic Surgery, Slotervaart Hospital, Louwesweg 6, Amsterdam 1066 EC, The Netherlands. [daniel@drhaverkamp.com](mailto:daniel@drhaverkamp.com)  
Telephone: +31-6-45628276

Received: January 24, 2017

Peer-review started: February 2, 2017

First decision: June 26, 2017

Revised: November 30, 2017

Accepted: December 1, 2017

Article in press: December 1, 2017

Published online: January 18, 2018

### Abstract

#### AIM

To translate the Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire into the Dutch language (VISA-A-NL), and to assess its reliability, validity, and applicability to non-athletes.

#### METHODS

After translation according to a forward-backward protocol, 101 patients with complaints of Achilles tendinopathy were asked to fill out the VISA-A-NL at two time points together with visual analogue scale, the Foot and Ankle Outcome Score, and the Short Form-36 questionnaires. Reliability, internal consistency, construct validity, and content validity were tested.

#### RESULTS

The VISA-A-NL showed high reliability (0.97, 95%CI: 0.95-0.98). Cronbach's alpha (internal consistency) was 0.80. It increased to 0.88 without activity domain. Correlation with other questionnaires was moderate or poorer.

## CONCLUSION

The VISA-A-NL proved to be an excellent evaluation instrument for the Dutch physician. If applied to non-athletes, using a modified score (questions 1-6) should be considered.

**Key words:** Achilles tendon; Victorian Institute of Sports Assessment-Achilles; Validity; Patient reported outcome measurement

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** This manuscript shows the validity and reliability of the Dutch version of the Victorian Institute of Sports Assessment-Achilles (VISA-A) in patients with Achilles tendinopathy. The most important finding is that the athletes and non-athletes cannot be compared. The effect of treatment, when using the VISA-A score to measure outcome, is underestimated in non-athletes. If applied to non-athletes, using a modified score (questions 1-6) should be considered.

Sierevelt I, van Sterkenburg M, Tol H, van Dalen B, van Dijk N, Haverkamp D. Dutch version of the Victorian Institute of Sports Assessment-Achilles questionnaire for Achilles tendinopathy: Reliability, validity and applicability to non-athletes. *World J Orthop* 2018; 9(1): 1-6 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i1/1.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i1.1>

## INTRODUCTION

Achilles tendinopathy is a major cause of chronic pain and disability, which may lead to suboptimal overall health as physical inactivity is a risk factor for cardiovascular disease<sup>[1]</sup>. Many studies have been published on a multitude of treatments for Achilles tendinopathy, but prospective series on the outcome are lacking. One of the factors limiting the quality of research may be the absence of standardised measures to evaluate the outcome of treatment<sup>[2]</sup>. A patient's subjective assessment of treatment outcome such as pain, functional ability, and satisfaction fulfils the criteria of being valid, reliable, and sensitive to change if gathered by a correctly designed and tested patient-centred questionnaire<sup>[3]</sup>. The Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire was created in 2001 to assess clinical severity for patients with Achilles tendinopathy. It is a self-administered questionnaire evaluating symptoms and their effect on physical activity, and displayed reliability and construct validity. Subjective scoring systems can be used in countries other than the ones in which they were developed if translated and validated for a specific language and population<sup>[4-6]</sup>. The VISA-A has been translated into Swedish, Italian, and German and proved to be able to determine the clinical severity and

provide information about the effect of the management of patients with Achilles tendinopathy who speak these languages<sup>[1,7,8]</sup>. The aim of this study was to translate the VISA-A questionnaire into the Dutch language (VISA-A-NL) and assess its reliability and validity to provide a valid questionnaire for the Dutch population. Moreover, the questionnaire seems to be designed only for athletes as 40% of the points account for activity. As approximately 30% of patients with complaints of Achilles tendinopathy have a sedentary lifestyle<sup>[9]</sup>, applicability to non-athletes was also evaluated in this study.

## MATERIALS AND METHODS

### Translation procedure

A Dutch translation was made using a forward-backward translation protocol according to the guidelines of Guillemin *et al.*<sup>[4,5]</sup>. Three people independently translated the English version of the VISA-A questionnaire to Dutch. All three were in the medical field, and spoke English as a second language. One independent native speaker who was not active in the medical field translated this Dutch version back into English. Discrepancies were discussed and adjusted for the final Dutch questionnaire (VISA-A-NL). It was assumed that no major cultural differences in lifestyle exist between the Dutch and Canadian populations, and therefore cultural adaptation of the questionnaire was not required<sup>[4,10]</sup>.

### Patients

The local accredited ethics committee (Dutch acronym: METC) reviewed this study in an expedited manner and determined, based on the Dutch Medical Research Involving Human Subjects Act (Dutch acronym: WMO), that the research activities described meet the requirements for exemption from METC review under the WMO. According to the Consensus-Based Standards for the Selection of Health Measurement Instruments criteria, we decided to choose a sample size of at least 100 patients. Actually, 104 consecutive patients from the outpatient clinic of three participating Dutch hospitals were included, of whom 47% were female; 79 (76%) were athletes and 25 (24%) were non-athletes. Their mean age was 48.5 years (SD, 11.6 years).

All patients had complaints of Achilles tendinopathy (including mid-portion and insertional tendinopathy, paratendinopathy, and retrocalcaneal bursitis)<sup>[11]</sup>.

They were clinically assessed and an American Orthopaedic Foot and Ankle Society (AOFAS) questionnaire was taken by the consulting physician. All patients were asked to fill out two sets of questionnaires; the first [A = VISA-A-NL, the Visual Analogue Scale (VAS) pain, VAS function, the Foot and Ankle Outcome Score (FAOS), and the Short Form-36 (SF-36)] was completed on the day of consultation, and the second (B = VISA-A-NL) was completed 5 d later<sup>[12]</sup>. Additionally, they were asked whether their complaints had changed since the first assessment.

### Questionnaires

The original English version of the VISA-A questionnaire as designed by Robinson and co-workers<sup>[2]</sup> contains eight questions that cover three domains; pain (questions 1-3), function (questions 4-6), and activity (questions 7-8). Scores are summed to yield a total of 100 points in an asymptomatic subject: questions 1-7 score a maximum of 10 points each; question 8, on sporting activity, carries a maximum of 30. Pain on undertaking sports will automatically lead to a loss of 10-20 points.

Since questions 7 and 8 refer to sport activities (accounting for 40% of points) and the study population contained both athletes and non-athletes, we modified the VISA-A score by deleting both questions and investigated the psychometric properties of both the VISA and the modified VISA.

FAOS is a 42-item questionnaire divided into five subscales: pain (9 items), other symptoms (7 items), activities of daily living (17 items), sport and recreation function (5 items), and foot and ankle related quality of life (4 items). Each question can be scored on a 5-point Likert scale (0-4) and each of the five subscale scores is calculated as the sum of the items included. Raw scores are then transformed to 0-100, worst to best score<sup>[13]</sup>.

SF-36 is a self-administered, generic HRQL (health related quality of life) instrument<sup>[14-17]</sup>. It comprises 36 items across eight dimensions (physical functioning, role limitation due to physical problems, bodily pain, perception of general health, energy and vitality, social functioning, role limitation due to emotional problems, and mental health). The eight dimensions of the SF-36 score are calculated on a 0-100 worst to best scale<sup>[18]</sup>.

The VAS is a 100 mm visual analogue scale and is used to determine the seriousness of pain and functional problems<sup>[19]</sup>.

In 1994, the AOFAS developed a questionnaire to provide a standard method for reporting clinical status of the ankle and foot. The AOFAS-ankle and hindfoot clinical rating system combines both subjective and objective factors into numerical scales to describe function, alignment, and pain. Since objective aspects are incorporated, this questionnaire has to be completed by the investigator<sup>[20]</sup>.

### Testing

When a questionnaire is developed or translated, the most important consideration is that it must be able to accurately measure that for which it is designed. To evaluate the psychometric properties of the VISA-A-NL, both reliability and validity were assessed.

### Reliability

Reliability is defined as the extent to which patients can be distinguished from each other, despite measurement errors<sup>[21]</sup>.

**Test-retest reliability:** Test-retest reliability refers to the repeatability of the test and measures the extent to which the same results are obtained on repeated

administration when no change in physical functioning has occurred<sup>[22]</sup>. To determine the test-retest reliability, a second VISA-A-NL (B) questionnaire was given to all patients; 67 patients responded. In 15 patients, complaints had changed at re-test measured by an anchor question (7 item Likert). Test-retest reliability was therefore assessed in 52 patients, using the intra-class coefficient (ICC<sub>agreement</sub>, two-way random effects model). An ICC > 0.75 was considered good<sup>[23]</sup>. A *t*-test was performed to determine the presence of a systematic difference between the first and second assessment. Additionally, standard error of measurement (SEM) was calculated as the square root of the within-subject variance. The smallest detectable change (SDC) was calculated as  $1.96 \times \sqrt{2} \times \text{SEM}$ . The SDC is the smallest measurement change that can be interpreted as real change<sup>[24]</sup>.

**Internal consistency:** Internal consistency of the scale is the extent to which the items are inter-correlated and cover the same construct (homogeneity of the scale). To evaluate the internal consistency of the VISA-A, Cronbach's alpha was calculated. A Cronbach's alpha of 0.7 was considered to represent an acceptable degree of internal consistency, 0.8 was considered as good, and 0.9 as excellent internal consistency<sup>[25]</sup>.

### Validity

Validity relates to the ability of a questionnaire to measure outcome parameter of interest.

**Construct validity:** Construct validity was tested by determining the association between the VISA-A-NL questionnaire and the FAOS, SF-36, VAS scores for pain and function, and the AOFAS, using Pearson correlation coefficients. We evaluated construct validity by hypothesizing that correlation coefficients between the VISA-A-NL (with and without the activity questions) and VAS pain, FAOS pain, symptoms, and sport and recreation, and SF-36 bodily pain and physical functioning would be higher than correlations with the other domains.

**Content validity:** Content validity examines the extent to which all concepts of interest are adequately represented by the items in the questionnaire<sup>[12]</sup>. It was evaluated by assessing distribution and floor and ceiling effects of the VISA-A-NL. These are considered to be present if more than 15% of responders achieve the lowest or highest possible score<sup>[12]</sup>.

### Statistical analysis

Statistical analyses were performed using PASW statistics 18.0 software (SPSS Inc., Chicago, IL, United States). A *P*-value < 0.05 was considered statistically significant.

## RESULTS

Of 104 participants, 11 returned questionnaires that

**Table 1** The ICC<sub>agreement</sub> and Cronbach's alpha of the questionnaire

	Athletes ( <i>n</i> = 39)	Non-athletes ( <i>n</i> = 13)	Total ( <i>n</i> = 52)
ICC <sub>VISA total</sub> (95% CI)	0.95 (0.91-0.97)	-	0.97 (0.95-0.98)
ICC <sub>VISA modified</sub> (95% CI)	0.96 (0.92-0.98)	0.98 (0.93-0.99)	0.97 (0.95-0.98)
SEM <sub>VISA total</sub>	4.41 (4.4%)	-	4.07 (4.1%)
SEM <sub>VISA modified</sub>	2.64 (4.4%)	2.42 (4.0%)	2.68 (4.5%)
SDC <sub>VISA total</sub>	12.21 (12.2%)	-	11.28 (11.3%)
SDC <sub>VISA modified</sub>	7.32 (12.2%)	6.70 (11.2%)	7.44 (12.4%)
Cronbach's alpha <sub>VISA total</sub>	0.72	0.82	0.78
Cronbach's alpha <sub>VISA modified</sub>	0.83	0.86	0.86

ICC: Intra-class correlation coefficient; SEM: Standard error of measurement; SDC: Smallest detectable change.

**Table 2** Pearson correlation coefficients of the Victorian Institute of Sports Assessment-Achilles-NL with the other questionnaires (with and without activity domain)

	VISA-A <sub>Total</sub> Athletes ( <i>n</i> = 71)	VISA-A <sub>Modified</sub> Athletes ( <i>n</i> = 71)	VISA-A <sub>Modified</sub> Non-athletes ( <i>n</i> = 22)	VISA-A <sub>Total</sub> Entire population ( <i>n</i> = 93)	VISA-A <sub>Modified</sub> Entire population ( <i>n</i> = 93)
VAS pain	-0.54 <sup>a</sup>	-0.58 <sup>a</sup>	-0.39	-0.54 <sup>a</sup>	-0.57 <sup>a</sup>
VAS function	0.52 <sup>a</sup>	0.51 <sup>a</sup>	0.44 <sup>a</sup>	0.50 <sup>a</sup>	0.52 <sup>a</sup>
AOFAS	0.48 <sup>a</sup>	0.46 <sup>a</sup>	0.31	0.56 <sup>a</sup>	0.50 <sup>a</sup>
FAOS symptoms	0.45 <sup>a</sup>	0.52 <sup>a</sup>	0.53 <sup>a</sup>	0.58 <sup>a</sup>	0.60 <sup>a</sup>
FAOS pain	0.53 <sup>a</sup>	0.56 <sup>a</sup>	0.52 <sup>a</sup>	0.58 <sup>a</sup>	0.60 <sup>a</sup>
FAOS ADL	0.56 <sup>a</sup>	0.55 <sup>a</sup>	0.47 <sup>a</sup>	0.59 <sup>a</sup>	0.58 <sup>a</sup>
FAOS sport	0.56 <sup>a</sup>	0.61 <sup>a</sup>	0.43 <sup>a</sup>	0.55 <sup>a</sup>	0.59 <sup>a</sup>
FAOS QOL	0.29 <sup>a</sup>	0.33 <sup>a</sup>	0.14	0.38 <sup>a</sup>	0.37 <sup>a</sup>
SF-36 physical functioning	0.55 <sup>a</sup>	0.63 <sup>a</sup>	0.66 <sup>a</sup>	0.70 <sup>a</sup>	0.71 <sup>a</sup>
SF-36 role physical	0.13	0.12	0.58 <sup>a</sup>	0.31 <sup>a</sup>	0.32 <sup>a</sup>
SF-36 bodily pain	0.31	0.40 <sup>a</sup>	0.46 <sup>a</sup>	0.49 <sup>a</sup>	0.51 <sup>a</sup>
SF-36 social functioning	0.01	-0.04	0.29	0.27 <sup>a</sup>	0.21
SF-36 mental health	-0.11	-0.07	0.39	0.21	0.20
SF-36 role emotional	-0.06	0.02	0.65 <sup>a</sup>	0.37 <sup>a</sup>	0.39 <sup>a</sup>
SF-36 vitality	-0.26	-0.25	0.26	-0.05	-0.09
SF-36 general health perception	-0.01	-0.02	0.28	0.25 <sup>a</sup>	0.21
SF-36 physical component scale	0.43 <sup>a</sup>	0.47 <sup>a</sup>	0.36	0.52 <sup>a</sup>	0.51 <sup>a</sup>
SF-36 mental component scale	-0.34 <sup>a</sup>	-0.32 <sup>a</sup>	0.49 <sup>a</sup>	0.04	0.03

<sup>a</sup>*P* < 0.05. VISA-A: Victorian Institute of Sports Assessment-Achilles; VAS: Visual analogue scale; AOFAS: American Orthopaedic Foot and Ankle Society; FAOS: Foot and ankle outcome score; SF-36: Short form-36.

were filled out incompletely or erroneously and were therefore excluded from analysis. Thus, 93 patients were finally included in the analysis.

### Reliability

Of 93 patients, 52 (56%) returned the second set of questionnaires. The ICC<sub>agreement</sub> of the questionnaire was 0.97 (95%CI: 0.95-0.98) and Cronbach's alpha was 0.78 for the entire study population (Table 1). A statistically significant difference between the two assessments was not observed for both versions of the VISA-A-NL in athletes, nor in non-athletes ( $0.29 < P < 0.67$ ).

### Validity

Pearson correlation coefficients of the VISA-A-NL with the other questionnaires are shown in Table 2. The subscale "SF-36 physical functioning" correlated well with the VISA-A-NL questionnaire, both with and without activity domain. Most other physical domains correlated moderately, but the subscales of FAOS quality of life showed a poor correlation with VISA-A. A

poor correlation was also observed for the psychological domains (SF-36 social functioning, mental health, role emotional, vitality, and general health perception).

The mean scores of the VISA-A-NL questionnaire were 52.4 (SD 19.7) and 22.0 (SD 15.7) for athletes and non-athletes, respectively. The mean scores of the modified VISA-A-NL questionnaire were 36.2 (SD 13.9) and again 22.0 (SD 15.7) for athletes and non-athletes, respectively. Floor and ceiling effects were not observed in both versions of the questionnaire, as only one (1%) subject scored 0 points, nobody scored 100 points, and one patient scored the maximum of 60 points in the modified VISA-A score.

## DISCUSSION

The aim of this study was to translate the original VISA-A questionnaire on the subjective complaints of patients with Achilles tendinopathy into the Dutch language, to validate it, and to assess its applicability to non-athletes.

The translation procedure did not create any pro-

blems, since the items are universal and there is no large cultural difference between Dutch and Canadian patients.

Reliability of the translation was excellent, with a statistically non-significant difference between assessments. This outcome may be explained by the fact that, as the procedure for the Dutch Oxford 12-item knee questionnaire taught us, we introduced a question if complaints had changed between assessments<sup>[26]</sup>. Fifteen (22%) of sixty-seven patients answered this question with "yes", and therefore they were excluded from reliability testing.

The SDC in this study indicated that under a stable condition, the VISA-A score can vary up to 12 points. For clinical studies, this implies that clinical changes can only be detected if they exceed the 12 points.

The study questionnaire showed good internal consistency (Cronbach's alpha = 0.80), but there indeed was a negative effect of the activity domain. Sub-analysis without these questions showed an increase of Cronbach's alpha to 0.88. However, when measuring the effect of a treatment in a mixed group of athletes and non-athletes, the effect of treatment could be underestimated. For example, an athlete can score 0 points with questions 7 and 8 before treatment as complaints withhold him/her from being sports active. After treatment, the athlete is complaint-free and scores 100 points. The non-athlete also scores 0 points for questions 7 and 8 before treatment, and is also complaint-free after treatment. However, he/she will never score higher than 60 points as questions 7 and 8 will not be answered differently between assessments. The effect of treatment, when using the VISA-A score to measure outcome, is therefore underestimated in non-athletes.

When choosing the VISA-A questionnaire for a mixed population of athletes and non-athletes, deleting questions 7 and 8 can be considered, since the psychometric properties of the modified VISA-A were comparable with those of the original version.

Generally, Pearson correlation coefficients were higher for physical than psychological components. Convergent and divergent validity is confirmed as correlation coefficients were higher for the physical domains of the questionnaires. However, for non-athletes, correlation with socio-emotional components was also higher. This could imply that physical restrictions in this subgroup with chronic Achilles tendinopathy have greater emotional and social consequences than in athletes. Noticeable is the moderate correlation of VISA-A with VAS, which is a validated subjective outcome measure frequently used for scientific means.

Low correlations can be explained by the fact that none of the questionnaires except for the VISA-A were validated for Achilles tendinopathy. Initially it was intended to do so, but this study aim was departed to not further enlarge patient burden as many of these questionnaires are extensive. Given the laborious inclusion of 104 patients in 3.5 years and a 56% response rate to

both assessments, this was well decided. This was also why responsiveness was not tested.

In conclusion, the VISA-A-NL questionnaire seems suitable for use in athletes. However, in a combined population of athletes and non-athletes, results will become incomparable as the highest possible score for non-athletes is 40 points lower than that for non-athletes. Psychometric properties of the VISA-A-NL, without questions 7 and 8, are satisfactory for both athletes and non-athletes. It is therefore proposed that the modified VISA-A-NL questionnaire is considered a mixed population of patients with Achilles tendinopathy, meaning a version with only questions 1-6 and the complete questionnaire (questions 1-8) is reserved for athletes only.

## ARTICLE HIGHLIGHTS

### Background

Achilles tendinopathy is a major cause of chronic pain and disability. Many studies have been published on a multitude of treatments for Achilles tendinopathy, but prospective series on the outcome are lacking. The Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire was created in 2001 to assess clinical severity for patients with Achilles tendinopathy. It is a self-administered questionnaire evaluating symptoms and their effect on physical activity, and displayed reliability and construct validity.

### Research frontiers

The VISA-A has been translated into Swedish, Italian, and German and proved to be able to determine the clinical severity and provide information about the effect of the management of patients with Achilles tendinopathy who speak these languages.

### Innovations and breakthroughs

This work translated the VISA-A questionnaire into the Dutch language (VISA-A-NL), assessed its validity and reliability, and provided a valid questionnaire for the Dutch population. The questionnaire seems to be designed only for athletes as 40% of the points account for activity. As approximately 30% of patients with complaints of Achilles tendinopathy have a sedentary lifestyle, applicability to non-athletes was also evaluated.

### Applications

Psychometric properties of the VISA-A-NL, without questions 7 and 8, are satisfactory for both athletes and non-athletes. It is therefore proposed that the modified VISA-A-NL questionnaire is considered for a mixed population of patients with Achilles tendinopathy.

## REFERENCES

- 1 **Maffulli N**, Longo UG, Testa V, Oliva F, Capasso G, Denaro V. Italian translation of the VISA-A score for tendinopathy of the main body of the Achilles tendon. *Disabil Rehabil* 2008; **30**: 1635-1639 [PMID: 18608373 DOI: 10.1080/09638280701785965]
- 2 **Robinson JM**, Cook JL, Purdam C, Visentini PJ, Ross J, Maffulli N, Taunton JE, Khan KM; Victorian Institute Of Sport Tendon Study Group. The VISA-A questionnaire: a valid and reliable index of the clinical severity of Achilles tendinopathy. *Br J Sports Med* 2001; **35**: 335-341 [PMID: 11579069 DOI: 10.1136/bjism.35.5.335]
- 3 **Dawson J**, Carr A. Outcomes evaluation in orthopaedics. *J Bone Joint Surg Br* 2001; **83**: 313-315 [PMID: 11341410 DOI: 10.1302/0301-620X.83B3.12148]
- 4 **Guillemin F**. Cross-cultural adaptation and validation of health status measures. *Scand J Rheumatol* 1995; **24**: 61-63 [PMID: 7747144 DOI: 10.3109/03009749509099285]
- 5 **Guillemin F**, Bombardier C, Beaton D. Cross-cultural adaptation

- of health-related quality of life measures: literature review and proposed guidelines. *J Clin Epidemiol* 1993; **46**: 1417-1432 [PMID: 8263569 DOI: 10.1016/0895-4356(93)90142-N]
- 6 **Mathias SD**, Fifer SK, Patrick DL. Rapid translation of quality of life measures for international clinical trials: avoiding errors in the minimalist approach. *Qual Life Res* 1994; **3**: 403-412 [PMID: 7866358 DOI: 10.1007/BF00435392]
  - 7 **Lohrer H**, Nauck T. Cross-cultural adaptation and validation of the VISA-A questionnaire for German-speaking achilles tendinopathy patients. *BMC Musculoskelet Disord* 2009; **10**: 134 [PMID: 19878572 DOI: 10.1186/1471-2474-10-134]
  - 8 **Silbernagel KG**, Thomeé R, Karlsson J. Cross-cultural adaptation of the VISA-A questionnaire, an index of clinical severity for patients with Achilles tendinopathy, with reliability, validity and structure evaluations. *BMC Musculoskelet Disord* 2005; **6**: 12 [PMID: 15748297 DOI: 10.1186/1471-2474-6-12]
  - 9 **Ames PR**, Longo UG, Denaro V, Maffulli N. Achilles tendon problems: not just an orthopaedic issue. *Disabil Rehabil* 2008; **30**: 1646-1650 [PMID: 18608383 DOI: 10.1080/09638280701785882]
  - 10 **Beaton DE**, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine (Phila Pa 1976)* 2000; **25**: 3186-3191 [PMID: 11124735 DOI: 10.1097/00007632-200012150-00014]
  - 11 **van Dijk CN**, van Sterkenburg MN, Wiegnerink JI, Karlsson J, Maffulli N. Terminology for Achilles tendon related disorders. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 835-841 [PMID: 21222102 DOI: 10.1007/s00167-010-1374-z]
  - 12 **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]
  - 13 **Roos EM**, Brandsson S, Karlsson J. Validation of the foot and ankle outcome score for ankle ligament reconstruction. *Foot Ankle Int* 2001; **22**: 788-794 [PMID: 11642530 DOI: 10.1177/107110070102201004]
  - 14 **Aaronson NK**, Muller M, Cohen PD, Essink-Bot ML, Fekkes M, Sanderman R, Sprangers MA, te Velde A, Verrips E. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998; **51**: 1055-1068 [PMID: 9817123 DOI: 10.1016/S0895-4356(98)00097-3]
  - 15 **Brazier JE**, Harper R, Jones NM, O’Cathain A, Thomas KJ, Usherwood T, Westlake L. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ* 1992; **305**: 160-164 [PMID: 1285753 DOI: 10.1136/bmj.305.6846.160]
  - 16 **Sullivan LM**, Dukes KA, Harris L, Dittus RS, Greenfield S, Kaplan SH. A comparison of various methods of collecting self-reported health outcomes data among low-income and minority patients. *Med Care* 1995; **33**: AS183-AS194 [PMID: 7723446]
  - 17 **Ware JE Jr**, 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]
  - 18 **Insall JN**, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. *Clin Orthop Relat Res* 1989; (248): 13-14 [PMID: 2805470 DOI: 10.1097/00003086-198911000-00004]
  - 19 **Price DD**, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain* 1983; **17**: 45-56 [PMID: 6226917 DOI: 10.1016/0304-3959(83)90126-4]
  - 20 **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]
  - 21 **Streiner DL**. Starting at the beginning: an introduction to coefficient alpha and internal consistency. *J Pers Assess* 2003; **80**: 99-103 [PMID: 12584072 DOI: 10.1207/S15327752JPA8001\_18]
  - 22 **Eechaute C**, Vaes P, Duquet W, Van Gheluwe B. Test-retest reliability of sudden ankle inversion measurements in subjects with healthy ankle joints. *J Athl Train* 2007; **42**: 60-65 [PMID: 17597945]
  - 23 **Fleiss JL**. The design and analysis of clinical experiments. 1986. New York: Wiley
  - 24 **Beckerman H**, Roebroeck ME, Lankhorst GJ, Becher JG, Bezemer PD, Verbeek AL. Smallest real difference, a link between reproducibility and responsiveness. *Qual Life Res* 2001; **10**: 571-578 [PMID: 11822790 DOI: 10.1023/A:1013138911638]
  - 25 **Dunbar MJ**, Robertsson O, Ryd L, Lidgren L. Translation and validation of the Oxford-12 item knee score for use in Sweden. *Acta Orthop Scand* 2000; **71**: 268-274 [PMID: 10919298 DOI: 10.1080/000164700317411861]
  - 26 **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]

**P- Reviewer:** Hernandez-Sanchez S **S- Editor:** Kong JX  
**L- Editor:** Wang TQ **E- Editor:** Li RF





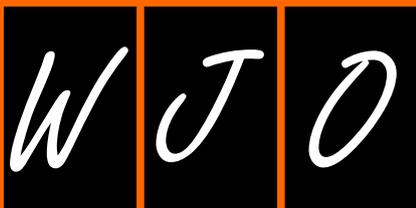
Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 February 18; 9(2): 7-13





**ORIGINAL ARTICLE**

**Basic Study**

- 7 Optimal surgical approach for the treatment of Quervains disease: A surgical-anatomical study  
*Poublon AR, Kleinrensink GJ, Kerver ALA, Coert JH, Walbeehm ET*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Albert Isidro, MD, PhD, Professor, Surgeon, Orthopaedic Surgery Department, Serv COT Hosp, Sagrat Cor Unidad Docente UB, Barcelona 08015, 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 Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central and Scopus.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Li-Jun Cui*  
**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, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com>

[www.wjgnet.com/2218-5836/editorialboard.htm](http://www.wjgnet.com/2218-5836/editorialboard.htm)

**EDITORIAL OFFICE**  
 Xiu-Xia Song, Director  
*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 February 18, 2018

**COPYRIGHT**  
 © 2018 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.f6publishing.com>

## Basic Study

**Optimal surgical approach for the treatment of Quervains disease: A surgical-anatomical study**

Alexander R Poublon, Gert-Jan Kleinrensink, Anton LA Kerver, J Henk Coert, Erik T Walbeehm

Alexander R Poublon, Gert-Jan Kleinrensink, Department of Neuroscience and Anatomy, Erasmus MC, Rotterdam, Zuid-Holland 3000 CA, Netherlands

Anton LA Kerver, Department of Plastic and Reconstructive surgery, Catharina Ziekenhuis, Eindhoven, Noord-Brabant 5623 EJ, Netherlands

J Henk Coert, Department of Plastic Surgery, UMC Utrecht, Utrecht, Utrecht 3584 CX, Netherlands

Erik T Walbeehm, Department of Plastic Surgery, Radboud UMC, Gelderland, Nijmegen 6500 HB, Netherlands

ORCID number: Alexander R Poublon (0000-0001-8326-4869); Gert-Jan Kleinrensink (0000-0002-9073-3181); Anton LA Kerver (0000-0002-1534-1399); J Henk Coert (0000-0002-1921-9737); Erik T Walbeehm (0000-0002-5319-2224).

**Author contributions:** Poublon AR and Kerver ALA performed the research, did the experiments and wrote the paper; Kleinrensink GJ, Coert JH and Walbeehm ET helped with study design and writing of the paper.

**Institutional review board statement:** As this is a cadaveric study, no institutional review board statement is required.

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

**Data sharing statement:** No additional data was 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:** Alexander R Poublon, MD, Academic

Research, Department of Neuroscience and Anatomy, Erasmus MC, Postbus 2040, Rotterdam, Zuid-Holland 3000 CA, Netherlands. [a.poublon@erasmusmc.nl](mailto:a.poublon@erasmusmc.nl)  
Telephone: +31-62-8426599  
Fax: +31-10-7043257

Received: September 7, 2017  
Peer-review started: September 24, 2017  
First decision: November 6, 2017  
Revised: January 6, 2018  
Accepted: January 23, 2018  
Article in press: January 23, 2018  
Published online: February 18, 2018

**Abstract****AIM**

To determine which of the common used incision techniques has the lowest chance of iatrogenic damage to the nerves which at risk are the superficial branch of the radial nerve (SBRN) and the Lateral Antebrachial Cutaneous Nerve (LABCN).

**METHODS**

Twenty embalmed arms were dissected and the course of the SBRN and the LABCN in each individual arm was marked and the distance between the two branches of the SBRN at the location of the First Extensor Compartment (FEC) was measured. This data was used as input in a visualization tool called Computer Assisted Anatomy Mapping (CASAM) to map the course of the nerves in each individual arm.

**RESULTS**

This image visualizes that in 90% of the arms, one branch of the SBRN crosses the FEC and one branch runs volar to the compartment. The distance between the two branches was 7.8 mm at the beginning of the FEC and 10.2 mm at the end. Finally the angle of incision at which the chance of damage to the nerves is lowest, is 19.4

degrees volar to the radius.

### CONCLUSION

CASAM shows the complexity of the course of the SBRN over the FEC. None of the four widely used incision techniques has a significantly lower chance of iatrogenic nerve damage. Surgical skills are paramount to prevent iatrogenic nerve damage.

**Key words:** De Quervain's tenosynovitis; First dorsal compartment release; Wrist surgery

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Although many incision techniques can be found in literature no consensus on the best incision technique has been established. The study shows a large variation in the course of the superficial branch of the radial nerve over the first extensor compartment. However no complete safe zone can be defined. The choice of incision remains surgeons' preference and surgical skills are paramount to prevent iatrogenic nerve damage.

Poublon AR, Kleinrensink GJ, Kerver ALA, Coert JH, Walbeehm ET. Optimal surgical approach for the treatment of Quervains disease: A surgical-anatomical study. *World J Orthop* 2018; 9(2): 7-13 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i2/7.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i2.7>

## INTRODUCTION

A study regarding de Quervains disease (QD) performed in the UK showed a prevalence of 0.5% in men and 1.3% in women<sup>[1]</sup>. The study also showed a higher prevalence in workers and black people. Since its first description in 1895 by Fritz de Quervain, various treatment options have been described, varying from non-invasive techniques, such as splinting<sup>[2-7]</sup>, to more invasive techniques such as injection<sup>[3,8-13]</sup> or even an operation one very debilitating complication after surgery for de Quervains disease, is nerve damage.

In previous studies four incision types have been suggested when applying surgical treatment: Transverse, longitudinal, lazy "s" or even specific angle technique. The transverse incision is designed to follow the lines of Langer and provide a superior cosmetic result<sup>[14,15]</sup>. The skin is incised transversely for 0.5 to 1 cm and the underlying tissue is bluntly dissected down to the extensor retinaculum overlying the first extensor compartment. The retinaculum is opened longitudinally and the first extensor compartment is released.

The longitudinal incision has been emphasized as being the safest incision<sup>[16,17]</sup>. The skin is incised longitudinally for 1.5 to 2 cm over the first extensor compartment and the underlying tissue is bluntly dissected down to the extensor retinaculum. The extensor retinaculum is opened

longitudinally and the first extensor compartment is released.

The "lazy S" incision has been described<sup>[18]</sup>. The skin is incised with a stretched S over a length of 2 cm over the first extensor compartment. As with the other techniques, the underlying tissue is bluntly dissected down to the extensor retinaculum and the extensor retinaculum is opened longitudinally to release the first extensor compartment.

Another technique, is an incision under a specific angle as described<sup>[19]</sup>. Firstly a line is drawn down the mid-shaft of the first metacarpal and secondly a line is drawn perpendicular to the first line one finger width proximal to the base of the first metacarpal. From the intersection of these two lines, a 1-1.5 cm long incision is directed proximally and directed towards the ulna at a 30 to 45-degree angle.

However until now no consensus has been established on a "golden standard" for the incision type used for surgical treatment of the de Quervains Disease. The ideal incision should provide the best exposure with minimal scar tissue formation, a low recurrence rate and a minimal chance of iatrogenic damage to anatomical structures, *i.e.* the superficial nerves.

The structures most at risk in case of surgical treatment of QD are the SBRN and the Lateral Antebrachial Cutaneous Nerve (LABCN). The course of these nerves has been described in many previous studies (ref anatomy). The course of these nerves makes them very susceptible to iatrogenic damage. Some form of Superficial nerve damage has been estimated to occur in 0.5% to 30% of release<sup>[15,20-25]</sup>.

As postulated in an earlier study<sup>[26]</sup>, iatrogenic nerve damage to these nerves can lead do debilitating neuropathic pain symptoms<sup>[27]</sup>.

The aim of this study is to identify, out of the four operative techniques described above, the technique with the lowest risk of iatrogenic damage to the nerve.

By using a new anatomical tool called Computer Assisted Anatomy Mapping (CASAM) it was possible to visualize statistics on the course of the nerves most at risk, such as the SBRN and LABCN.

CASAM is a tool that made it possible to visually map the course of the two branches of the SBRN and the course of the LABCN in each of the twenty arms that were dissected. By enlarging and/or reducing the size of all twenty individual visual images to the size of the average length of all twenty arms and then layering all individual images over each other, a visual image was created that represents the jointly course of the nerves in the average arm<sup>[28,29]</sup> (see the CASAM paragraph below).

This image, created by using CASAM, shows the complexity of the course and density of the nerves at risk in the operative area and thus providing a tool to evaluate the four incision techniques when operating.

## MATERIALS AND METHODS

Twenty embalmed arms were dissected and the course

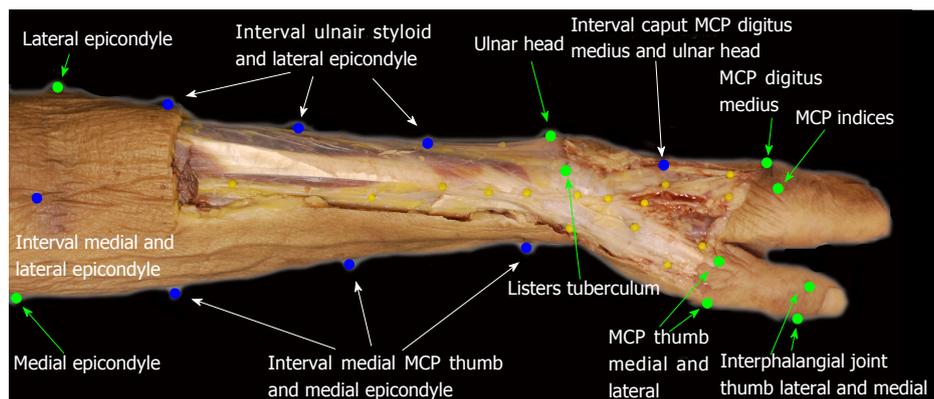


Figure 1 Landmarks used to outline the arm. MCP: Metacarpo phalangeal.

of the SBRN and LABCN were identified and marked using colored pins. All arms [9 male, 11 female; mean age 79.35 (range 61-90); 15 Right, 5 Left] were embalmed using the anubifix embalming solution. The dissections were then performed under a magnifying loupe with a 2.5 times magnification.

### Dissection

A standardized dissection technique was used. An incision was made from approximately 10 cm above the elbow down to the Metacarpo phalangeal (MCP) joint. At the proximal and distal end of the first incision, two perpendicular incisions were placed, by making these incisions a skin flap was created which could be removed laterally and medially. The Musculocutaneous Nerve was identified under the biceps and the LABCN was followed down to the MCP. At the distal 1/3 of the arm, the brachioradialis muscle was identified and bluntly dissected from the underlying tissue. The SBRN was found running under to the brachioradialis muscle (BR). Once the SBRN was found deep to the BR its course was followed to the muscle tendon transition from where the SBRN runs a superficial course. The SBRN was dissected distally to the Metacarpal joint and the nerve was identified using colored pins. After the SBRN was dissected down to the MCP the first extensor compartment was identified and the contour was marked using colored pins. Each arm was photographed with a Nikon D 60 with Sigma 50 mm 1:2.8 DG MACRO lens using a standardized setup<sup>[29]</sup>. The camera was positioned perpendicular to the specimen at a fixed distance and the arms were placed in specially designed clamps to ensure standard alignment.

### Measurements

The width and length of the first extensor compartment was measured using digital calipers. Also, the distance between the first two branches of the SBRN was measured at 5 mm intervals. Finally, the angle was measured in which an incision would pose a minimal threat to the SBRN.

### CASAM

Since the dissected arms vary in size, making comparisons

is difficult. By using CASAM it is possible to compare digital images of all dissected arm directly by warping them to an average dimension.

CASAM is based on the fact that the bony landmarks, such as Lister's tuberculum, are relatively constant in the same position in every arm. These are called "bony landmarks" (BL). From "bony landmarks" so called "shape defining landmarks" (SDL) were calculated, to mark the outline of each arm, by dividing the space between two BL's into equal parts. The BL's and SDL's were used to define the shape of each arm and average locations for these landmarks were computed, thus creating an "average" arm. All arms were then warped to the dimensions of the "average" arm making it possible to compare all the arms directly. The "scaled" course of the SBRN and the LABCN of all individual arms could then be compared directly. In the near future, the data collected in the anatomical study will be stored in a database which is made accessible via the internet. Then, a digital picture of a patient can be uploaded and warped to the "average" arm of the CASAM database to predict the course of the SBRN making more precise, individual preoperative planning possible.

The "bony landmarks" and "shape defining landmarks" used in this study can be found in Figure 1 (green marks and blue marks). An image is then created of each arm with average dimensions of all specimen. This shows the average course of the SBRN.

The mean distance between a line through the lateral and medial epicondyle and Lister's tuberculum, was 239.15 mm (range 209-281 mm), this distance was used as the reference length of the arm.

### Photoshop procedure

The course of the SBRN and LABCN was traced using Photoshop CS4, furthermore the shape of the first extensor compartment was also traced in photoshop. These photoshop layers could then be compiled into one picture for further analysis.

The four incision types could then be superimposed on the database of nerves and the proximity to nerve fibers could be assessed.

The area between the first and second branch of the SBRN was defined and subsequently 'filled' with a color

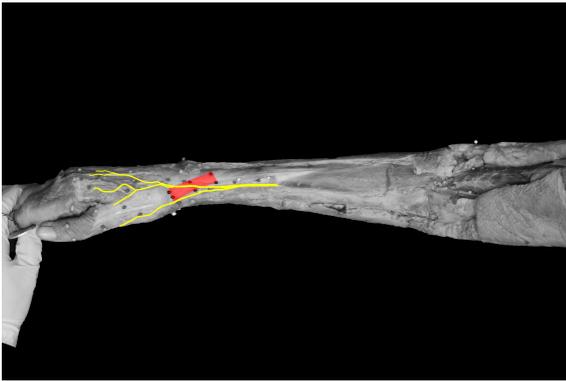


Figure 2 Course of the superficial branch of the radial nerve compared to the first extensor compartment.

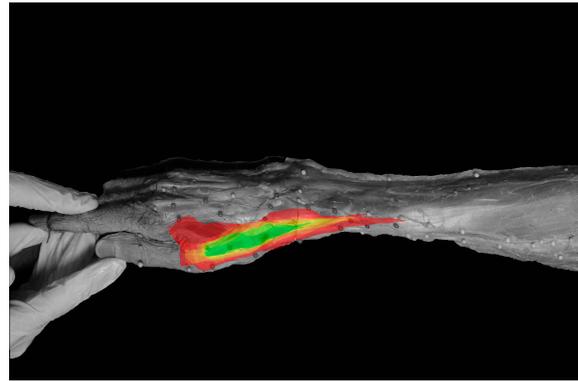


Figure 3 "Safe zone" gradient from red (95% nerve density) to green (0% nerve density).

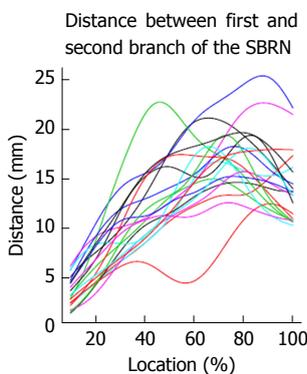


Figure 4 Distance between first and second branch of the superficial branch of the radial nerve for all 20 arms. SBRN: Superficial branch of the radial nerve.



Figure 5 Course of 20 superficial branch of the radial nerve (Yellow) and 20 lateral antebrachial cutaneous nerve (Green) compared to the first extensor compartment.

with 5% opacity. By compiling all 20 arms, an area could be defined in which the nerve was present in 5% of all cases and subsequently an area can be identified in which the nerve is present in 10% of cases *etc.* In this fashion a colored gradient map could be produced showing the 0 to 100% safe zone.

## RESULTS

The first extensor compartment can be found at a distance of 8 mm proximal to Lister's tuberculum and has a mean length of 26.6 mm (SD 5.3) and a mean width of 8.2 mm (SD 1.1). The mean angle between the first extensor compartment and the radius was 19.4° (SD 4.4). In all twenty specimens one or two branches of the SBRN ran across the first extensor compartment. The first branching of the SBRN was found 43.8 mm (SD 18.6) proximal to Lister's tuberculum.

CASAM shows that in 90% of all cases one branch of the SBRN (SR 2) runs across the first extensor compartment in a longitudinal direction. Also, a second branch (SR 1) runs volar to the first extensor compartment (Figure 2). In the present 20 specimen, no complete safe zone (a zone in which no nerve fibers are present) could be identified near the first extensor compartment. However, the CASAM images (Figure 2) show that the direction of

the SBRN over the first extensor compartment is at an angle of 19.4 degrees volar to the radius. Also one of the images created in CASAM shows a very small safe zone in which none of the nerves in the 20 specimen are present over the FEC (Figure 3).

The distance between the two branches of the SBRN crossing the first extensor compartment is 7.8 mm (SD 3.6) at the beginning of the first extensor compartment. 10.2 mm (SD 2.7) halfway down the first extensor compartment and 12.6mm (SD 2.7) at the end of the first extensor compartment (Figure 4). The branch running through the first extensor compartment divides in two more branches crossing the path of longitudinal path. The mean distance between the first branching point and the second is 43.5mm (SD 19.17), *e.g.*, the maximum length of a longitudinal incision.

During dissection it was not possible to follow the LABCN over the first extensor compartment because the nerve runs mostly intradermally. Furthermore, the course of the LABCN varies tremendously and no correlations between the courses of the LABCN could be found (Figure 5). No recommendation to prevent damage to the LABCN during Quervains disease surgery could be made. Therefore, the LABCN was left out. However as seen in earlier studies<sup>[26]</sup> the close relation between the LABCN and SBRN could be a major contributor to the cause of

neuropathic pain in the distal wrist.

## DISCUSSION

Since the description of the first surgical treatment of Quervains disease, many surgeons have tried to perfect the operating technique and hence tried to minimize the complications. This study focusses on aspects of the incision. However, this treatment modality too has its complications. Recurrent tendovaginitis is a complication which occurs and often requires a second operation<sup>[30,31]</sup>. Also (iatrogenic) nerve damage is frequently seen, varying from neurapraxia to total transection of the nerve, are reported in literature<sup>[20,22-25]</sup>.

The surgical treatment of Quervains disease is the treatment of choice after conservative measures have failed. To operate safely in the area of the dorso-radial part of the distal radius and the first metacarpus immediately introduces the problem of crossing and intertwining superficial branches of the radial nerve and the lateral cutaneous nerves (branches of the musculocutaneous nerve).

Three types of incisions are used to operate in this region; the transverse, the longitudinal and the "lazy S" type incision. Each of which has its advantages and disadvantages and no best practice ('golden standard') could be found in literature. In the present study an attempt is made to make an inventory of the course of the surgically relevant nerves related to the four incision types. Data was visualized using CASAM to give the surgeon concise information that allows him to make a choice between the four incisions.

### Transverse incision technique

The transverse technique offers a good exposure while keeping the scar small and provides the best esthetic result<sup>[14,15]</sup>. Also because the skin incision is perpendicular to the first extensor compartment, contraction of scar tissue is less likely to cause compression of the first extensor compartment and thus is less likely to cause a recurrence of the symptoms of Quervains disease. However, the transverse direction of the skin incision implicates a high risk of iatrogenic nerve damage demonstrated by the images provided by CASAM (Figure 5). Furthermore, the distance between the two branches of the SBRN is 11.4 mm (0-26.3), therefore a transverse incision not only increases risk of injury to one branch but to the second branch as well.

### Longitudinal incision technique

The longitudinal techniques offers more exposure than a transverse incision<sup>[16,17,32]</sup> with a lower chance of iatrogenic nerve damage<sup>[33]</sup>. However this technique offers a suboptimal cosmetic result and because the scar is directly over the first extensor compartment the retraction of scar tissue could cause compression of the first extensor compartment and recurrence of the symptoms of Quervains disease. The average length for the incision placed between the first two branches of the

SBRN is 43.5 mm (SD 18.2). The nerve remains at risk due to its location over the first extensor compartment.

### "Lazy S" incision technique

The "lazy S" technique has both advantages and disadvantages. The incision offers a good exposure and less chance of iatrogenic damage than the transverse incision<sup>[17,18]</sup>. However the scar as a result of this incision is not as cosmetic as the transverse incision and the incision has a greater chance of iatrogenic damage to the nerves than the longitudinal incision.

### Specific angle technique

This technique offers a good exposure and minimizes the chance of iatrogenic damage to the nerve. It also offers a relatively cosmetically acceptable scar. However the determination of the angle of the incision takes time and is labor-intensive.

The technique described by<sup>[19]</sup> suggests a relatively acute angle to the radius which introduces a relatively high risk of damage to the SBRN. The present study shows that this risk can be significantly reduced by using a less acute angle.

The present study was performed using embalmed specimen which always means that the measurements cannot be extrapolated directly to the normal situation. However, since this concerns only relative measurements, the conclusions can be seen as representative. Furthermore by using Anubifix™ the shrinkage of tissue due to embalming is minimized and comparable to the fresh frozen specimen, the next best situation when compared with the *in vivo* situation.

Two- dimensional pictures are used in CASAM to warp the arms, but when operating the arm is a three-dimensional object. However, by taking the pictures in the same plane as the surgeon would use to make the incision, the third dimension is less relevant.

By using CASAM it was possible to virtually compare the incision techniques on the same arms. All techniques described above for the treatment of Quervains disease have their own advantages and disadvantages. The choice of which technique to use, depends on the priorities set by the surgeon. The main goal of this study was to identify the technique where iatrogenic damage to the SBRN is minimal. The conclusion that can be taken from the data is that despite the technique used, is that the retinaculum of the first dorsal compartment needs to be exposed by careful blunt dissection and divided under direct vision, so that the surgeon can see that the superficial nerves are not damaged. For beginning surgeons the longitudinal offers good exposure and less chance of iatrogenic nerve damage.

## ARTICLE HIGHLIGHTS

### Research background

Surgery is a widely applied as a treatment for the de Quervains Disease (QD). However, in 0.5 to 30% of cases, damage to the neurological structures have been reported this study was performed to try and provide a better

understanding of the anatomy of the forearm to be able to decrease iatrogenic damage to the nerves of the forearm.

### Research motivation

In this study the goal was to find the optimal incision technique for the first dorsal compartment release for the Quervains disease. Up till now 4 main incision techniques have been described and no golden standard has been established. By using a new visualization technique the goal was to identify the best technique in order to prevent iatrogenic nerve damage during the first extensor compartment release procedure.

### Research objectives

The goal of this study is to determine which of the common used incision techniques has the lowest chance of iatrogenic damage to the nerves. The nerves at risk are the superficial branch of the Radial Nerve (SBRN) and the Lateral Antebrachial Cutaneous Nerve (LABCN).

### Research methods

20 anubifix embalmed arms were dissected in a standardized way. Then the outline of the arm was marked and the arm was photographed in order to process it in the CASAM system. By using this system all arms could be rescaled to the dimensions of the average of the 20 embalmed arms. This ensures that the 20 nerve courses could be compared directly. Besides using CASAM the distance between the two branches of the SBRN running over de First Extensor Compartment (FEC) was measured.

### Research results

The image created in CASAM showed that in 90% of the arms, one branch of the SBRN crosses the FEC and one branch runs volar to the compartment. The distance between the two branches was 7.8 mm at the beginning of the FEC and 10.2 mm at the end. Finally the angle of incision at which the chance of damage to the nerves is lowest, is 19.4 degrees volar to the radius.

### Research conclusions

The study shows a large variation in the course of the superficial branch of the radial nerve over the first extensor compartment. However no complete safe zone can be defined. The choice of incision remains surgeons' preference and surgical skills are paramount to prevent iatrogenic nerve damage. The pre-study hypothesis was that there was a safe zone in which an incision for the Quervains disease could be made without chance of iatrogenic damage to the superficial branch of the radial nerve. This however was found not to be the case.

### Research perspectives

Although many incision techniques can be found in literature no consensus on the best incision technique has been established. The study shows a large variation in the course of the superficial branch of the radial nerve over the first extensor compartment. However no complete safe zone can be defined. The choice of incision remains surgeons' preference and surgical skills are paramount to prevent iatrogenic nerve damage. A randomized control trial comparing the incision techniques and their outcome could provide more evidence for the best possible incision technique in the future.

## ACKNOWLEDGEMENTS

The authors would especially like to thank Y. Steinvooort and B.J. Kompanje for all the help in providing room for dissection and all specimens.

## REFERENCES

- 1 Walker-Bone K, Palmer KT, Reading I, Coggon D, Cooper C. Prevalence and impact of musculoskeletal disorders of the upper limb in the general population. *Arthritis Rheum* 2004; **51**: 642-651 [PMID: 15334439 DOI: 10.1002/art.20535]
- 2 Mehdinasab SA, Alemohammad SA. Methylprednisolone acetate

- injection plus casting versus casting alone for the treatment of de Quervain's tenosynovitis. *Arch Iran Med* 2010; **13**: 270-274 [PMID: 20597558 DOI: 010134/AIM.004]
- 3 Richie CA 3rd, Briner WW Jr. Corticosteroid injection for treatment of de Quervain's tenosynovitis: a pooled quantitative literature evaluation. *J Am Board Fam Pract* 2003; **16**: 102-106 [PMID: 12665175 DOI: 10.3122/jabfm.16.2.102]
- 4 Moore JS. De Quervain's tenosynovitis. Stenosing tenosynovitis of the first dorsal compartment. *J Occup Environ Med* 1997; **39**: 990-1002 [PMID: 9343764 DOI: 10.1097/00043764-199710000-00011]
- 5 Avci S, Yilmaz C, Sayli U. Comparison of nonsurgical treatment measures for de Quervain's disease of pregnancy and lactation. *J Hand Surg Am* 2002; **27**: 322-324 [PMID: 11901392 DOI: 10.1053/jhsu.2002.32084]
- 6 Menendez ME, Thornton E, Kent S, Kalajian T, Ring D. A prospective randomized clinical trial of prescription of full-time versus as-desired splint wear for de Quervain tendinopathy. *Int Orthop* 2015; **39**: 1563-1569 [PMID: 25916954 DOI: 10.1007/s00264-015-2779-6]
- 7 Lane LB, Boretz RS, Stuchin SA. Treatment of de Quervain's disease: role of conservative management. *J Hand Surg Br* 2001; **26**: 258-260 [PMID: 11386780 DOI: 10.1054/jhsb.2001.0568]
- 8 Ilyas AM. Nonsurgical treatment for de Quervain's tenosynovitis. *J Hand Surg Am* 2009; **34**: 928-929 [PMID: 19410999 DOI: 10.1016/j.jhsa.2008.12.030]
- 9 Peters-Veluthamaningal C, van der Windt DA, Winters JC, Meyboom-de Jong B. Corticosteroid injection for de Quervain's tenosynovitis. *Cochrane Database Syst Rev* 2009; Jul 8;(3): CD005616 [PMID: 19588376 DOI: 10.1002/14651858.CD005616.pub2]
- 10 Peters-Veluthamaningal C, Winters JC, Groenier KH, Meyboom-DeJong B. Randomised controlled trial of local corticosteroid injections for de Quervain's tenosynovitis in general practice. *BMC Musculoskelet Disord* 2009; **10**: 131 [PMID: 19860883 DOI: 10.1186/1471-2474-10-131]
- 11 Earp BE, Han CH, Floyd WE, Rozental TD, Blazar PE. De Quervain tendinopathy: survivorship and prognostic indicators of recurrence following a single corticosteroid injection. *J Hand Surg Am* 2015; **40**: 1161-1165 [PMID: 25936736 DOI: 10.1016/j.jhsa.2014.12.027]
- 12 Mardani-Kivi M, Karimi Mobarakeh M, Bahrami F, Hashemi-Motlagh K, Saheb-Ekhtiari K, Akhoondzadeh N. Corticosteroid injection with or without thumb spica cast for de Quervain tenosynovitis. *J Hand Surg Am* 2014; **39**: 37-41 [PMID: 24315492 DOI: 10.1016/j.jhsa.2013.10.013]
- 13 Rowland P, Phelan N, Gardiner S, Linton KN, Galvin R. The Effectiveness of Corticosteroid Injection for De Quervain's Stenosing Tenosynovitis (DQST): A Systematic Review and Meta-Analysis. *Open Orthop J* 2015; **9**: 437-444 [PMID: 26587059 DOI: 10.2174/1874325001509010456]
- 14 Altay MA, Erturk C, Isikan UE. De Quervain's disease treatment using partial resection of the extensor retinaculum: A short-term results survey. *Orthop Traumatol Surg Res* 2011; **97**: 489-493 [PMID: 21680275 DOI: 10.1016/j.otsr.2011.03.015]
- 15 Suresh SS, Zaki H. De quervain disease: Ibrri technique to avoid superficial radial nerve injury. *Tech Hand Up Extrem Surg* 2009; **13**: 113-115 [PMID: 19516139 DOI: 10.1097/BTH.0b013e31819f6cdd]
- 16 Gundes H, Tosun B. Longitudinal incision in surgical release of De Quervain disease. *Tech Hand Up Extrem Surg* 2005; **9**: 149-152 [PMID: 16175118 DOI: 10.1097/01.bth.0000181105.24124.c0]
- 17 Bruner JM. Optimum skin incisions for the surgical relief of stenosing tenosynovitis in the hand. *Plast Reconstr Surg* 1966; **38**: 197-201 [PMID: 5919602 DOI: 10.1097/00006534-196609000-00003]
- 18 Bouras Y, El Andaloussi Y, Zaouari T, Touil N, Fnini S, Chikhaoui N, Largab A. Surgical treatment in De Quervain's tenosynovitis. About 20 cases. *Ann Chir Plast Esthet* 2010; **55**: 42-45 [PMID: 19939537 DOI: 10.1016/j.anplas.2009.08.006]
- 19 Ostric SA, Martin WJ, Derman GH. Intersecting the intersection: a

- reliable incision for the treatment of de Quervain's and second dorsal compartment tenosynovitis. *Plast Reconstr Surg* 2007; **119**: 2341-2342 [PMID: 17519769 DOI: 10.1097/01.prs.0000261070.92579.f5]
- 20 **Mellor SJ**, Ferris BD. Complications of a simple procedure: de Quervain's disease revisited. *Int J Clin Pract* 2000; **54**: 76-77 [PMID: 10824360]
- 21 **Scheller A**, Schuh R, Hönle W, Schuh A. Long-term results of surgical release of de Quervain's stenosing tenosynovitis. *Int Orthop* 2009; **33**: 1301-1303 [PMID: 18956185 DOI: 10.1007/s00264-008-0667-z]
- 22 **Arons MS**. de Quervain's release in working women: a report of failures, complications, and associated diagnoses. *J Hand Surg Am* 1987; **12**: 540-544 [PMID: 2956316 DOI: 10.1016/S0363-5023(87)80204-6]
- 23 **Rask MR**. Superficial radial neuritis and De Quervain's disease. Report of three cases. *Clin Orthop Relat Res* 1978; **(131)**: 176-182 [PMID: 657617]
- 24 **Braidwood AS**. Superficial radial neuropathy. *J Bone Joint Surg Br* 1975; **57**: 380-383 [PMID: 1158953]
- 25 **Kang HJ**, Hahn SB, Kim SH, Choi YR. Does endoscopic release of the first extensor compartment have benefits over open release in de Quervain's disease? *J Plast Reconstr Aesthet Surg* 2011; **64**: 1306-1311 [PMID: 21684826 DOI: 10.1016/j.bjps.2011.05.015]
- 26 **Poublon AR**, Walbeehm ET, Duraku LS, Eilers PH, Kerver AL, Kleinrensink GJ, Coert JH. The anatomical relationship of the superficial radial nerve and the lateral antebrachial cutaneous nerve: A possible factor in persistent neuropathic pain. *J Plast Reconstr Aesthet Surg* 2015; **68**: 237-242 [PMID: 25455286 DOI: 10.1016/j.bjps.2014.10.010]
- 27 **Stokvis A**, van der Avoort DJ, van Neck JW, Hovius SE, Coert JH. Surgical management of neuroma pain: a prospective follow-up study. *Pain* 2010; **151**: 862-869 [PMID: 20974520 DOI: 10.1016/j.pain.2010.09.032]
- 28 **Kerver AL**, Carati L, Eilers PH, Langezaal AC, Kleinrensink GJ, Walbeehm ET. An anatomical study of the ECRL and ECRB: feasibility of developing a preoperative test for evaluating the strength of the individual wrist extensors. *J Plast Reconstr Aesthet Surg* 2013; **66**: 543-550 [PMID: 23369737 DOI: 10.1016/j.bjps.2012.12.015]
- 29 **Kerver AL**, van der Ham AC, Theeuwes HP, Eilers PH, Poublon AR, Kerver AJ, Kleinrensink GJ. The surgical anatomy of the small saphenous vein and adjacent nerves in relation to endovenous thermal ablation. *J Vasc Surg* 2012; **56**: 181-188 [PMID: 22503186 DOI: 10.1016/j.jvs.2011.11.127]
- 30 **Alegado RB**, Meals RA. An unusual complication following surgical treatment of deQuervain's disease. *J Hand Surg Am* 1979; **4**: 185-186 [PMID: 217905 DOI: 10.1016/S0363-5023(79)80140-9]
- 31 **Picart P**. Symposium on the examination of equilibration function. Functional exploration of the vestibular apparatus. *J Fr Otorhinolaryngol Audiophonol Chir Maxillofac* 1967; **16**: 475-477 [PMID: 4233219 DOI: 10.4055/cios.2014.6.4.405]
- 32 **Menné T**, Hjorth N. Routine patch testing with paraben esters. *Contact Dermatitis* 1988; **19**: 189-191 [PMID: 3191679 DOI: 10.1111/j.1600-0536.1988.tb02892.x]
- 33 **Kumar K**. Outcome of longitudinal versus transverse incision in de Quervain's disease and its implications in Indian population. *Musculoskelet Surg* 2016; **100**: 49-52 [PMID: 26645452 DOI: 10.1007/s12306-015-0388-6]

P- Reviewer: Angoules A S- Editor: Cui LJ L- Editor: A  
E- Editor: Li RF





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 March 18; 9(3): 14-59



**W****J****O****ORIGINAL ARTICLE****Basic Study**

- 14 Sacroiliac joint stability: Finite element analysis of implant number, orientation, and superior implant length

*Lindsey DP, Kiapour A, Yerby SA, Goel VK*

**Retrospective Study**

- 24 Complex knee injuries treated in acute phase: Long-term results using Ligament Augmentation and Reconstruction System artificial ligament

*Gliatis J, Anagnostou K, Tsoumpas P, Billis E, Papandreou M, Plessas S*

- 35 Neglected traumatic hip dislocation: Influence of the increased intracapsular pressure

*Massoud EIE*

**Clinical Practice Study**

- 41 Establishing minimum clinically important difference values for the Patient-Reported Outcomes Measurement Information System Physical Function, hip disability and osteoarthritis outcome score for joint reconstruction, and knee injury and osteoarthritis outcome score for joint reconstruction in orthopaedics

*Hung M, Bounsanga J, Voss MW, Saltzman CL*

- 50 Use of ketamine sedation for the management of displaced paediatric forearm fractures

*Wiik AV, Patel P, Bovis J, Cowper A, Pastides PS, Hulme A, Evans S, Stewart C*

**RETRACTION NOTE**

- 58 Retraction note to four articles published in *World Journal of Orthopaedics*

*Cui Q*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Nigel Zheng, PhD, Professor, Center for Biomedical Engineering and Science, Department of Mechanical Engineering and Science, University of North Carolina at Charlotte, Charlotte, NC 28223, 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 Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central and Scopus.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Li-Jun Cui*  
**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, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com>

[www.wjgnet.com/2218-5836/editorialboard.htm](http://www.wjgnet.com/2218-5836/editorialboard.htm)

**EDITORIAL OFFICE**  
 Xiu-Xia Song, Director  
*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 March 18, 2018

**COPYRIGHT**  
 © 2018 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.f6publishing.com>

## Basic Study

**Sacroiliac joint stability: Finite element analysis of implant number, orientation, and superior implant length**

Derek P Lindsey, Ali Kiapour, Scott A Yerby, Vijay K Goel

Derek P Lindsey, Scott A Yerby, Research and Development, SI-BONE, Inc., San Jose, CA 95128, United States

Ali Kiapour, Vijay K Goel, Engineering Center for Orthopaedic Research Excellence, Departments of Bioengineering and Orthopaedic Surgery, Colleges of Engineering and Medicine, University of Toledo, Toledo, OH 43606, United States

ORCID number: Derek P Lindsey (0000-0003-2699-8190); Ali Kiapour (0000-0002-7837-9191); Scott A Yerby (0000-0002-0378-2576); Vijay K Goel (0000-0002-9175-5366).

Author contributions: Lindsey DP, Yerby SA and Goel VK designed the research; Kiapour A performed the finite element analysis; Lindsey DP analyzed the results; Lindsey DP, Kiapour A, Yerby SA and Goel VK wrote the paper.

Supported by SI-BONE, Inc., San Jose, CA, United States.

Conflict-of-interest statement: Lindsey DP and Yerby SA are employees of SI-BONE, Inc.

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: Derek P Lindsey, MSc, Research Scientist, Research and Development, SI-BONE, Inc., 3055 Olin Avenue, Suite 2200, San Jose, CA 95218, United States. [dlindsey@si-bone.com](mailto:dlindsey@si-bone.com)  
Telephone: +1-408-2070700  
Fax: +1-408-5578312

Received: December 5, 2017

Peer-review started: December 6, 2017

First decision: December 18, 2017

Revised: December 22, 2017

Accepted: February 4, 2018

Article in press: February 5, 2018

Published online: March 18, 2018

**Abstract****AIM**

To analyze how various implants placement variables affect sacroiliac (SI) joint range of motion.

**METHODS**

An experimentally validated finite element model of the lumbar spine and pelvis was used to simulate a fusion of the SI joint using various placement configurations of triangular implants (iFuse Implant System®). Placement configurations were varied by changing implant orientation, superior implant length, and number of implants. The range of motion of the SI joint was calculated using a constant moment of 10 N-m with a follower load of 400 N. The changes in motion were compared between the treatment groups to assess how the different variables affected the overall motion of the SI joint.

**RESULTS**

Transarticular placement of 3 implants with superior implants that end in the middle of the sacrum resulted in the greatest reduction in range of motion (flexion/extension = 73%, lateral bending = 42%, axial rotation = 72%). The range of motions of the SI joints were reduced with use of transarticular orientation (9%-18%) when compared with an inline orientation. The use of a superior implant that ended mid-sacrum resulted in median reductions of (8%-14%) when compared with a superior implant that ended in the middle of the ala. Reducing the number of implants, resulted in increased SI joint range of motions for the 1 and 2 implant models of 29%-133% and 2%-39%, respectively,

when compared with the 3 implant model.

### CONCLUSION

Using a validated finite element model we demonstrated that placement of 3 implants across the SI joint using a transarticular orientation with superior implant reaching the sacral midline resulted in the most stable construct. Additional clinical studies may be required to confirm these results.

**Key words:** Fusion; Biomechanics; Minimally invasive surgery; Sacroiliac joint dysfunction; Finite element analysis

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Minimally invasive fusion of the sacroiliac (SI) joint is a potential treatment for patients suffering with symptoms related to the SI joint. This study used finite element analysis to investigate how implant orientation, superior implant length, and implant number affect SI joint range of motion. The results of this study demonstrate that placement of 3 implants across the SI joint using a transarticular orientation with superior implant reaching the sacral midline resulted in the most stable construct.

Lindsey DP, Kiapour A, Yerby SA, Goel VK. Sacroiliac joint stability: Finite element analysis of implant number, orientation and superior implant length. *World J Orthop* 2018; 9(3): 14-23 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i3/14.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i3.14>

### INTRODUCTION

Minimally invasive fusion of the sacroiliac (SI) joint is a potential treatment for patients suffering with symptoms related to the SI joint. Although diagnosis of the primary pain generator in low back pain is challenging<sup>[1]</sup>, proper diagnosis allows for the most effective treatment. Of patients dealing with low back pain, between 15% and 30% have the SI joint as a pain generator<sup>[2-4]</sup>.

Recently, minimally invasive fusion of the SI joint has been shown to be an effective method for reducing SI joint pain<sup>[5]</sup>. In addition, minimally invasive procedures have been shown to reduce blood loss, length of stay, and surgical time, while resulting in more positive outcomes for the patient compared with traditional open fusion procedures<sup>[5]</sup>.

There are many factors that influence the choice and placement of implants placed across the SI joint. The sacral anatomy allows for placement of iliosacral hardware within sacral safe zones, although differences in anatomy have a significant effect on the location and size of the safe zones<sup>[6]</sup>. There is evidence that placement of multiple implants in unstable pelvic fracture models results in the greatest biomechanical

stability<sup>[7-9]</sup>. Additional studies have demonstrated that placement of iliosacral screws within regions of higher bone density result in higher extraction forces<sup>[10,11]</sup>.

Previous *ex vivo* experimental studies have investigated the biomechanical effects of placing SI joint fusion devices<sup>[12,13]</sup>. These studies have shown that placement of 3 triangular titanium plasma spray (TPS) coated titanium implants significantly reduced motion of the treated SI joint. A comparison of two lateral placement variations, inline (posterior) and transarticular, showed that both variations significantly reduced motion, and suggested that the transarticular orientation may provide more initial stability.

Finite element modeling is another technique used to investigate the biomechanics of the SI joint and pelvis<sup>[14-17]</sup>. Ivanov *et al.*<sup>[14,15]</sup> validated an SI joint FE model by comparing the FEA model ROM with experimental data for the intact and sequential ligament sectioning conditions from Simonian *et al.*<sup>[18]</sup>. This SI joint model was later confirmed<sup>[17]</sup> to demonstrate that SI joint treatment using implants resulted in comparable reductions in motion to those reported in cadavers by Soriano-Baron *et al.*<sup>[13]</sup>.

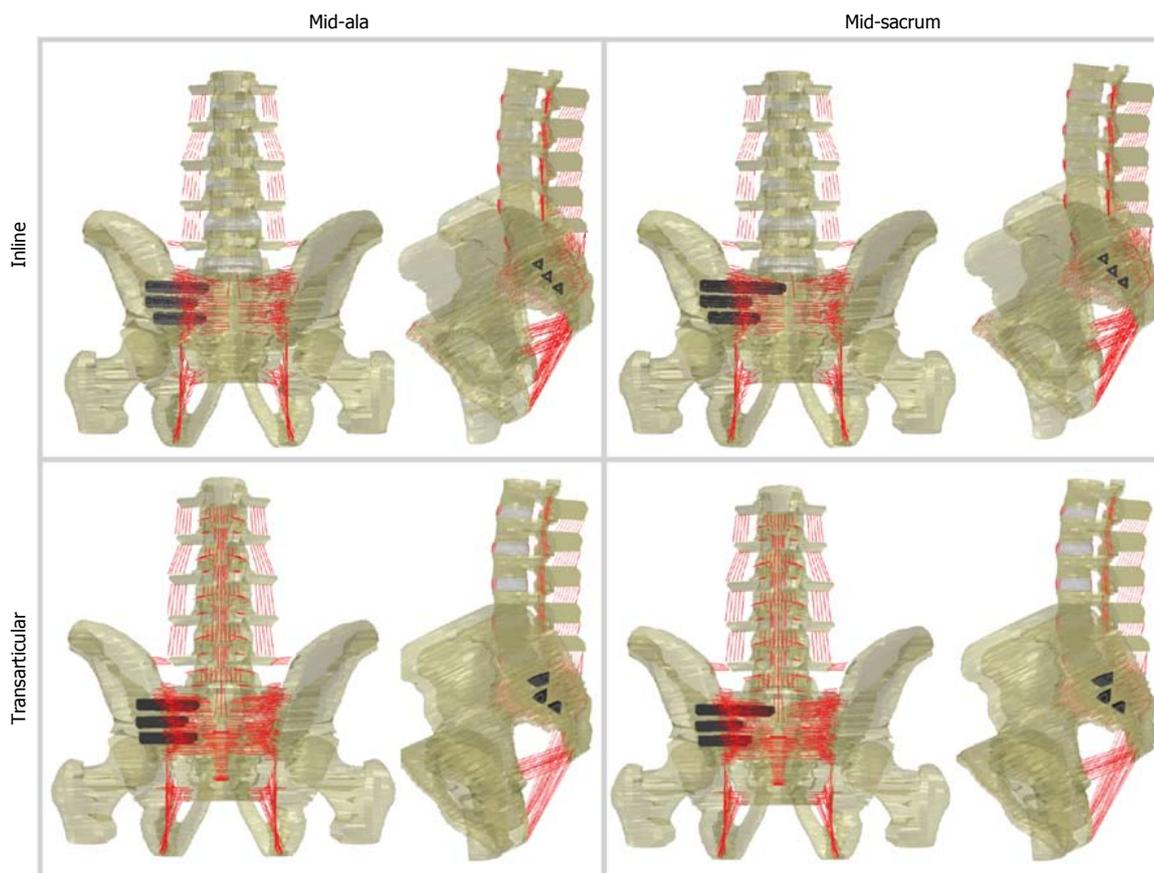
Although, clinical and experimental evidence shows that placing 3 triangular TPS coated implants has successful clinical and biomechanical results, questions remain concerning the optimal parameters for implant placement. The objective of this study was to investigate and quantify the effect of implant orientation, superior implant length, and implant number on SI joint range of motion.

### MATERIALS AND METHODS

A finite element model of the lumbar spine, pelvis, and both femurs was used to simulate SI joint motion; this model has previously been used to evaluate the effects of leg length discrepancy, effects of lumbar spine fusion on the SI joint, and effects of SI joint fusion on the lumbar spine<sup>[14-17]</sup>. The femoral head was fixed into the acetabular cup to ensure loading, but that no motion occurred at the hip joint. Briefly, a pelvis was scanned using computed tomography (CT) and material properties for bones, ligaments, and joints were assigned<sup>[14,15]</sup>. The material properties of the sacral cancellous bone were assumed to be isotropic and varied in accordance to the apparent bone mineral density from a normal sacrum ( $t$ -score > -1)<sup>[19]</sup> using a power law distribution ( $\alpha = 2$ )<sup>[20]</sup>. For treated models, the core of the titanium plasma spray (TPS) coated implants (iFuse Implant 7.0 mm; SI-BONE, Inc., San Jose, CA, United States) was assigned the material properties of Ti6Al4V ELI ( $E = 115$  GPa), the interface between the implant core and adjacent bone can be found in Lindsey *et al.*<sup>[17]</sup>.

#### Loading conditions/outcomes

The intact and instrumented model loads were simulated using a compressive follower load of 400 N,



**Figure 1** Finite element models tested in this study used either an inline or transarticular orientation. For models that included a superior implant, the length was varied such that the implant ended above the S1 foramen (mid-ala) or the midline of the sacrum (mid-sacrum).

and a 10 N-m bending moment applied at the superior surface of the L1 vertebra<sup>[21,22]</sup>. The compressive follower load was extended to the sacrum level and the angle of the connector elements defined such that the entire lumbo-pelvic segment did not go into any rotational motion following contraction of the connector elements. Loading was simulated in flexion-extension, lateral bending (left and right), and axial rotation (left and right) during double-leg stance. The range of motion of the SI joint was determined for each loading direction<sup>[14]</sup>.

### Treatment groups

Three treatment variables were investigated: Implant orientation, superior implant length, and implant number. Two potential implant orientations, inline (posterior) and transarticular, have been previously investigated<sup>[13]</sup> and both were further investigated here (Figure 1). Clinically, the superior implant length is often chosen to end within the middle of the ala (*i.e.*, directly above the S1 foramen); based upon previous trauma literature<sup>[11]</sup>, we also investigated a longer superior implant that extended to the midline of the sacrum (Figure 1). Typically, three implants are placed<sup>[23]</sup>, for this investigation either 1, 2, or 3 implants were placed. All potential instrumented combinations were simulated, resulting in 22 unique models (Table 1). The superior

implant was either 55 mm long (mid-ala) or 75 mm long (mid-sacrum) for both the inline and transarticular orientation (placement of the superior implant is identical for the two orientations). The middle implants were 45 mm long for both the inline and transarticular orientations, while the inferior implant was 45 mm long for the inline orientation and 50 mm long for the transarticular orientation.

### Statistical analysis

The effect of treatment was assessed by calculating the difference in ROM between the intact and treated configurations for each combination of implant orientation, superior implant length, and number of implants in flexion-extension, lateral bending, and axial rotation. The percent change was calculated in comparison with the intact ROM. The median and range for the difference in ROM and percent change were determined for each motion. Effects of individual treatment variables are described below.

**Implant orientation:** The effect of implant orientation was assessed by calculating the difference between the inline and transarticular (TA) configurations. Differences in ROM were calculated as a function of superior implant length (SIL) (mid-ala, mid-sacrum, or none) and number of implants (3-superior/middle/inferior, 2-

**Table 1** Sacroiliac joint range of motion for an intact model and 22 configurations of implant orientation, superior implant length, and number of implants

Treatment/orientation	Implant placed			Superior implant ending point	SI joint ROM (°) [Reduction in ROM (%)]		
	Superior	Middle	Inferior		Flexion-extension	Lateral bending	Axial rotation
Intact	-	-	-	- <sup>1</sup>	1.94° (-)	0.66° (-)	1.11° (-)
Inline orientation	X	X	X	Mid-ala	0.7° (64%)	0.45° (32%)	0.41° (63%)
				Mid-sacrum	0.63° (68%)	0.41° (38%)	0.38° (66%)
	X	-	X	Mid-ala	0.82° (58%)	0.47° (29%)	0.44° (60%)
				Mid-sacrum	0.69° (64%)	0.43° (35%)	0.4° (64%)
	X	X	-	Mid-ala	0.97° (50%)	0.5° (24%)	0.49° (56%)
				Mid-sacrum	0.76° (61%)	0.45° (32%)	0.43° (61%)
	-	X	X	- <sup>1</sup>	0.91° (53%)	0.53° (20%)	0.55° (50%)
	X	-	-	Mid-ala	1.36° (30%)	0.58° (12%)	0.67° (40%)
				Mid-sacrum	1.21° (38%)	0.58° (12%)	0.61° (45%)
		X	-	- <sup>1</sup>	1.32° (32%)	0.65° (2%)	0.73° (34%)
Transarticular orientation			X	- <sup>1</sup>	1.25° (36%)	0.69° (-5%)	0.79° (29%)
	X	X	X	Mid-ala	0.59° (70%)	0.41° (38%)	0.34° (69%)
				Mid-sacrum	0.52° (73%)	0.38° (42%)	0.31° (72%)
	X	-	X	Mid-ala	0.69° (64%)	0.42° (36%)	0.36° (68%)
				Mid-sacrum	0.58° (70%)	0.39° (41%)	0.32° (71%)
	X	X	-	Mid-ala	0.81° (58%)	0.45° (32%)	0.4° (64%)
				Mid-sacrum	0.64° (67%)	0.41° (38%)	0.35° (68%)
	-	X	X	- <sup>1</sup>	0.76° (61%)	0.47° (29%)	0.46° (59%)
	X	-	-	Mid-ala	1.36° (30%)	0.58° (12%)	0.67° (40%)
				Mid-sacrum	1.21° (38%)	0.58° (12%)	0.61° (45%)
	-	X	-	- <sup>1</sup>	1.11° (43%)	0.6° (9%)	0.7° (37%)
	-	-	X	- <sup>1</sup>	1.05° (46%)	0.62° (6%)	0.73° (34%)

<sup>1</sup>Configuration does not include a superior implant. SI: Sacroiliac; ROM: Range of motion.

superior/inferior, 2-superior/middle, 2-middle/inferior, 1-middle, and 1-inferior), for a total of 9 combinations. The percent change was calculated in comparison with the inline ROM. The treatment of one implant in the superior position was not compared between orientations since the configurations are identical for the inline and transarticular orientations. The median and range for the difference in ROM and percent change were determined.

**Superior implant length:** The effect of the superior implant length was assessed by calculating the difference between the mid-sacrum (MS) and mid-ala (MA) configurations. Differences in ROM were calculated as a function of orientation (Inline, Transarticular) and number of implants (3-superior/middle/inferior, 2-superior/inferior, 2-superior/middle, and 1-superior), for a total of 8 combinations. The percent change was calculated in comparison with the ROM of mid-ala superior implant length. The median and range for the difference in ROM and percent change were determined.

**Implant number:** The effect of implant number was assessed by calculating the difference in ROM between all single or dual implant configurations and the corresponding 3 implant configuration as a function of orientation (Inline, Transarticular) and superior implant length (SIL) (mid-ala, mid-sacrum) for a total of 18 combinations, and normalizing by the corresponding 3 implant configuration (implants without a superior implant were normalized to the mid-ala configuration). The median and range for the difference in ROM and

percent change were determined for each single or dual implant configuration.

### Animal care and use statement

The article does not contain any studies with human participants or animals performed by any of the authors.

## RESULTS

Placement of 3 implants using the inline and transarticular orientations resulted in reductions in motion of 64%, 32%, 63%, and 70%, 38%, 69%, in flexion-extension, lateral bending, and axial rotation, respectively (Table 1). These reductions are consistent with the range of reductions reported by Soriano-Baron *et al.*<sup>13)</sup> and provided confidence that this FE model is sufficient to make comparisons between treatment variables that have not previously been investigated in cadaver studies (*i.e.*, implant number, placement technique, and superior implant length).

Transarticular placement of 3 implants with a mid-sacrum length superior implant resulted in the greatest reduction in range of motion (Table 1). One superior implant (mid-ala length) has the least reduction in range of motion in flexion-extension; one inferior implant placed using the inline orientation has the least reduction in range of motion in lateral bending and axial rotation. Transarticular placement of a superior (mid-sacrum length) and inferior implant has the most reduction in range of motion for a 2 implant configuration.

**Table 2** Reduction in sacroiliac joint range of motion (°) between transarticular and inline orientation groups

Orientation	Implants (positions)	Superior implant ending point	Reduction in SI joint ROM (°) (%)		
			Flexion-extension	Lateral bending	Axial rotation
Transarticular <i>vs</i> inline	3 (S, M, I)	Mid-ala	0.11° (16%)	0.04° (9%)	0.07° (17%)
		Mid-sacrum	0.11° (17%)	0.03° (7%)	0.07° (18%)
	2 (S, -, I)	Mid-ala	0.13° (16%)	0.05° (11%)	0.08° (18%)
		Mid-sacrum	0.11° (16%)	0.04° (9%)	0.08° (20%)
	2 (S, M, -)	Mid-ala	0.16° (16%)	0.05° (10%)	0.09° (18%)
		Mid-sacrum	0.12° (16%)	0.04° (9%)	0.08° (19%)
	2 (-, M, I)	<sup>-1</sup>	0.15° (16%)	0.06° (11%)	0.09° (16%)
	1 (-, M, -)	<sup>-1</sup>	0.21° (16%)	0.05° (8%)	0.03° (4%)
	1 (-, -, I)	<sup>-1</sup>	0.20° (16%)	0.07° (10%)	0.06° (8%)
		<b>Median (°) (Range)</b>	<b>0.13° (0.11-0.21)</b>	<b>0.05° (0.03-0.07)</b>	<b>0.08° (0.03-0.09)</b>
	<b>Median (%) (Range)</b>	<b>16% (16-17)</b>	<b>9% (7-11)</b>	<b>18% (4-20)</b>	

<sup>1</sup>Configuration does not include a superior implant. S: Superior; M: Middle; I: Inferior.

Altering the implant orientation from the inline to the transarticular placement technique resulted in median reductions in motion of 16%, 9% and 18%, in flexion-extension, lateral bending, and axial rotation, respectively (Table 2).

Extending the superior implant to the midline of the sacrum resulted in median reductions in motion of 14%, 8% and 9%, in flexion-extension, lateral bending, and axial rotation, respectively (Table 3).

The two implant models with superior and inferior implants resulted in increased motions of 10%-17%, 2%-5% and 3%-7% compared with the 3 implant model, in flexion-extension, lateral bending, and axial rotation, respectively (Figure 2). Two implant models configurations with the implants placed close together (superior/middle, and middle/inferior) resulted in increased motions when compared with the 3 implant configuration of 21%-39%, 8%-18%, and 13%-35% in flexion-extension, lateral bending, and axial rotation, respectively (Figure 2; Tables 4-6). For single implant models, the motion increases ranged from 78% to 133%, 29% to 53% and 61% to 115%, in flexion-extension, lateral bending, and axial rotation, respectively (Figure 2).

## DISCUSSION

The finite element model used in this study resulted in intact and treated SI joint motions that are consistent with previous experimental studies<sup>[13]</sup>. The combination of the current results and the previous validations confirm that both the intact and treated models in this study are functioning in a physiologic manner.

The current study demonstrated that the implant orientations across the SI joint can alter the range of motion. The SI joint contains both cartilaginous and fibrocartilaginous portions, with the cartilaginous portion exhibiting greater subchondral sacral bone density<sup>[19]</sup>. The transarticular orientation positions the middle and inferior implants more ventrally (approximately 15°-20°) and across the cartilaginous portion of the SI joint (Figure 1). Soriano-Baron *et al.*<sup>[13]</sup> reported that the

transarticular orientation had larger average reduction in SI joint ROM, although this was not determined to be significant.

The current study also demonstrated that placement of a longer superior implant resulted in reduced SI joint range of motion. Kraemer *et al.*<sup>[11]</sup> demonstrated that iliosacral screws had a higher pullout force when the threads were positioned in the sacral midbody compared with those positioned in the ala. The results from Kraemer *et al.*<sup>[11]</sup> are consistent with later anatomical studies that have reported reduced bone mineral density within the ala<sup>[24]</sup>. The current study demonstrated that increasing the length of the superior implant to the higher density bone of the sacral midline reduces the range of motion of the SI joint in flexion-extension, lateral bending, and axial rotation. Clinically, anatomic constraints must be considered prior to placement of a longer first implant.

The current study also demonstrated that placement of 3 implants resulted in greater motion reduction than any combination of two implants. Multiple studies have demonstrated that the use of a single SI screw results in less stability when compared with 2 SI screws<sup>[7-9]</sup>. The current study investigated treatment with 1, 2, or 3 implants to evaluate the treated SI joint range of motion as a function of implant number. Clinically, a prospective randomized trial documented 3 implants being placed in 91% of cases; with the rest of the cases using either 2 implants (5% cases) or 4 implants (4% cases)<sup>[23]</sup>. Although a small portion of clinical cases used 4 implants, this condition was not investigated in this study as placement is highly dependent on the size of the sacrum. The results from the current study demonstrate that reducing the number of placed implants results in increased initial SI joint range of motion. Two implants with increased separation, however, are more stable than 2 implants placed close together.

The current study is not without limitations. As with all finite element models, certain assumptions must be made to model the system. As previously noted, the current model is based on a single patient and did not

**Table 3 Reduction in sacroiliac joint range of motion (°) between mid-sacrum and mid-ala placement groups**

Superior implant ending point	Orientation	Implants (position)	Reduction in SI joint ROM (°) (%)		
			Flexion-extension	Lateral bending	Axial rotation
Mid-sacrum vs mid-ala	Inline	3 (S, M, I)	0.07° (10%)	0.04° (9%)	0.03° (7%)
		2 (S, -, I)	0.13° (16%)	0.04° (9%)	0.04° (9%)
		2 (S, M, -)	0.21° (22%)	0.05° (10%)	0.06° (12%)
	Trans-articular	1 (S, -, -)	0.15° (11%)	0.00° (0%)	0.06° (9%)
		3 (S, M, I)	0.07° (12%)	0.03° (7%)	0.03° (9%)
		2 (S, -, I)	0.11° (16%)	0.03° (7%)	0.04° (11%)
		2 (S, M, -)	0.17° (21%)	0.04° (9%)	0.05° (13%)
		1 (S, -, -)	0.15° (11%)	0.00° (0%)	0.06° (9%)
		<b>Median (°) (Range)</b>	<b>0.14° (0.07-0.21)</b>	<b>0.035° (0.00-0.05)</b>	<b>0.045° (0.03-0.06)</b>
		<b>Median (%) (Range)</b>	<b>14% (10-22)</b>	<b>8% (0-10)</b>	<b>9% (7-13)</b>

The reduction in range of motion (%) was calculated in comparison to the to the mid-ala superior implant length. S: Superior; M: Middle; I: Inferior.

**Table 4 Change in sacroiliac joint flexion-extension range of motion (°) as a result of reducing the number of implants**

Treatment	Implants (positions)	Superior implant ending point	Range of motion (°)	Motion increase (°)	% 3 Implant motion
Intact	-	- <sup>1</sup>	1.94	-	-
Inline	3 (S, M, I)	Mid-ala	0.7	Reference configuration	
Inline	2 (S, M, -)	Mid-ala	0.97	0.27	39
Inline	2 (S, -, I)	Mid-ala	0.82	0.12	17
Inline	2 (-, M, I)	- <sup>1</sup>	0.91	0.21	30
Inline	1 (S, -, -)	Mid-ala	1.36	0.66	94
Inline	1 (-, M, -)	- <sup>1</sup>	1.32	0.62	89
Inline	1 (-, -, I)	- <sup>1</sup>	1.25	0.55	79
Inline	3 (S, M, I)	Mid-sacrum	0.63	Reference configuration	
Inline	2 (S, M, -)	Mid-sacrum	0.76	0.13	21
Inline	2 (S, -, I)	Mid-sacrum	0.69	0.06	10
Inline	1 (S, -, -)	Mid-sacrum	1.21	0.58	92
Transarticular	3 (S, M, I)	Mid-ala	0.59	Reference configuration	
Transarticular	2 (S, M, -)	Mid-ala	0.81	0.22	37
Transarticular	2 (S, -, I)	Mid-ala	0.69	0.1	17
Transarticular	2 (-, M, I)	- <sup>1</sup>	0.76	0.17	29
Transarticular	1 (S, -, -)	Mid-ala	1.36	0.77	131
Transarticular	1 (-, M, -)	- <sup>1</sup>	1.11	0.52	88
Transarticular	1 (-, -, I)	- <sup>1</sup>	1.05	0.46	78
Transarticular	3 (S, M, I)	Mid-sacrum	0.52	Reference configuration	
Transarticular	2 (S, M, -)	Mid-sacrum	0.64	0.12	23
Transarticular	2 (S, -, I)	Mid-sacrum	0.58	0.06	12
Transarticular	1 (S, -, -)	Mid-sacrum	1.21	0.69	133
<b>Treatment</b>	<b>Implants (positions)</b>	<b>Superior implant ending point</b>	<b>% 3 Implant motion</b>	<b>Implants (positions)</b>	<b>Median (%) [range]</b>
Inline	2 (S, -, I)	Mid-ala	17	2 (S, -, I)	14.5% (10-17)
Inline	2 (S, -, I)	Mid-sacrum	10		
Transarticular	2 (S, -, I)	Mid-ala	17		
Transarticular	2 (S, -, I)	Mid-sacrum	12		
Inline	2 (S, M, -)	Mid-ala	39	2 (S, M, -)	30% (21-39)
Inline	2 (S, M, -)	Mid-sacrum	21		
Transarticular	2 (S, M, -)	Mid-ala	37		
Transarticular	2 (S, M, -)	Mid-sacrum	23		
Inline	2 (-, M, I)	- <sup>1</sup>	30	2 (-, M, I)	29.5% (29-30)
Transarticular	2 (-, M, I)	- <sup>1</sup>	29		
Inline	1 (S, -, -)	Mid-ala	94	1 (S, -, -)	112.5% (92-133)
Inline	1 (S, -, -)	Mid-sacrum	92		
Transarticular	1 (S, -, -)	Mid-ala	131		
Transarticular	1 (S, -, -)	Mid-sacrum	133		
Inline	1 (-, M, -)	- <sup>1</sup>	89	1 (-, M, -)	88.5% (88-89)
Transarticular	1 (-, M, -)	- <sup>1</sup>	88		
Inline	1 (-, -, I)	- <sup>1</sup>	79	1 (-, -, I)	78.5% (78-79)
Transarticular	1 (-, -, I)	- <sup>1</sup>	78		

<sup>1</sup>Configuration does not include a superior implant. S: Superior; M: Middle; I: Inferior.

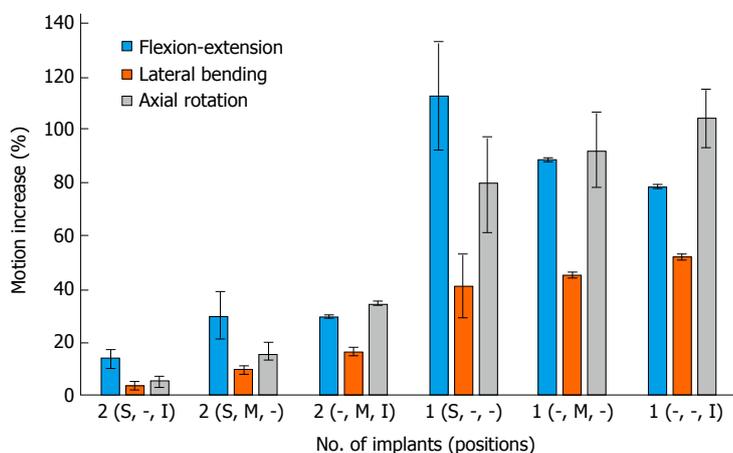
simulate SI joint dysfunction, therefore generalizing the results to the general patient population should be made with care<sup>[17]</sup>. The current study assumed

sacral cancellous bone material properties based on those found in normal cancellous bone (*t*-score > -1). Although the reported bone mineral densities are

**Table 5** Change in sacroiliac joint lateral bending range of motion (°) as a result of reducing the number of implants

Treatment	Implants (positions)	Superior implant ending point	Range of motion (°)	Motion increase (°)	% 3 implant motion
Intact	-	<sup>1</sup>	0.66	-	-
Inline	3 (S, M, I)	Mid-ala	0.45	Reference configuration	
Inline	2 (S, M, -)	Mid-ala	0.5	0.05	11
Inline	2 (S, -, I)	Mid-ala	0.47	0.02	4
Inline	2 (-, M, I)	<sup>1</sup>	0.53	0.08	18
Inline	1 (S, -, -)	Mid-ala	0.58	0.13	29
Inline	1 (-, M, -)	<sup>1</sup>	0.65	0.2	44
Inline	1 (-, -, I)	<sup>1</sup>	0.69	0.24	53
Inline	3 (S, M, I)	Mid-sacrum	0.41	Reference configuration	
Inline	2 (S, M, -)	Mid-sacrum	0.45	0.04	10
Inline	2 (S, -, I)	Mid-sacrum	0.43	0.02	5
Inline	1 (S, -, -)	Mid-sacrum	0.58	0.17	41
Transarticular	3 (S, M, I)	Mid-ala	0.41	Reference configuration	
Transarticular	2 (S, M, -)	Mid-ala	0.45	0.04	10
Transarticular	2 (S, -, I)	Mid-ala	0.42	0.01	2
Transarticular	2 (-, M, I)	<sup>1</sup>	0.47	0.06	15
Transarticular	1 (S, -, -)	Mid-ala	0.58	0.17	41
Transarticular	1 (-, M, -)	<sup>1</sup>	0.6	0.19	46
Transarticular	1 (-, -, I)	<sup>1</sup>	0.62	0.21	51
Transarticular	3 (S, M, I)	Mid-sacrum	0.38	Reference configuration	
Transarticular	2 (S, M, -)	Mid-sacrum	0.41	0.03	8
Transarticular	2 (S, -, I)	Mid-sacrum	0.39	0.01	3
Transarticular	1 (S, -, -)	Mid-sacrum	0.58	0.2	53
Treatment	Implants (positions)	Superior implant ending point	% 3 Implant motion	Implants (positions)	Median (%) [range]
Inline	2 (S, -, I)	Mid-ala	4	2 (S, -, I)	3.5% (2-5)
Inline	2 (S, -, I)	Mid-sacrum	5		
Transarticular	2 (S, -, I)	Mid-ala	2		
Transarticular	2 (S, -, I)	Mid-sacrum	3		
Inline	2 (S, M, -)	Mid-ala	11	2 (S, M, -)	10% (8-11)
Inline	2 (S, M, -)	Mid-sacrum	10		
Transarticular	2 (S, M, -)	Mid-ala	10		
Transarticular	2 (S, M, -)	Mid-sacrum	8		
Inline	2 (-, M, I)	<sup>1</sup>	18	2 (-, M, I)	16.5% (15-18)
Transarticular	2 (-, M, I)	<sup>1</sup>	15		
Inline	1 (S, -, -)	Mid-ala	29	1 (S, -, -)	41% (29-53)
Inline	1 (S, -, -)	Mid-sacrum	41		
Transarticular	1 (S, -, -)	Mid-ala	41		
Transarticular	1 (S, -, -)	Mid-sacrum	53		
Inline	1 (-, M, -)	<sup>1</sup>	44	1 (-, M, -)	45% (44-46)
Transarticular	1 (-, M, -)	<sup>1</sup>	46		
Inline	1 (-, -, I)	<sup>1</sup>	53	1 (-, -, I)	52% (51-53)
Transarticular	1 (-, -, I)	<sup>1</sup>	51		

<sup>1</sup>Configuration does not include a superior implant. S: Superior; M: Middle; I: Inferior.



**Figure 2** Motion increase (%) for configurations with a reduced number of implants. The increase for each condition was normalized by the corresponding model that contained 3 implants. Note that a smaller increase in motion represents more reduction in range of motion. S: Superior; M: Middle; I: Inferior. Data is shown as median ± range.

**Table 6** Change in sacroiliac joint axial rotation range of motion (°) as a result of reducing the number of implants

Treatment	Implants (positions)	Superior implant ending point	Range of motion	Motion increase (°)	% 3 implant motion
Intact	-	<sup>1</sup>	1.11	-	-
Inline	3 (S, M, I)	Mid-ala	0.41	Reference configuration	
Inline	2 (S, M, -)	Mid-ala	0.49	0.08	20
Inline	2 (S, -, I)	Mid-ala	0.44	0.03	7
Inline	2 (-, M, I)	<sup>1</sup>	0.55	0.14	34
Inline	1 (S, -, -)	Mid-ala	0.67	0.26	63
Inline	1 (-, M, -)	<sup>1</sup>	0.73	0.32	78
Inline	1 (-, -, I)	<sup>1</sup>	0.79	0.38	93
Inline	3 (S, M, I)	Mid-sacrum	0.38	Reference configuration	
Inline	2 (S, M, -)	Mid-sacrum	0.43	0.05	13
Inline	2 (S, -, I)	Mid-sacrum	0.4	0.02	5
Inline	1 (S, -, -)	Mid-sacrum	0.61	0.23	61
Transarticular	3 (S, M, I)	Mid-ala	0.34	Reference configuration	
Transarticular	2 (S, M, -)	Mid-ala	0.4	0.06	18
Transarticular	2 (S, -, I)	Mid-ala	0.36	0.02	6
Transarticular	2 (-, M, I)	<sup>1</sup>	0.46	0.12	35
Transarticular	1 (S, -, -)	Mid-ala	0.67	0.33	97
Transarticular	1 (-, M, -)	<sup>1</sup>	0.7	0.36	106
Transarticular	1 (-, -, I)	<sup>1</sup>	0.73	0.39	115
Transarticular	3 (S, M, I)	Mid-sacrum	0.31	Reference configuration	
Transarticular	2 (S, M, -)	Mid-sacrum	0.35	0.04	13
Transarticular	2 (S, -, I)	Mid-sacrum	0.32	0.01	3
Transarticular	1 (S, -, -)	Mid-sacrum	0.61	0.3	97
Treatment	Implants (positions)	Superior implant ending point	% 3 Implant motion	Implants (positions)	Median (%) [range]
Inline	2 (S, -, I)	Mid-ala	7	2 (S, -, I)	5.5% (3-7)
Inline	2 (S, -, I)	Mid-sacrum	5		
Transarticular	2 (S, -, I)	Mid-ala	6		
Transarticular	2 (S, -, I)	Mid-sacrum	3		
Inline	2 (S, M, -)	Mid-ala	20	2 (S, M, -)	15.5% (13-20)
Inline	2 (S, M, -)	Mid-sacrum	13		
Transarticular	2 (S, M, -)	Mid-ala	18		
Transarticular	2 (S, M, -)	Mid-sacrum	13		
Inline	2 (-, M, I)	<sup>1</sup>	34	2 (-, M, I)	34.5% (34-35)
Transarticular	2 (-, M, I)	<sup>1</sup>	35		
Inline	1 (S, -, -)	Mid-ala	63	1 (S, -, -)	80% (61-97)
Inline	1 (S, -, -)	Mid-sacrum	61		
Transarticular	1 (S, -, -)	Mid-ala	97		
Transarticular	1 (S, -, -)	Mid-sacrum	97		
Inline	1 (-, M, -)	<sup>1</sup>	78	1 (-, M, -)	92% (78-106)
Transarticular	1 (-, M, -)	<sup>1</sup>	106		
Inline	1 (-, -, I)	<sup>1</sup>	93	1 (-, -, I)	104% (93-115)
Transarticular	1 (-, -, I)	<sup>1</sup>	115		

<sup>1</sup>Configuration does not include a superior implant. S: Superior; M: Middle; I: Inferior.

different in the normal, osteopenic, and osteoporotic sacra, the distribution of low and high density locations are consistent in all three cases<sup>[19,24]</sup>; as such, we expect that the findings in the different bone quality groups will be consistent. The current model and previous experimental study had consistent intact ROM and motion reductions after treatment, but there are some differences for the loading conditions simulated in this study (double-leg stance, follower load, and larger applied moment). Although the loading conditions were different, the consistency in intact ROM suggested that these disparities were counteracting each (*e.g.*, follower load and double-leg stance increase stability; higher applied moment increase ROM)<sup>[17]</sup>, and demonstrated that the SI joint and treatment were being effectively modeled. Lastly, the theoretical model used in this study did not model all *in vivo* characteristics (*e.g.*, biological healing response after surgery); as such, additional

clinical studies may be required to confirm these results.

While the minimum biomechanical requirements for clinically successful fixation of the SI joint are currently unknown, the current study investigated 3 clinical implant placement parameters and compared the resulting SI joint reduction in range of motion with a baseline model. The baseline model investigated here (inline orientation, mid-ala superior implant length, 3 implants) is a common technique that has positive clinical outcomes<sup>[23]</sup>. The range of motion of the SI joint in the current study was assessed in 3 anatomical loading directions, of which flexion-extension demonstrated both the largest intact range of motion (1.94°) and, after treatment, overall reductions in motion (0.58°-1.42°). Lateral bending and axial rotation resulted in small median reductions in motion (< 0.1°) when the variables were investigated, which may not be clinically significant by themselves. In contrast, flexion-

extension was more sensitive to altering the variables with median reductions in motion  $> 0.1^\circ$ . Although the 3 motions investigated had varying sensitivity, they consistently (*i.e.*, positively/negatively) altered the reductions in motion. These results demonstrate that in flexion-extension, when compared with the baseline model, placement of the implants in areas of thicker cortical bone (transarticular orientation) and higher bone density (longer superior implant) leads to similar median increased reductions in motion of 16% and 14%, respectively. This study suggests that a surgeon can optimize implant placement in 3 ways: (1) Longer superior implants; (2) transarticular placement; and (3) using 3 implants (and/or increasing implant separation). Although the long-term clinical outcomes from these placement variations is unknown, the current study provides clinicians with insight and rationale into determining optimal implant placement.

## ARTICLE HIGHLIGHTS

### Research background

Minimally invasive fusion of the sacroiliac (SI) joint is a potential treatment for patients suffering with symptoms related to the SI joint. The use of a lateral procedure for SI joint fusion has been shown to be an effective method for reducing SI joint pain. Previous anatomical studies have demonstrated significant variability in sacral anatomy and the resultant location and size of safe zones for implant placement.

### Research motivation

A surgeon has options regarding the number of implants, length of implants, and their orientation; the optimal placement parameters for SI joint fixation are currently unknown. Quantification of the changes in SI joint motion as a result of varying the potential implant placement variables will provide a surgeon input when performing an SI joint fusion procedure.

### Research objectives

The objective of this study was to investigate and quantify the effect of implant orientation, superior implant length, and implant number on SI joint range of motion.

### Research methods

This study used a previously validated finite element analysis to investigate how implant orientation, superior implant length, and implant number affect SI joint range of motion. Implant orientation was simulated using either an inline or a transarticular placement. The length of the superior implant was varied to end either in the middle of the ala or at the sacral midline. The number of implants was 1, 2, or 3 implants. The SI joint range of motion was calculated using a constant moment of 10 N-m with a follower load of 400 N in flexion-extension, lateral bending, and axial rotation. A total of 23 model configurations were tested and the difference in SI joint range of motion compared.

### Research results

The use of a transarticular placement with a mid-sacrum length superior implant resulted in the greatest reduction in SI joint ROM. The use of transarticular placement resulted in median reductions in motion of 16%, 9%, and 18%, in flexion-extension, lateral bending, and axial rotation, respectively. Extending the superior implant to the sacral midline resulted in median reductions in motion of 14%, 8%, and 9%, in flexion-extension, lateral bending, and axial rotation, respectively. Reducing the number of implants (*i.e.*, 1 or 2 implants) resulted in increased motions in all directions. Implant configurations with 2 implants placed farthest apart had the smallest increases.

### Research conclusions

This study demonstrates that the treated SI joint range of motion is affected by implant orientation, superior implant length, and implant number. These results show that the optimal placement investigated was 3 implants placed using a transarticular placement with a superior implant that reaches the sacral midline. This study suggests that a surgeon can optimize implant placement in 3 ways: (1) Longer superior implants; (2) transarticular placement; and (3) using 3 implants (and/or increasing implant separation).

### Research perspectives

The use of a finite element model to simulate the SI joint and treatment effects allows for investigation of many variables and provides valuable insight regarding how each variable effects SI joint stability. These results allow for more detailed investigation using either *in vitro* or *in vivo* studies.

## REFERENCES

- 1 **Dreyfuss P**, Dreyer SJ, Cole A, Mayo K. Sacroiliac joint pain. *J Am Acad Orthop Surg* 2004; **12**: 255-265 [PMID: 15473677 DOI: 10.5435/00124635-200407000-00006]
- 2 **Bernard TN Jr**, Kirkaldy-Willis WH. Recognizing specific characteristics of nonspecific low back pain. *Clin Orthop Relat Res* 1987; (**217**): 266-280 [PMID: 2951048 DOI: 10.1097/00003086-198704000-00029]
- 3 **Schwarzer AC**, Aprill CN, Bogduk N. The sacroiliac joint in chronic low back pain. *Spine (Phila Pa 1976)* 1995; **20**: 31-37 [PMID: 7709277 DOI: 10.1097/00007632-199501000-00007]
- 4 **Sembrano JN**, Polly DW Jr. How often is low back pain not coming from the back? *Spine (Phila Pa 1976)* 2009; **34**: E27-E32 [PMID: 19127145 DOI: 10.1097/BRS.0b013e31818b8882]
- 5 **Heiney J**, Capobianco R, Cher D. A systematic review of minimally invasive sacroiliac joint fusion utilizing a lateral transarticular technique. *Int J Spine Surg* 2015; **9**: 40 [PMID: 26273558 DOI: 10.14444/2040]
- 6 **Gardner MJ**, Morshed S, Nork SE, Ricci WM, Chip Routh ML Jr. Quantification of the upper and second sacral segment safe zones in normal and dysmorphic sacra. *J Orthop Trauma* 2010; **24**: 622-629 [PMID: 20871250 DOI: 10.1097/BOT.0b013e3181cf0404]
- 7 **Yinger K**, Scalise J, Olson SA, Bay BK, Finkemeier CG. Biomechanical comparison of posterior pelvic ring fixation. *J Orthop Trauma* 2003; **17**: 481-487 [PMID: 12902785 DOI: 10.1097/00005131-200308000-00002]
- 8 **van Zwienen CM**, van den Bosch EW, Snijders CJ, Kleinrensink GJ, van Vugt AB. Biomechanical comparison of sacroiliac screw techniques for unstable pelvic ring fractures. *J Orthop Trauma* 2004; **18**: 589-595 [PMID: 15448446 DOI: 10.1097/00005131-200410000-00002]
- 9 **van Zwienen CM**, van den Bosch EW, Hoek van Dijke GA, Snijders CJ, van Vugt AB. Cyclic loading of sacroiliac screws in Tile C pelvic fractures. *J Trauma* 2005; **58**: 1029-1034 [PMID: 15920420 DOI: 10.1097/01.TA.0000158515.58494.11]
- 10 **Smith SA**, Abitbol JJ, Carlson GD, Anderson DR, Taggart KW, Garfin SR. The effects of depth of penetration, screw orientation, and bone density on sacral screw fixation. *Spine (Phila Pa 1976)* 1993; **18**: 1006-1010 [PMID: 8367767 DOI: 10.1097/00007632-199306150-00009]
- 11 **Kraemer W**, Heam T, Tile M, Powell J. The effect of thread length and location on extraction strengths of iliosacral lag screws. *Injury* 1994; **25**: 5-9 [PMID: 8132312 DOI: 10.1016/0020-1383(94)90176-7]
- 12 **Lindsey DP**, Perez-Orribo L, Rodriguez-Martinez N, Reyes PM, Newcomb A, Cable A, Hickam G, Yerby SA, Crawford NR. Evaluation of a minimally invasive procedure for sacroiliac joint fusion - an *in vitro* biomechanical analysis of initial and cycled properties. *Med Devices (Auckl)* 2014; **7**: 131-137 [PMID: 24868175 DOI: 10.2147/MDER.S63499]
- 13 **Soriano-Baron H**, Lindsey DP, Rodriguez-Martinez N, Reyes PM, Newcomb A, Yerby SA, Crawford NR. The effect of implant

- placement on sacroiliac joint range of motion: posterior versus transarticular. *Spine* (Phila Pa 1976) 2015; **40**: E525-E530 [PMID: 25705956 DOI: 10.1097/BRS.0000000000000839]
- 14 **Ivanov AA**, Alexander A. Development, validation and clinical application of finite element human pelvis model. 2008
- 15 **Ivanov AA**, Kiapour A, Ebraheim NA, Goel V. Lumbar fusion leads to increases in angular motion and stress across sacroiliac joint: a finite element study. *Spine* (Phila Pa 1976) 2009; **34**: E162-E169 [PMID: 19247155 DOI: 10.1097/BRS.0b013e3181978ea3]
- 16 **Kiapour A**, Abdelgawad AA, Goel VK, Souccar A, Terai T, Ebraheim NA. Relationship between limb length discrepancy and load distribution across the sacroiliac joint--a finite element study. *J Orthop Res* 2012; **30**: 1577-1580 [PMID: 22488899 DOI: 10.1002/jor.22119]
- 17 **Lindsey D**, Kiapour A, Yerby S, Goel V. Sacroiliac Joint Fusion Minimally Affects Adjacent Lumbar Segment Motion: A Finite Element Study. *Int J Spine Surg* 2015; [cited 2015 Nov 17] Available from: URL: <http://ijssurgery.com/10.14444/2064>
- 18 **Simonian PT**, Routt ML Jr, Harrington RM, Mayo KA, Tencer AF. Biomechanical simulation of the anteroposterior compression injury of the pelvis. An understanding of instability and fixation. *Clin Orthop Relat Res* 1994; (**309**): 245-256 [PMID: 7994968]
- 19 **Richards AM**, Coleman NW, Knight TA, Belkoff SM, Mears SC. Bone density and cortical thickness in normal, osteopenic, and osteoporotic sacra. *J Osteoporos* 2010; **2010**: pii: 504078 [PMID: 20948574 DOI: 10.4061/2010/504078]
- 20 **Rice JC**, Cowin SC, Bowman JA. On the dependence of the elasticity and strength of cancellous bone on apparent density. *J Biomech* 1988; **21**: 155-168 [PMID: 3350829]
- 21 **Patwardhan AG**, Havey RM, Meade KP, Lee B, Dunlap B. A follower load increases the load-carrying capacity of the lumbar spine in compression. *Spine* (Phila Pa 1976) 1999; **24**: 1003-1009 [PMID: 10332793]
- 22 **Panjabi M**, Malcolmson G, Teng E, Tominaga Y, Henderson G, Serhan H. Hybrid testing of lumbar CHARITE discs versus fusions. *Spine* (Phila Pa 1976) 2007; **32**: 959-966; discussion 967 [PMID: 17450069 DOI: 10.1097/01.brs.0000260792.13893.88]
- 23 **Polly DW**, Cher DJ, Wine KD, Whang PG, Frank CJ, Harvey CF, Lockstadt H, Glaser JA, Limoni RP, Sembrano JN; INSITE Study Group. Randomized Controlled Trial of Minimally Invasive Sacroiliac Joint Fusion Using Triangular Titanium Implants vs Nonsurgical Management for Sacroiliac Joint Dysfunction: 12-Month Outcomes. *Neurosurgery* 2015; **77**: 674-690; discussion 690-691 [PMID: 26291338 DOI: 10.1227/NEU.0000000000000988]
- 24 **Peretz AM**, Hipp JA, Heggeness MH. The internal bony architecture of the sacrum. *Spine* (Phila Pa 1976) 1998; **23**: 971-974 [PMID: 9589533]

**P- Reviewer:** Angoules A, Cui QJ, Emara KM, Guerado E

**S- Editor:** Cui LJ **L- Editor:** A **E- Editor:** Li D



## Retrospective Study

**Complex knee injuries treated in acute phase: Long-term results using Ligament Augmentation and Reconstruction System artificial ligament**

John Gliatis, Konstantinos Anagnostou, Pantelis Tsoumpos, Evdokia Billis, Maria Papandreou, Spyridon Plessas

John Gliatis, Konstantinos Anagnostou, Pantelis Tsoumpos, Department of Orthopaedic, University Hospital of Patras, Patras 25100, Greece

Evdokia Billis, Department of Physical Therapy, Technological Educational Institute of Western Greece, Aigion 25100, Greece

Maria Papandreou, Department of Physiotherapy, Technological Educational Institute of Athens, Aigion 25100, Greece

Spyridon Plessas, Department of Orthopaedic, General Hospital of Nikaia "Snt.Panteleimon", Piraeus 26504, Greece

ORCID number: John Gliatis (0000-0002-1216-354X); Konstantinos Anagnostou (0000-0001-7923-9732); Pantelis Tsoumpos (0000-0003-4773-5066); Evdokia Billis (0000-0002-5828-809X); Maria Papandreou (0000-0003-0353-4182); Spyridon Plessas (0000-0003-3695-0529).

**Author contributions:** Gliatis J has designed the research; Anagnostou K conducted the data collection, analysis and wrote the manuscript; Gliatis J and Plessas S were the senior surgeons; Billis E and Papandreou M were the senior physiotherapists of the team.

**Institutional review board statement:** The study was reviewed and approved by the Ethical Committee of University Hospital of Patras.

**Informed consent statement:** All study participants, provided informed written consent prior to study enrollment.

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

**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:** John Gliatis, PhD, Assistant Professor, Department of Orthopaedic, University Hospital of Patras Western Greece, Parodos Ipeirou, Agios Basileios, Patras 25100, Greece. [igliat@upatras.gr](mailto:igliat@upatras.gr)  
**Telephone:** +30-2610-999553  
**Fax:** +30-2610-931025

**Received:** January 26, 2017

**Peer-review started:** February 7, 2017

**First decision:** December 18, 2017

**Revised:** December 21, 2017

**Accepted:** February 4, 2018

**Article in press:** February 5, 2018

**Published online:** March 18, 2018

**Abstract****AIM**

To present the long-term results of complex knee injuries, treated early using the Ligament Augmentation and Reconstruction System (LARS) artificial ligament to reconstruct posterior cruciate ligament (PCL).

**METHODS**

From September 1997 to June 2010, thirty-eight complex knee injuries were treated, where early arthroscopic PCL reconstructions were undergone, using the LARS (Surgical Implants and Devices, Arc-sur-Tille, France) artificial ligament. Exclusion criteria were: Late (> 4 wk) reconstruction, open technique, isolated PCL reconstruction, knee degenerative disease, combined

fracture or vascular injury and use of allograft or autograft for PCL reconstruction. Clinical and functional outcomes were assessed with IKDC Subjective Knee Form, KOS-ADLS questionnaire, Lysholm scale and SF-12 Health Survey. Posterior displacement (PD) was measured with the Telos Stress Device.

### RESULTS

Seven patients were excluded; two because of co-existing knee osteoarthritis and the remaining five because of failure to attend the final follow-up. The sample consisted of 31 patients with mean age at the time of reconstruction  $33.2 \pm 12.5$  years (range 17-61). The postoperative follow-up was on average  $9.27 \pm 4.27$  years (range 5-18). The mean average IKDC and KOS scores were  $79.32 \pm 17.1$  and  $88.1 \pm 12.47\%$  respectively. Average PD was  $3.61 \pm 2.15$  mm compared to  $0.91 \pm 1.17$  mm in the uninjured knees (one with grade 1 + and two with grade 2 +). Dial test was found positive in one patient, whereas the quadriceps active drawer test was positive in three patients. None was tested positive on the reverse-pivot shift test. The range of motion (ROM) was normal in thirty knees, in comparison with the contralateral one. There was no extension deficit. Osteoarthritic changes were found in three knees (9.6%).

### CONCLUSION

Early treatment of complex knee injuries, using LARS artificial ligament for PCL reconstruction sufficiently reduces posterior tibia displacement and provides satisfactory long-term functional outcomes.

**Key words:** Complex knee injuries; Posterior cruciate ligament; Acute reconstruction; Ligament Augmentation and Reconstruction System

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Complex knee injuries pose a difficult problem while the treatment remains controversial. There are only few studies with long-term follow-up and with homogenous sample, regarding the timing of operation, the type of the graft and the type of reconstruction. In our study with a long-term follow-up, we have operated all the patients in the acute phase, using a standardized protocol regarding the technique, the type of the graft and the postoperative rehabilitation. Furthermore we have excluded the knee dislocations with vascular injuries, since these injuries have a different prognosis and they consist a separate category.

Gliatis J, Anagnostou K, Tsoumpos P, Billis E, Papandreou M, Plessas S. Complex knee injuries treated in acute phase: Long-term results using Ligament Augmentation and Reconstruction System artificial ligament. *World J Orthop* 2018; 9(3): 24-34 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i3/24.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i3.24>

## INTRODUCTION

Although most complex knee injuries are thought to occur due to a knee dislocation, in real practice a complete knee dislocation is very rare. Almost all complex knee injuries involve either the anterior cruciate ligament (ACL) and/or posterior cruciate ligament (PCL). This may be combined with injury to the medial knee structures and/or posterolateral corner structures of the knee. "Benign knee dislocation", described by Wascher *et al*<sup>[1]</sup> features isolated knee injury with mild or no neurovascular compromise and intact bony structure. Controversies also exist regarding various parameters, including early vs delayed surgery, type of reconstruction technique being chosen and postoperative rehabilitation program<sup>[2,3]</sup>. Very few studies exist with long term follow-up, whilst most of them include cases with complex injuries and true dislocations being classified within the same category.

Amongst the controversies regarding reconstruction of the multiple-injured knee is the choice of PCL graft tissue and the timing of the operation<sup>[4]</sup>. Posterior cruciate ligament is considered the primary restraint to posterior translation of the knee and the central stabilizer of the knee<sup>[5-8]</sup>. The incidence of PCL injuries is lower than that of ACL, occurring in approximately 3.4% to 20% of all knee ligament injuries<sup>[9]</sup>. PCL injuries are presented either as isolated tears or combined with other knee ligament injuries. Multiple knee ligament injuries usually need surgical treatment<sup>[10,11]</sup>. Despite the variety of operative techniques, PCL reconstruction still remains a challenge<sup>[10,12,13]</sup>. Autografts like Patella tendon (Bone-Tendon-Bone), Hamstrings and Quadriceps tendon or allografts like Achilles tendon, Anterior and Posterior Tibialis tendon are the most commonly used grafts<sup>[4]</sup>. Artificial grafts are rarely indicated because of their previous failure in ACL reconstruction<sup>[14-16]</sup>. The new generation artificial ligaments offer the advantages of less surgical time, absence of donor site morbidity, avoidance of possible spread of diseases (like Hepatitis C, HIV or knee infection), and faster postoperative rehabilitation<sup>[4,17-21]</sup>.

As far as the timing of the operation is concerned, previous studies have stress out the risk of arthrofibrosis after early treatment<sup>[22,23]</sup>. However in other reports, there is evidence that early reconstruction, in the first 4-6 wk usually provides better results compared to delayed reconstruction<sup>[2,24]</sup>, which could be explained by the good healing capacity of the early ruptured PCL<sup>[25-29]</sup>. The limit of early treatment though arbitrary is considered 3 wk. Recently Fanelli *et al*<sup>[3]</sup> set the limit of early reconstruction in six weeks long.

In our retrospective study we have included patients with complex knee injuries being treated acutely and followed-up long-term, utilizing a standardized treatment protocol. Early (during 4 wk post injury) PCL reconstruction using an artificial ligament as a temporary restraint to posterior translation of tibia,

**Table 1 Patients data**

Patient	Gender	Age	Cause and time of Injury	Injury	Operation time after injury (wk)	Follow-up (yr)
1	Male	35	MVA (2007)	(R) PCL/MCL/MM	2	8
2	Male	46	MVA (2007)	(R)PCL/ACL/MCL part	4	8
3	Male	52	MVA (2003)	(L) PCL/ACL/LM	1	12
4	Male	19	MVA (2004)	(R) PCL/PLC/LM	4	11
5	Male	41	MVA (1997)	(L) PCL/ACL/LM	2	18
6	Male	36	MVA (2003)	(L) PCL/ACL	1	12
7	Male	25	MVA (2007)	(R) PCL/ACL/PLC	4	8
8	Male	20	MVA (2001)	(L) PCL/MCL/MM	4	14
9	Male	61	FALL (2006)	(R) PCL/ACL/MCL	1	9
10	Male	60	FALL (2007)	(R) PCL/ACL/PLC	3	8
11	Fem.	54	FALL (2000)	(R) PCL/ACL/	3	15
12	Male	37	MVA (2002)	(R) PCL/ACL	3	13
13	Male	25	MVA (2004)	(R)PCL/PLC/ACL/LM	1	11
14	Male	51	MVA (2007)	(L) PCL/MCL	4	8
15	Female	17	FALL (1999)	(L)PCL/ACL/LM	1	16
16	Female	28	FALL (2005)	(R)PCL/ACL/MCL part	1	10
17	Male	20	MVA (2000)	(L) PCL/MCL	4	15
18	Male	23	MVA (2003)	(R) PCL/PLC/LM	2	12
19	Male	38	MVA (2004)	(L) PCL/MCL	3	11
20	Male	37	MVA (2007)	(R) PCL/PLC	2	8
21	Male	27	FALL (2009)	(L) PCL/ACL	4	6
22	Female	36	MVA (2009)	(R) PCL/ACL/PLC	4	6
23	Male	33	MVA (2009)	(R) PCL/ACL/MCL/MM	4	6
24	Male	30	MVA (2010)	(L) PCL/ACL	1	5
25	Male	27	MVA (2010)	(L) PCL/ACL/PLC	3	5
26	Male	21	MVA (2010)	(R) PCL/ACL/MCL	2	5
27	Male	22	MVA (2011)	(R) PCL/ACL	1	6
28	Male	35	FALL (2010)	(R) PCL/ACL	4	5
29	Male	26	MVA (2010)	(R) PCL/ACL/MCL	2	5
30	Male	26	MVA (2010)	(R) PCL/ACL/MCL	4	5
31	Male	21	MVA (2011)	(R) PCL/ACL	4	7
Average ± SD		33.2 ± 12.5			2.67 ± 1.24	9.2 ± 4.27

allows the PCL remnants to heal<sup>[26,30-35]</sup> and can give satisfactory early and long-term results concerning posterior stability. In addition the augmentation of the posterolateral corner reconstruction allows the repaired soft tissues to heal in the correct position. We thus, retrospectively present the results of complex knee injuries treated in the early post-injury period using the artificial ligament LARS (Ligament Augmentation Reconstruction System)<sup>[36-38]</sup> to reconstruct PCL. The purpose of this study was to post-operatively assess the stability and clinical outcomes of the knee in mid-term to long-term follow-up, and to identify the progress of any degenerative changes in acutely operated knees.

## MATERIALS AND METHODS

### Sample

Multiple ligament knee injuries where PCL was reconstructed with LARS artificial ligament were retrospectively studied. The study period was from 1997 to 2010. Thirty-eight operations were undergone in this period. Inclusion criteria were the early arthroscopically-assisted, multiple ligament reconstruction, always including single bundle PCL reconstruction with LARS artificial ligament. Exclusion criteria were the open technique, the use of allografts or autografts such Hamstrings or Patella tendon for PCL reconstruction,

the isolated PCL reconstruction, the presence of degenerative knee disease and the concomitant fracture or vascular injury that could influence the postoperative rehabilitation program. All patients were operated in the first four weeks after injury, which is the elapsed time to consider an injury as an acute one (Table 1).

### Graft selection

The graft used for PCL reconstruction was the LARS (Ligament Augmentation and Reconstruction System, Surgical Implants and Devices, Arc-sur-Tille, France) artificial ligament, made of polyethylene terephthalate. LARS is a system of artificial ligament devices used for ACL, PCL, PLC (posterolateral corner) reconstructions and also Achilles tendon ruptures and acromioclavicular joint injuries<sup>[18,19,36,37,39]</sup>. We have used PC 80 in our cases.

### Operative technique

All the operations were performed by the two senior authors, which were experienced in multiple ligament reconstructions. Under general anesthesia in supine position, a tourniquet was applied to the affected limb without being inflated. The foot of the operated leg was seated on a post over the operative table with a lateral support to maintain the knee in 90° of flexion. Leg position adjustments were possible. We used fluids with

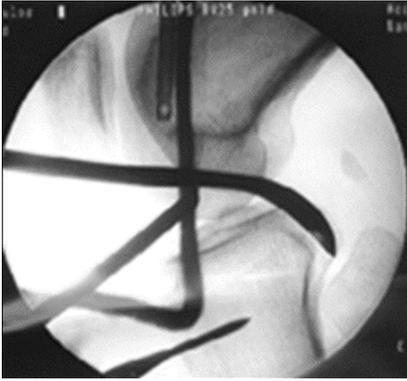


Figure 1 Tibial tunnel opening under image intensifier.

gravity flow and not a pump. An image intensifier was necessary in the theatre. In all cases, we performed a routine arthroscopic examination of the knee joint through the standard anterolateral and anteromedial portals. These portals were made immediately adjacent to the lateral and medial borders of the patellar tendon and 1 cm above the joint line to allow an easy passage of an arthroscope through the intercondylar notch to provide access to PCL tibial attachment. In PCL injuries, it is easier for the arthroscope to pass from the anterolateral portal to the posteromedial compartment through the intercondylar notch. In cases of meniscal or cartilage injury, if debridement was needed, the medial portal was used as well. Posteromedial portal was not used. Initial intra-articular bleeding was controlled with the aid of intermittent tourniquet inflation. A thorough evaluation of the intra-articular injuries was performed. The meniscal and cartilage injuries were treated first, either with fragments removal or meniscal repair. In all cases PCL was reconstructed, first of all injured ligaments, with LARS artificial ligament. The PCL remnants were always left intact and the tibial tunnel was created first, under image intensifier control (Figure 1). With the LARS instrument there was no need to debride the tibial PCL attachment. Then the femoral tunnel was created aiming just inferior to the native anterolateral bundle attachment of the PCL. The graft was passed afterwards through the tunnels with the aid of flexible wires, leaving the functional part of the graft inside the knee joint. The femoral side was fixed first and the normal step off was restored under image intensifier before the fixation of the tibial side with one screw and one staple. In cases of coexisting ACL rupture, we reconstructed the ligament in the early cases with LARS artificial ligament in the first 12 cases, while in the other 13 cases we used Hamstrings tendons. Posterolateral instability (PLI) was detected clinically with increased external rotation (Dial test) and arthroscopically with the "drive through sign" in 9 cases. We reconstructed posterolateral corner (PLC) addressing the popliteal and popliteo-fibular ligament (Warren procedure)<sup>[35,40]</sup>. In all cases we used Hamstrings tendons from the contralateral knee to augment the



Figure 2 Proper position of tibia and femur for Telos Stress Device.

repaired PLC structures. In none of the cases MCL reconstruction was necessary<sup>[41]</sup>. Postoperatively we used continuous passive motion (CPM) from day one. The patients were allowed to partial weight-bear for 6 wk and gradually to full weight-bear up to two months. Postoperatively conventional functional braces were utilized<sup>[20,21]</sup>.

### Evaluation

All patients were assessed clinically and functionally in an outpatient office by an independent observer who was an appropriately trained senior resident. Clinical evaluation included Lachman and reverse-Lachman test, Anterior and Posterior Drawer tests (grading: 1 +: 0-5 mm, 2 +: 5-10 mm, 3 +: > 10 mm anterior or posterior translation respectively), Quadriceps Active Drawer test, Dial test for PLI and Varus-Valgus stress tests (grading I : 0-5 mm, II : 5-10 mm, III : > 10 mm opening) for collateral ligaments' assessment<sup>[42]</sup>. The functional outcome was assessed with ROM evaluation, KOS-ADLS score and IKDC Subjective Knee Form, while Lysholm knee scoring, and SF-12 Health Survey completed the clinical outcomes<sup>[43-47]</sup>. The examiner used the Telos Stress Device to evaluate the posterior displacement of the injured knee in comparison to the contralateral healthy one<sup>[48,49]</sup>. A lateral x-ray imaging was performed in 90° of knee flexion under a standard anteroposterior force of 150N from Telos Stress Device (Figure 2). The standard force is widely accepted since 80N are adequate to induce posterior displacement of the tibia, while a greater than 180N force will cause pain and muscle contraction, influencing the reliability of measurements<sup>[50]</sup>. The total posterior tibial translation was measured and the side to side difference between normal and affected knee was compared during the force applied and not<sup>[50-53]</sup> (Figure 3). Arthritis was assessed by AP radiographs. Arthritis was rated as either present or absent based on joint space narrowing and/or the presence of osteophytes. This methodology is similar to that used in the Kellgren and Lawrence (KL) grading system<sup>[54]</sup>. Patients without evidence of osteoarthritis would be considered (KL) Grade 0 to 1, whereas patients with radiographic evidence of

**Table 2 Functional scores**

Patient code	KOS-ADSL/70 × 100%	IKDC/87 × 100	Lysholm/100	SF-12	
				Physical subscale (%)	Mental subscale (%)
1	94.2%	88.5	91	51.1	62.4
2	98.5%	79.3	100	54.8	59.8
3	88.5%	83.9	85	49.3	61.4
4	95.7%	98.8	91	56.6	60.8
5	92.8%	77.0	88	56.6	60.8
6	74.2%	65.5	83	48.7	61.5
7	98.5%	98.8	100	56.6	60.8
8	100%	94.2	100	57.2	33.8
9	88.5%	62.0	94	48.0	62.5
10	100%	98.5	100	56.6	60.8
11	77.1%	72.0	88	56.6	60.8
12	78.5%	80.4	90	53.1	59.9
13	88.5%	83.9	69	53.0	57.0
14	41.4%	24.1	48	30.8	40.5
15	90.0%	93.1	85	56.6	60.8
16	100%	95.4	100	56.6	60.8
17	80.0%	52.8	90	38.8	61.5
18	75.7%	60.9	58	47.6	48.6
19	85.7%	81.6	95	54.1	53.8
20	97.1%	95.4	99	56.6	60.8
21	90.0%	81.6	99	55.3	60.7
22	97.1%	95.4	99	55.3	60.7
23	58.5%	49.4	67	42.8	57.0
24	92.8%	81.6	94	55.3	60.7
25	98.5%	100	100	56.6	60.8
26	92.8%	86.2	85	53.2	49.8
27	95.7%	90.8	94	56.6	60.8
28	77.1%	55.1	81	36.0	60.4
29	98.5%	89.6	94	56.6	60.8
30	92.8%	85.0	94	56.6	60.8
31	92.8%	81.6	86	55.3	60.7
Average ± SD	88.1 ± 12.47	79.32 ± 17.1	88 ± 12.4		

osteoarthritis would be considered (KL) Grade 2 to 4.

## RESULTS

Thirty-eight patients in total over the 17 years' period sustained a complex knee injury including PCL rupture and underwent a reconstruction of PCL with LARS artificial ligament. From these, two patients were excluded because of co-existing knee osteoarthritis, while five more did not manage to attend the final follow-up. So, the final sample consisted of 31 patients. From the 31 patients, 27 were males and 4 females. From the reconstructed knees 20 were right side and 11 left. The mean age at the time of reconstruction was 34.5 (± 12.5) years (range 17-61). The average time from injury to surgery was 2.67 (± 1.24) wk (range 1-4) and the mean time of postoperative follow-up was 9.2 (± 4.27) years (range 5-18), (Table 1). From the 31 cases, 24 were motor vehicle accidents (MVA) and 7 were sport injuries and falls (Table 1). All patients were examined clinically (clinical examination) functionally (with functional outcome questionnaires) (Table 2), and radiologically with the Telos stress device (Table 3).

### Time interval between injury and operation

Three patients (8.8%) were operated during the first

week (< 1/52); specifically two patients were operated three days post-injury and one patient on the accident day. Also five patients (17.6%) were operated 1 wk (1/52) after the trauma and six patients (17.6%) 2 wk (2/52) after their accident, respectively. Five patients (17.6%) underwent operation three weeks (3/52) post injury, while twelve patients (38.2%) were treated four weeks (4/52) after injury.

### Functional scores and clinical findings

The mean KOS-ADLS score (Knee Outcome Survey - Activities of Daily Living Score) was 88.1% (± 12.47). Twenty-two patients (70.9%) had score greater than 60/70 and two of them (6.4%) reached the absolute 70/70, indicating excellent functionality. Only one patient (3.2%) had score of less than 35/70. The mean IKDC (International Knee Documentation Committee) Subjective Knee Form was 79.32 (± 17.1). Twenty patients (64.5%) reached 70/87 score and above but four patients (12.9%) pointed a score lower than 50/87.

The evaluation according to the Lysholm knee scoring revealed excellent (95-100) results for ten (32.2%) patients, good (84-94) for sixteen (51.6%), fair (65-83) for three (9.6%) and poor (< 64) for only two (6.4%) patients (Table 2). Regarding the SF-12 Health Survey, all patients except three declared very satisfied from

**Table 3** Radiological results with Telos device

Patient code	Telos posterior displacement (mm) X-ray measured	
	Operated knee	Healthy knee (contralateral)
1	8	0
2	6	3
3	5	2
4	1	0
5	4	0
6	2	5
7	0	0
8	0	2
9	6	0
10	3	1
11	2	1
12	4	0
13	6	1
14	7	2
15	5	0
16	3	3
17	3	0
18	3	0
19	4	1
20	3	1
21	4	0
22	2	1
23	8	0
24	4	1
25	0	2
26	5	0
27	1	1
28	3	0
29	0	0
30	3	0
31	4	0
Average (SD)	3.61 ( $\pm$ 2.15)	0.91 ( $\pm$ 1.17)

the postoperative outcome in both physical and mental health fields (ranging from 30.8-56.6 and 33.8-62.5 respectively), and further indicated that if again needed, they would undergo the same procedure under the same circumstances (Table 3).

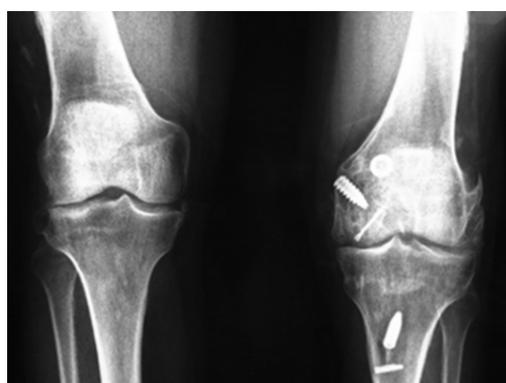
The posterior drawer test was positive (grade 2+) in six ( $n = 6$ ) patients, the anterior drawer test was positive in three ( $n = 3$ ) (one with grade 1+ and two with grade 2+), the varus stress test in five ( $n = 5$ ) (three with grade I and two with grade II) and the valgus stress test in three ( $n = 3$ ) patients (all with grade II). The dial test was found positive ( $> 15^\circ$  side to side difference) in one ( $n = 1$ ) patient, whereas the quadriceps active drawer test was positive in three ( $n = 3$ ) patients. None was tested positive on the reverse-pivot shift test. The range of motion (ROM) was normal in thirty knees, in comparison with the contralateral one, with a  $0^\circ$ - $121.2^\circ$  ( $\pm 10.14$ ) average flexion arc and had no extension deficit. Only in one knee there was a limitation of ROM:  $0^\circ$ - $90^\circ$ .

### Radiographic evaluation

The evaluation of knee X-rays (AP weight-bearing-standing) revealed a medial joint space narrowing ( $> 2$  mm in comparison with lateral joint space) in three ( $n = 3$ ) patients; in a 66 year old woman at the last



**Figure 3** Anteroposterior force on tibia through Telos Device leading to posterior translation.



**Figure 4** Anteroposterior knee x-rays for evaluation of arthritis progression (Kellgren and Lawrence grade 3).

follow-up, 15 years postoperatively with (KL) grade 3 (Figure 4), and in two men 64 and 54 years old, 8 and 15 years after operation, respectively both with (KL) grade 2. The remaining twenty-eight ( $n = 31$ ) patients had no radiographic findings of joint space narrowing (KL grade 0 or 1). The mean tibial posterior displacement of the operated knees as measured with the Telos Stress Device was  $3.61$  ( $\pm 2.15$ ) mm. The value for the normal contralateral knees was  $0.91$  ( $\pm 1.17$ ) mm respectively. Twenty-five patients (80.6%) were found with posterior translation of less than 5 mm (Grade I) and six patients (19.3%) with posterior displacement in the range 6-10 mm (Grade II). No one patient was classified in the group of 11-15 mm or greater than 15 mm (Grades III and IV, respectively) (Table 3).

## DISCUSSION

In our study we treated complex knee injuries in the acute phase, at four weeks' time, reconstructing PCL with LARS artificial ligament in all our cases. The clinical outcome was satisfactory in most of the cases long-term. The rate of posttraumatic arthritis was very low, too. Most of our patients in this study maintained a good clinical outcome in the long-term follow-up. We assessed the stability with the Telos Stress Device

postoperatively<sup>[48-53]</sup>. The posterior translation was more than 5 mm in only six patients, but none of them had an over 10 mm posterior displacement. The mean side-to-side difference was 2.7 mm, which is comparable with other series with long-term follow-ups. Hermans *et al*<sup>[55]</sup> found a 4.7 mm mean difference in their patients. Similar results have been reported in other studies using autografts or allografts<sup>[56]</sup>. The functional and clinical outcome was assessed through three knee-specific questionnaires: The IKDC Subjective Knee Form, the KOS-ADLS, the Lysholm scale, as well as a general health questionnaire, the SF-12 Health Survey<sup>[43-45]</sup>. More than 70% of our patients scored good to excellent results in all measures used. Only one patient yielded disappointing results even though the objective assessment was normal. In our study the rate of post-traumatic arthritis was low (three out of 34 patients) compared to other studies with similar follow-up time<sup>[3,57,58]</sup>.

Very few studies underwent long-term follow-up<sup>[2,3,57-61]</sup> and only two studies exceeded the ten-year follow-up limit<sup>[3,59]</sup>. However most of these previous studies included both true dislocations and complex knee injuries together. Thus, making the sample heterogeneous, because the soft tissue injury is usually worse after a complete dislocation. In one of those, Engebretsen *et al*<sup>[58]</sup> also included patients with different type of injuries, where they concluded that high-energy injuries had significantly lower functional scores. Furthermore in some of these studies with long term follow-up the type of treatment was not consistent, either treating the patients in two stages<sup>[57]</sup> or conservatively<sup>[61]</sup>. Another issue, which was not consistent in these studies, was the timing of operative treatment. In some of those the operation was performed in a later stage<sup>[57]</sup>, in others in an early stage<sup>[58,59]</sup> and some of these studies included patients, who had treatment both in early and late stage<sup>[58]</sup>. Recently, a study<sup>[2]</sup> presented good results after long-term follow-up in patients with traumatic knee dislocations. However they included patients with vascular injury requiring repair, as well as some patients with high-energy injuries. In these cases, soft tissues very rarely heal in the first three weeks after the injury making impossible reconstruction in early stage, thus influencing negatively the final outcome. Treatment regime was not the same for all the patients since they used various grafts for ligament reconstruction, especially for the PCL. The incidence of posttraumatic arthritis also, was not reported. Fanelli *et al*<sup>[3]</sup>, presented the study with the longest follow-up (over 10 years) and the patients had a standardized treatment protocol, utilizing allografts in a delayed fashion in the majority of the cases. They reported that the knee stability was restored but one fourth of the patients had developed post-traumatic arthritis. Interestingly, the same authors in a previously reported study<sup>[62]</sup> with 10 years follow-up did not provide any information about post-traumatic

arthritis. Engebretsen *et al*<sup>[58]</sup> on the other hand reported high incidence of arthritis in his patients but they included all high-energy traumatic complete knee dislocations.

Our treatment regime included several standardized procedures. Firstly, the requirement for operating was to have a "quiet" knee with no blisters or edema, and with smooth range of knee motion. In all of our cases we achieved this goal using early CPM and active quadriceps exercises, at the limits of the pain. Therefore, we excluded the cases of knee dislocations requiring revascularization, as in these cases the repair had to be protected with knee immobilization, using an external fixator. This is the reason we used the term "complex" knee injuries and not knee dislocations. In our experience, the latter is a different entity because of the severity of the soft tissue injury and the possible fasciotomies, associated with vascular reconstruction, which usually preclude early treatment of the knee ligaments. Secondly, our aim was to operate in an early stage, trying to preserve the remnants of both, the ruptured PCL and the ruptured collateral ligaments. There is debate in the literature regarding the timing for treating complex knee injuries. Two systematic reviews, published both in 2009<sup>[63,64]</sup> reported different conclusions regarding the timing of the operation. Levy *et al*<sup>[63]</sup> suggested that early operative treatment of the multi-ligament injured knee yields improved functional and clinical outcomes compared to non-operative management or delayed surgery. On the other hand, Mook *et al*<sup>[24]</sup> reported that delayed reconstructions of severe multiple-ligament knee injuries could potentially yield equivalent outcomes in terms of stability when compared with acute surgery. This is justified by the fact that acute surgery is highly associated with range-of-motion deficits. Hirschmann *et al*<sup>[59]</sup> reported in 12 years follow-up (average) study with early reconstruction very good results regarding knee stability, but one fifth of the patients had extension deficits and one third of the patients had not satisfactory clinical outcome. The authors did not include patients with vascular repair but the ligament reconstruction was performed with open surgery. Recently Khakha *et al*<sup>[2]</sup> reported a high level of overall knee function following acute surgical reconstruction with a 10-year average follow-up. However, the treatment protocol was not consistent, since they used different grafts for PCL and PLRI reconstruction. They also included patients requiring vascular repair, who needed postoperative immobilization; they however, have reported immediate knee motion postoperatively.

We have used also the artificial LARS ligament to reconstruct PCL. The artificial graft acts as a scaffold for the PCL remnants. The stable joint environment and the scaffold function of the LARS ligament promotes the healing procedure<sup>[25,27,29,31,32,39,51]</sup>. Its use in ACL reconstruction as an isolated graft is contraindicated because it has failed in the majority of the cases

even though it seemed successful in the short-term<sup>[14-17,26,37,41,64]</sup>. The difference in PCL reconstruction is that the function of the graft in the acute phase is to act as the central support system, allowing the PCL remnants to heal in the correct position with minimal posterior laxity in the knee<sup>[30,31,34,65]</sup>. Another advantage of the artificial graft is that there is no need for intensive postoperative rehabilitation using sophisticated devices. In all the cases we did not restrict the range of motion postoperatively. The surgical technique also is simpler than the conventional PCL reconstruction techniques, because the posterior portals are not needed, since the posterior exit of the tibial tunnel is assessed fluoroscopically, using the special guide of the LARS system. The risk of synovitis was reduced as we did not notice any case of synovitis in our sample and we are aware of only one case in the literature<sup>[14,15]</sup>. Another benefit of this reconstructive procedure is that it permits fast return to daily activities and sooner to sports. In contrast to this fast return, hamstrings or other autografts require a period of graft revascularization, where activities are limited and rehabilitation program is extended. In addition, allografts always pose the risk of disease transmission<sup>[18,20,21]</sup>. The advantage of preserving the PCL remnants was stressed out in two studies. Both Ahn *et al.*<sup>[32]</sup> and Zhao *et al.*<sup>[66]</sup> reported a preserving reconstruction method for chronic, however PCL injuries. The only study available to describe the results of remnant-preserving PCL reconstruction in the acute and sub-acute stage was presented by Jung *et al.*<sup>[31]</sup> but the authors have included patients in the sub-acute phase (3 mo post-injury). They also used hamstrings grafts, which require protection in the early postoperative period. Recently various reports have published good results after PCL reconstruction using LARS artificial ligaments<sup>[19,37]</sup>. However only in one study the operation was performed in an early stage<sup>[19]</sup> and the follow-up was relatively short (less than 5 years), which is considered a limitation when artificial grafts are used, because of their tendency to fail in a later phase<sup>[15,16]</sup>.

Despite our efforts, there are limitations in our study. It is a retrospective study, but the majority of similar studies are also retrospective, since the incidence of these injuries is very rare. A second limitation is the sample size, which seems rather small, however it is considered a homogenous sample, since we used a standardized protocol regarding the timing of surgery and the treatment method. We have also excluded patients with vascular injuries, which require different treatment protocol and they also have different prognosis. The follow-up was long enough, compared to other similar studies, reported in the literature. Therefore, we believe that our proposed treatment protocol to treat complex knee injuries, operating in an early fashion and reconstructing PCL with LARS artificial ligament may restore knee stability and provide satisfactory long term clinical outcome.

## ARTICLE HIGHLIGHTS

### Research background

Complex knee injuries pose a difficult problem across the literature in terms of diagnostic classification while the treatment remains controversial. In particular, there is conflict regarding: (1) Their classification (as benign knee dislocations with intact neurovascular status and knee dislocations with arterial injury are not well classified); (2) their postoperative rehabilitation (as knee dislocations with arterial injury require a period of knee immobilization, whereas "benign" knee dislocations can be treated with aggressive postoperative rehabilitation); (3) the timing of the operation; (4) the graft type; and (5) the lack of long term follow-up. In our study we have tried to address all these issues, because we present a homogenous sample, with a long-term follow-up, using LARS artificial ligament to reconstruct PCL and all patients had the operations in the acute phase. Therefore, we feel that the results presented here are reliable since our study, although retrospective has a clear and robust methodology.

### Research motivation

In medicine and in any other research processes, the researcher first he observes a phenomenon, secondly he tries to explain it with a theory, and lastly, he has to reproduce it, to confirm the theory. Taking this into account, we have observed that early reconstruction of these injuries provide better outcomes, because the injured soft tissues, have a better healing potential in the acute phase. There is also always a fear for knee arthrofibrosis, when operating early these injuries; we have therefore, allowed (in all our cases) the inflammation to settle down with the help of intensive physiotherapy after the injury. The artificial ligament also provides the scaffold, necessary for the tissue healing in the appropriate position. Furthermore, it allows early rehabilitation because primary stability is achieved during the operation and no need for further protection is needed during the early postoperative period. The satisfactory outcome after this study's long-term follow-up is supporting the theory of early intervention following our treatment protocol.

### Research objectives

The main objective of our study was to present a standard treatment protocol to manage complex knee injuries, taking into account parameters which have not been clearly elaborated in previous studies, such as postoperative rehabilitation, timing of the operation, follow-up *etc.* The various parameters of the protocol have been well defined and we suggest this protocol, since we have found very promising outcomes for our patient sample.

### Research methods

In this retrospective study, we have used a range of clinical outcome measures and radiological parameters. Clinical measures included three knee-specific measures; the Knee Outcome Survey for Activities of Daily Living (KOS-ADLS), the Lysholm scale, the Knee Osteoarthritis Outcome Survey (KOOS) as well as a generic health measure, the SF-12 Health Survey, all of which present as the most commonly used self-reported outcomes in similar type of studies. In addition, for detecting any anteroposterior (AP) instability we have used the Telos devise. We have also used plain radiographs to detect any possible remaining instability and post-traumatic arthritis. However, we believe that the main advantages of our methodology is (1) Our homogenous sample selection (not including patients with vascular injury or major fracture around the knee); (2) the fact that the sample were all treated with the same standardized protocol; and (3) that postoperative rehabilitation was also intensive with no serious precautions regarding sophisticated and expensive braces.

### Research results

Authors study we have found satisfactory clinical outcomes after a long period of time. The functional scores, which have been used in our study yielded very good results. The remaining instability was minimal in most cases and the rate of posttraumatic arthritis was not detectable in most of our cases, given the long follow-up. In future, we may have to include an MRI to detect any occult meniscal or cartilage injuries.

### Research conclusions

The new findings of this study support the theory of early intervention following

complex knee injuries (without concomitant serious vascular or bony injuries) as clinical, functional and radiological outcomes have all been satisfactory during our long follow-up. We propose to treat early these injuries, providing that the patient has achieved a good range of motion preoperatively. We also suggest augmenting PCL remnants with LARS artificial ligament, which has been proven adequate in the long-term follow-up. In summary, the proposed treatment protocol is efficient in complex knee injuries, providing there is no concomitant serious vascular or bony injuries. The new hypothesis proposed by this study is the reconstruction of complex knee injuries in the acute phase. The cornerstone of our approach is to start early intensive physiotherapy, to operate as soon as the inflammation settles down and to repair all tissues in one stage. We augment the PCL with LARS artificial ligament and we also augment the repair of collateral ligaments. Based on these findings, we feel that all these injuries should be treated in the acute phase. The new methods are the use of LARS artificial ligament, only for PCL reconstruction and the repair of all the injuries in one stage. With this approach the patients may return earlier to their previous functional level. We feel that this is a major achievement because these injuries may be disabling when they are not treated appropriately.

### Research perspectives

The experience learnt from this study was to proceed for proper classification of complex knee injuries. We cannot classify them all in the same category since the prognosis and the treatment protocol is different in injuries complicated with vascular or serious bony injuries. The direction of the future research should be oriented towards the better classification of these injuries and to determine the use of the various available grafts. The methods for future research, is either biomechanical or clinical. The problem with clinical studies, is the rarity of the injury, therefore multicenter studies are required.

## REFERENCES

- 1 **Wascher DC**, Becker JR, Dexter JG, Blevins FT. Reconstruction of the anterior and posterior cruciate ligaments after knee dislocation. Results using fresh-frozen nonirradiated allografts. *Am J Sports Med* 1999; **27**: 189-196 [PMID: 10102100]
- 2 **Khakha RS**, Day AC, Gibbs J, Allen S, Hill P, Hull J, Perry A, Chissell H. Acute surgical management of traumatic knee dislocations--Average follow-up of 10 years. *Knee* 2016; **23**: 267-275 [PMID: 26545616 DOI: 10.1016/j.knee.2015.09.019]
- 3 **Fanelli GC**, Sousa PL, Edson CJ. Long-term followup of surgically treated knee dislocations: stability restored, but arthritis is common. *Clin Orthop Relat Res* 2014; **472**: 2712-2717 [PMID: 24898528 DOI: 10.1007/s11999-014-3707-6]
- 4 **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]
- 5 **Harner CD**, Höher J. Evaluation and treatment of posterior cruciate ligament injuries. *Am J Sports Med* 1998; **26**: 471-482 [PMID: 9617416]
- 6 **Wang D**, Berger N, Cohen JR, Lord EL, Wang JC, Hame SL. Surgical treatment of posterior cruciate ligament insufficiency in the United States. *Orthopedics* 2015; **38**: e281-e286 [PMID: 25901620 DOI: 10.3928/01477447-20150402-55]
- 7 **Voos JE**, Mauro CS, Wente T, Warren RF, Wickiewicz TL. Posterior cruciate ligament: anatomy, biomechanics, and outcomes. *Am J Sports Med* 2012; **40**: 222-231 [PMID: 21803977 DOI: 10.1177/0363546511416316]
- 8 **Papannagari R**, DeFrate LE, Nha KW, Moses JM, Moussa M, Gill TJ, Li G. Function of posterior cruciate ligament bundles during in vivo knee flexion. *Am J Sports Med* 2007; **35**: 1507-1512 [PMID: 17376856 DOI: 10.1177/0363546507300061]
- 9 **Miyasaka KC**, Daniel DM, Stone ML. The incidence of knee ligament injuries in the general population. *Am J Knee Surg* 1991; **4**: 3-8
- 10 **Lee BK**, Nam SW. Rupture of posterior cruciate ligament: diagnosis and treatment principles. *Knee Surg Relat Res* 2011; **23**: 135-141 [PMID: 22570824 DOI: 10.5792/ksrr.2011.23.3.135]
- 11 **Apsingi S**, Nguyen T, Bull AM, Unwin A, Deehan DJ, Amis AA. The role of PCL reconstruction in knees with combined PCL and posterolateral corner deficiency. *Knee Surg Sports Traumatol Arthrosc* 2008; **16**: 104-111 [PMID: 18060383 DOI: 10.1007/s00167-007-0444-3]
- 12 **Kohen RB**, Sekiya JK. Single-bundle versus double-bundle posterior cruciate ligament reconstruction. *Arthroscopy* 2009; **25**: 1470-1477 [PMID: 19962075 DOI: 10.1016/j.arthro.2008.11.006]
- 13 **Kim SJ**, Kim TE, Jo SB, Kung YP. Comparison of the clinical results of three posterior cruciate ligament reconstruction techniques. *J Bone Joint Surg Am* 2009; **91**: 2543-2549 [PMID: 19884425 DOI: 10.2106/JBJS.H.01819]
- 14 **Li H**, Yao Z, Jiang J, Hua Y, Chen J, Li Y, Gao K, Chen S. Biologic failure of a ligament advanced reinforcement system artificial ligament in anterior cruciate ligament reconstruction: a report of serious knee synovitis. *Arthroscopy* 2012; **28**: 583-586 [PMID: 22361004 DOI: 10.1016/j.arthro.2011.12.008]
- 15 **Klein W**, Jensen KU. Synovitis and artificial ligaments. *Arthroscopy* 1992; **8**: 116-124 [PMID: 1532312]
- 16 **Viateau V**, Manassero M, Anagnostou F, Guérard S, Mitton D, Mignonney V. Biological and biomechanical evaluation of the ligament advanced reinforcement system (LARS AC) in a sheep model of anterior cruciate ligament replacement: a 3-month and 12-month study. *Arthroscopy* 2013; **29**: 1079-1088 [PMID: 23726110 DOI: 10.1016/j.arthro.2013.02.025]
- 17 **Batty LM**, Norsworthy CJ, Lash NJ, Wasiak J, Richmond AK, Feller JA. Synthetic devices for reconstructive surgery of the cruciate ligaments: a systematic review. *Arthroscopy* 2015; **31**: 957-968 [PMID: 25620500 DOI: 10.1016/j.arthro.2014.11.032]
- 18 **Smith C**, Ajuied A, Wong F, Norris M, Back D, Davies A. The use of the ligament augmentation and reconstruction system (LARS) for posterior cruciate reconstruction. *Arthroscopy* 2014; **30**: 111-120 [PMID: 24290790 DOI: 10.1016/j.arthro.2013.09.081]
- 19 **Shen G**, Xu Y, Dong Q, Zhou H, Yu C. Arthroscopic posterior cruciate ligament reconstruction using LARS artificial ligament: a retrospective study. *J Surg Res* 2012; **173**: 75-82 [PMID: 20888585 DOI: 10.1016/j.jss.2010.08.015]
- 20 **Lee YS**, Kim NK. Rehabilitation after posterior cruciate ligament reconstruction. *Minerva Ortop Traumatol* 2011; **62**: 291-295
- 21 **Edson CJ**, Fanelli GC, Beck JD. Postoperative rehabilitation of the posterior cruciate ligament. *Sports Med Arthrosc* 2010; **18**: 275-279 [PMID: 21079508 DOI: 10.1097/JSA.0b013e3181f2f23d]
- 22 **Harner CD**, Irrgang JJ, Paul J, Dearwater S, Fu FH. Loss of motion after anterior cruciate ligament reconstruction. *Am J Sports Med* 1992; **20**: 499-506 [PMID: 1443315]
- 23 **Jari S**, Shelbourne KD. Non-operative or delayed surgical treatment of combined cruciate ligaments and medial side knee injuries. *Sports Med Arthrosc Rev* 2001; **9**: 185-192
- 24 **Mook WR**, Miller MD, Diduch DR, Hertel J, Boachie-Adjei Y, Hart JM. Multiple-ligament knee injuries: a systematic review of the timing of operative intervention and postoperative rehabilitation. *J Bone Joint Surg Am* 2009; **91**: 2946-2957 [PMID: 19952260 DOI: 10.2106/JBJS.H.01328]
- 25 **Bray RC**, Leonard CA, Salo PT. Vascular physiology and long-term healing of partial ligament tears. *J Orthop Res* 2002; **20**: 984-989 [PMID: 12382963 DOI: 10.1016/S0736-0266(02)00012-8]
- 26 **Woo SL**, Vogrin TM, Abramowitch SD. Healing and repair of ligament injuries in the knee. *J Am Acad Orthop Surg* 2000; **8**: 364-372 [PMID: 11104400]
- 27 **Akisue T**, Kurosaka M, Yoshiya S, Kuroda R, Mizuno K. Evaluation of healing of the injured posterior cruciate ligament: Analysis of instability and magnetic resonance imaging. *Arthroscopy* 2001; **17**: 264-269 [PMID: 11239346]
- 28 **Shelbourne KD**, Jennings RW, Vahey TN. Magnetic resonance imaging of posterior cruciate ligament injuries: assessment of healing. *Am J Knee Surg* 1999; **12**: 209-213 [PMID: 10626911]
- 29 **Scapinelli R**. Comment on W. Petersen and B. Tillmann, "Blood and lymph supply of the posterior cruciate ligament". *Knee Surg Sports Traumatol Arthrosc* 1999; **7**: 337, author reply 338 [PMID: 10525706 DOI: 10.1007/s001670050174]
- 30 **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]
- 31 **Jung YB**, Jung HJ, Song KS, Kim JY, Lee HJ, Lee JS. Remnant posterior cruciate ligament-augmenting stent procedure for injuries in the acute or subacute stage. *Arthroscopy* 2010; **26**: 223-229 [PMID: 20141985 DOI: 10.1016/j.arthro.2009.07.017]
- 32 **Ahn JH**, Yang HS, Jeong WK, Koh KH. Arthroscopic transtibial posterior cruciate ligament reconstruction with preservation of posterior cruciate ligament fibers: clinical results of minimum 2-year follow-up. *Am J Sports Med* 2006; **34**: 194-204 [PMID: 16303881 DOI: 10.1177/0363546505279915]
- 33 **Yoon KH**, Bae DK, Song SJ, Cho HJ, Lee JH. A prospective randomized study comparing arthroscopic single-bundle and double-bundle posterior cruciate ligament reconstructions preserving remnant fibers. *Am J Sports Med* 2011; **39**: 474-480 [PMID: 21098819 DOI: 10.1177/0363546510382206]
- 34 **Jung HJ**, Kim JH, Lee HJ, Koo S, Chang SH, Jung YB, Lee SH. The isometry of two different paths for remnant-preserving posterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 1029-1035 [PMID: 22763568 DOI: 10.1007/s00167-012-2111-6]
- 35 **Fanelli GC**, Giannotti BF, Edson CJ. Arthroscopically assisted combined posterior cruciate ligament/posterior lateral complex reconstruction. *Arthroscopy* 1996; **12**: 521-530 [PMID: 8902124]
- 36 **LARS**. Accessed June 2013. Available from: URL: [www.lars-ligaments.com](http://www.lars-ligaments.com)
- 37 **Huang JM**, Wang Q, Shen F, Wang ZM, Kang YF. Cruciate ligament reconstruction using LARS artificial ligament under arthroscopy: 81 cases report. *Chin Med J (Engl)* 2010; **123**: 160-164 [PMID: 20137364]
- 38 **Tzurbakis M**, Diamantopoulos A, Xenakis T, Georgoulis A. Surgical treatment of multiple knee ligament injuries in 44 patients: 2-8 years follow-up results. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 739-749 [PMID: 16602025 DOI: 10.1007/s00167-006-0039-4]
- 39 **Xu X**, Huang T, Liu Z, Wen H, Ye L, Hu Y, Yu H, Pan X. Hamstring tendon autograft versus LARS artificial ligament for arthroscopic posterior cruciate ligament reconstruction in a long-term follow-up. *Arch Orthop Trauma Surg* 2014; **134**: 1753-1759 [PMID: 25376713 DOI: 10.1007/s00402-014-2104-7]
- 40 **Wiley WB**, Askew MJ, Melby A 3rd, Noe DA. Kinematics of the posterior cruciate ligament/posterolateral corner-injured knee after reconstruction by single- and double-bundle intra-articular grafts. *Am J Sports Med* 2006; **34**: 741-748 [PMID: 16382008 DOI: 10.1177/0363546505282615]
- 41 **Shelbourne KD**, Carr DR. Combined anterior and posterior cruciate and medial collateral ligament injury: nonsurgical and delayed surgical treatment. *Instr Course Lect* 2003; **52**: 413-418 [PMID: 12690868]
- 42 **Rubinstein RA Jr**, Shelbourne KD, McCarroll JR, VanMeter CD, Rettig AC. The accuracy of the clinical examination in the setting of posterior cruciate ligament injuries. *Am J Sports Med* 1994; **22**: 550-557 [PMID: 7943523]
- 43 **Kapreli E**, Panelli G, Strimpakos N, Billis E, Zacharopoulos A, Athanopoulos S. Cross-cultural adaptation of the Greek version of the Knee Outcome Survey--activities of Daily Living Scale (KOS-ADLS). *Knee* 2011; **18**: 424-427 [PMID: 20869875 DOI: 10.1016/j.knee.2010.09.001]
- 44 **Koumantakis GA**, Tsiglikas K, Papoutsidakis A, Ververidis A, Drosos GI. Cross-cultural adaptation and validation of the International Knee Documentation Committee Subjective Knee Form in Greek. *J Orthop Traumatol* 2016; **17**: 123-129 [PMID: 26093603 DOI: 10.1007/s10195-015-0362-y]
- 45 **Kontodimopoulos N**, Pappa E, Niakas D, Tountas Y. Validity of SF-12 summary scores in a Greek general population. *Health Qual Life Outcomes* 2007; **5**: 55 [PMID: 17900374 DOI: 10.1186/1477-7525-5-55]
- 46 **Zayni R**, Hager JP, Archbold P, Fournier Y, Quelard B, Chambat P, Sonnery-Cottet B. Activity level recovery after arthroscopic PCL reconstruction: a series of 21 patients with a mean follow-up of 29 months. *Knee* 2011; **18**: 392-395 [PMID: 21144755 DOI: 10.1016/j.knee.2010.11.005]
- 47 **Hammoud S**, Reinhardt KR, Marx RG. Outcomes of posterior cruciate ligament treatment: a review of the evidence. *Sports Med Arthrosc* 2010; **18**: 280-291 [PMID: 21079509 DOI: 10.1097/JSA.0b013e3181eaf8b4]
- 48 **Margheritini F**, Mancini L, Mauro CS, Mariani PP. Stress radiography for quantifying posterior cruciate ligament deficiency. *Arthroscopy* 2003; **19**: 706-711 [PMID: 12966377]
- 49 **Stäubli HU**, Noesberger B, Jakob RP. Stressradiography of the knee. Cruciate ligament function studied in 138 patients. *Acta Orthop Scand Suppl* 1992; **249**: 1-27 [PMID: 1529706]
- 50 **Jung TM**, Reinhardt C, Scheffler SU, Weiler A. Stress radiography to measure posterior cruciate ligament insufficiency: a comparison of five different techniques. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 1116-1121 [PMID: 16799824 DOI: 10.1007/s00167-006-0137-3]
- 51 **Mariani PP**, Margheritini F, Christel P, Bellelli A. Evaluation of posterior cruciate ligament healing: a study using magnetic resonance imaging and stress radiography. *Arthroscopy* 2005; **21**: 1354-1361 [PMID: 16325087 DOI: 10.1016/j.arthro.2005.07.028]
- 52 **Schulz MS**, Russe K, Lampakis G, Strobel MJ. Reliability of stress radiography for evaluation of posterior knee laxity. *Am J Sports Med* 2005; **33**: 502-506 [PMID: 15722285 DOI: 10.1177/0363546504269723]
- 53 **Wirz P**, von Stokar P, Jakob RP. The effect of knee position on the reproducibility of measurements taken from stress films: a comparison of four measurement methods. *Knee Surg Sports Traumatol Arthrosc* 2000; **8**: 143-148 [PMID: 10883424 DOI: 10.1007/s001670050204]
- 54 **Kellgren JH**, Lawrence JS. Radiological assessment of osteoarthrosis. *Ann Rheum Dis* 1957; **16**: 494-502 [PMID: 13498604]
- 55 **Hermans S**, Corten K, Bellemans J. Long-term results of isolated anterolateral bundle reconstructions of the posterior cruciate ligament: a 6- to 12-year follow-up study. *Am J Sports Med* 2009; **37**: 1499-1507 [PMID: 19451096 DOI: 10.1177/0363546509333479]
- 56 **Cooper DE**, Stewart D. Posterior cruciate ligament reconstruction using single-bundle patella tendon graft with tibial inlay fixation: 2- to 10-year follow-up. *Am J Sports Med* 2004; **32**: 346-360 [PMID: 14977658]
- 57 **Bin SI**, Nam TS. Surgical outcome of 2-stage management of multiple knee ligament injuries after knee dislocation. *Arthroscopy* 2007; **23**: 1066-1072 [PMID: 17916471 DOI: 10.1016/j.arthro.2007.05.008]
- 58 **Engebretsen L**, Risberg MA, Robertson B, Ludvigsen TC, Johansen S. Outcome after knee dislocations: a 2-9 years follow-up of 85 consecutive patients. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 1013-1026 [PMID: 19609504 DOI: 10.1007/s00167-009-0869-y]
- 59 **Hirschmann MT**, Zimmermann N, Rycken T, Candrian C, Hudetz D, Lorez LG, Amsler F, Müller W, Friederich NF. Clinical and radiological outcomes after management of traumatic knee dislocation by open single stage complete reconstruction/repair. *BMC Musculoskelet Disord* 2010; **11**: 102 [PMID: 20507623 DOI: 10.1186/1471-2474-11-102]
- 60 **Plancher KD**, Siliski J. Long-term functional results and complications in patients with knee dislocations. *J Knee Surg* 2008; **21**: 261-268 [PMID: 18979926]
- 61 **Roman PD**, Hopson CN, Zenni EJ Jr. Traumatic dislocation of the knee: a report of 30 cases and literature review. *Orthop Rev* 1987; **16**: 917-924 [PMID: 3333596]
- 62 **Fanelli GC**, Edson CJ. Arthroscopically assisted combined anterior and posterior cruciate ligament reconstruction in the multiple ligament injured knee: 2- to 10-year follow-up. *Arthroscopy* 2002; **18**: 703-714 [PMID: 12209427]
- 63 **Levy BA**, Dajani KA, Whelan DB, Stannard JP, Fanelli GC, Stuart MJ, Boyd JL, MacDonald PA, Marx RG. Decision making in the multiligament-injured knee: an evidence-based systematic review. *Arthroscopy* 2009; **25**: 430-438 [PMID: 19341932 DOI: 10.1016/j.arthro.2009.01.008]

- 64 **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]
- 65 **Lessim S**, Migonney V, Thoreux P, Lutomski D, Changotade S. PolyNaSS bioactivation of LARS artificial ligament promotes human ligament fibroblast colonisation in vitro. *Biomed Mater Eng* 2013; **23**: 289-297 [PMID: 23798650 DOI: 10.3233/BME-130753]
- 66 **Zhao J**, Xiaoqiao H, He Y, Yang X, Liu C, Lu Z. Sandwich-style posterior cruciate ligament reconstruction. *Arthroscopy* 2008; **24**: 650-659 [PMID: 18514108 DOI: 10.1016/j.arthro.2008.01.005]

**P- Reviewer:** Ohishi T **S- Editor:** Cui LJ **L- Editor:** A  
**E- Editor:** Li D



## Retrospective Study

**Neglected traumatic hip dislocation: Influence of the increased intracapsular pressure**

Elsayed Ibraheem Elsayed Massoud

Elsayed Ibraheem Elsayed Massoud, Department of Orthopaedic, Sohag Teaching Hospital, General Organization for Teaching Hospitals and Institutes, Sohag 0026280, Egypt

ORCID number: Elsayed Ibraheem Elsayed Massoud (0000-0003-1993-0825).

**Author contributions:** Massoud EIE has made all of the following: (1) The conception and design of the study, acquisition of data, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the version to be submitted.

**Institutional review board statement:** This study was reviewed and approved by the Local Ethics Committee of the Sohag Teaching 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 or his relatives agreed to treatment by written consent.

**Conflict-of-interest statement:** Author declares no conflicts-of-interest related to 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: Elsayed Ibraheem Elsayed Massoud, MD, MSc, Professor, Department of Orthopaedic, Sohag Teaching Hospital, General Organization for Teaching Hospitals and Institutes, Nil street, Sohag 0026280, Egypt. [elsayedmassoud@hotmail.com](mailto:elsayedmassoud@hotmail.com)  
Telephone: +2-93-4790632

Received: December 24, 2017

Peer-review started: December 25, 2017

First decision: January 6, 2018

Revised: January 12, 2018

Accepted: February 4, 2018

Article in press: February 5, 2018

Published online: March 18, 2018

**Abstract****AIM**

To investigate that the increased intracapsular pressure, during the delay period, can interrupt the blood flow to the femoral head.

**METHODS**

An observational retrospective study included a group of 17 patients with traumatic hip dislocation, their ages at time of injury averaged 26 (range from 3 to 70) years. Outcomes were assessed clinically and radiographically at a period averaged 11.5 (range from 4 to 20) years.

**RESULTS**

Minor trauma caused dislocation in seven and severe trauma in ten patients. All dislocations were posterior, six isolated dislocation and 11 were associated with other injuries. The negligence period averaged 2.5 (ranged from 1 to 4) d. At the latest visit, the radiography revealed normal hip in 11 and avascular necrosis (AVN) in six patients. Clinically, eight patients were rated as excellent, three good, three fair and three poor.

**CONCLUSION**

We believe the factors that contribute to increased intracapsular pressure also increase the influence of delayed reduction toward the development of AVN.

**Key words:** Avascular necrosis; Intracapsular pressure; Traumatic hip dislocation; Delayed reduction

© The Author(s) 2018. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Factors influencing outcomes of traumatic hip dislocation include reduction time, the severity of trauma, patients' ages and direction of dislocation. Although these factors have been thoroughly investigated, any of them was not assigned as the causative for the development of the avascular necrosis (AVN). Does the increased intracapsular pressure is the foremost factor? We believe that the factors as hemarthrosis, the position of the limb during the pre-reduction period particularly in posterior dislocation and traction in post-reduction period can increase the intracapsular pressure to a level sufficient for occlusion of intracapsular blood vessels. Delayed reduction accentuates influence of increased intracapsular pressure in favour of the development of AVN.

Massoud EIE. Neglected traumatic hip dislocation: Influence of the increased intracapsular pressure. *World J Orthop* 2018; 9(3): 35-40 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i3/35.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i3.35>

## INTRODUCTION

As the hip is an inherently stable joint, a substantial force is required for its dislocation. Therefore, associated injuries must be sought<sup>[1,2]</sup>. However, some biological factors can predispose to dislocation even with minor trauma, for instance, increased the head-shaft angle and diminished or increased femoral torsion<sup>[3-5]</sup>. In children, hip dislocates mostly after relatively trivial accidents such as slipping or tripping<sup>[2,6]</sup>. Consequently, the associated injuries are uncommon. The prominence of the associated injury or insignificance of the causative trauma leads to the negligence of hip dislocation<sup>[6,7]</sup>.

There is almost a consensus regarding the prompt reduction of the dislocated hip in order to minimize the incidence of avascular necrosis (AVN)<sup>[6-9]</sup>. However, an experimental study reported that the reduction time did not consider a critical factor in the appearance of AVN<sup>[10]</sup>.

Effusion of the hip joint was detected with traumatic dislocation at about 35 d post injury<sup>[11]</sup>. The effusion increases the intracapsular pressure to a level sufficient for tamponade of the retinacular blood vessels<sup>[2,11,12]</sup>. Likewise, placement of the injured limb in the particular positions during the pre and/or post-reduction periods can tighten the capsule, which increases the intracapsular pressure<sup>[13-15]</sup>. These reasons explain why some authors noted AVN despite early reduction<sup>[6,9]</sup>.

Over a period of twenty-year, we observed a group of patients with missed traumatic hip dislocations. Although all hips were reduced late and received the same post reduction management, however, only about 35% developed AVN. Therefore, we hypothesized that the delayed reduction is not only the direct factor that

contributes to the development of AVN. However, the factors that increase intracapsular pressure may play an important role in the development of AVN.

In order to investigate our hypothesis, we present this study using the patients' records as a source of the outcomes.

## MATERIALS AND METHODS

Between February 1993 and March 2013, we have observed and followed a group of 17 patients with a neglected traumatic hip dislocation. Local Ethics Committee approved this retrospective study. Patients were not required to give informed consent to the study because the analysis used anonymous clinical data. The included patients are seven females and ten males their ages at time of injury averaged 26 (range from 3 to 70) years. Baseline details are listed in Table 1. The causative trauma was graded into minor trauma as running, tripping or falling and severe trauma as high-energy impact, crushing, excessive speed (cycling) or excessive force (football)<sup>[7]</sup>. Dislocation was classified according to the direction into anterior, posterior and central. Then the posterior dislocation was classified according to the Thompson-Epstein classification system<sup>[16]</sup>. Additionally, dislocation was classified as an isolated or associated with other injuries, which were then classified into polytrauma, or injuries related to the dislocated side as sciatic nerve injury, femoral fractures or knee injuries. Negligence period was estimated from time of the trauma to the time of the certain reduction.

All dislocations were reduced closed and received the same post reduction management, which consists of aspiration of the hip joint, skin or skeletal traction for three weeks followed by another three weeks of non-weight bearing. In case of the dislocations associated with fractures, full weight bearing was allowed when the fractures healed.

Follow-up reviews were undertaken at every other week for 6 wk, and then at three, six and twelve months. After first year, patients were re-evaluated twice per year for 3 years, and then they invited once per year. The follow-up period averaged 11.5 (range from 4 to 20) years.

### Outcome measures

**Radiological assessment:** In order to assess the stability of reduction, plain radiography was repeated every other week for 6 wk. Development of AVN was assessed every 6 mo for 3 years and then once per year. AVN was defined as the appearance of subchondral sclerosis or the presence of segmental collapse. Associated fractures were considered during the follow-up visits.

**Clinical assessment:** Clinical outcome was evaluated according to Matta clinical evaluation system<sup>[17]</sup> that evaluates with points the pain, walking and range of hip

**Table 1** Baseline data and outcome for a group of patients, they were treated late for traumatic hip dislocation

No.	Baseline data						Outcomes			
	Age	Sex	NP in days	Trauma	Dislocation type	Associated injury	Follow-up period, yr	Clinical		Radiologic
								Score	Rating	
1	3	M	4	Minor	T-E type 1	Isolated	20	18 point	Excellent	Normal
2	33	M	3	Severe	T-E type 1	Polytrauma	18	14 point	Fair	AVN
3	5	F	3	Minor	T-E type 1	Isolated	18	18 point	Excellent	Normal
4	27	M	2	Severe	T-E type 1	Polytrauma	16	12 point	Poor	AVN
5	55	M	1	Severe	T-E type 4	Polytrauma	15	14 point	Fair	AVN
6	26	M	1	Severe	T-E type 2	Acetabular fracture	15	16 point	Good	Normal
7	19	M	2	Severe	T-E type 3	Acetabular fracture	13	14 point	Fair	AVN
8	6	F	2	Minor	T-E type 1	Isolated	12	18 point	Excellent	Normal
9	4	M	3	Minor	T-E type 1	Sciatic	12	18 point	Excellent	Normal
10	70	F	3	Minor	T-E type 1	Isolated	9	18 point	Excellent	Normal
11	36	F	4	Severe	T-E type 4	Polytrauma	8	12 point	Poor	AVN
12	4	F	3	Minor	T-E type 1	Isolated	8	18 point	Excellent	Normal
13	36	M	2	Severe	T-E type 2	Acetabular fracture	8	17 point	Good	Normal
14	24	F	2	Severe	T-E type 2	Acetabular fracture	7	16 point	Good	Normal
15	6	F	2	Severe	T-E type 1	Femoral fracture	7	18 point	Excellent	Normal
16	29	M	4	Severe	T-E type 1	Polytrauma	6	12 point	Poor	AVN
17	57	M	1	Minor	T-E type 1	Isolated	4	18 point	Excellent	Normal

NP: Negligence period; M: Male; F: Female; T-E: Thompson-Epstein; AVN: Avascular necrosis.

motion. The clinical scores were classified as excellent = 18 points, good = 15-17 points, fair = 13-14 points and poor  $\leq$  13 points<sup>[17]</sup>.

## RESULTS

The causative trauma was classified as minor in seven cases and severe trauma in ten cases. The direction of the hip dislocations was posterior in all cases. According to the Thompson-Epstein classification system<sup>[16]</sup>, 11 cases were classified as a type 1, three cases type 2, one case type 3, and two cases type 4. Six cases were classified as isolated dislocation and 11 cases were associated with other injuries (Table 1). The negligence period averaged 2.5 (ranged from 1 to 4) d.

Post-reduction aspiration of the hip joints revealed hemarthrosis in six, synovial fluid in four, and negative aspiration in seven hip joints.

### Radiographic outcome

The normal appearance of the femoral head compared to the contralateral side was observed in 11 patients and AVN signs were observed in six patients.

### Clinical outcome

According to Matta<sup>[17]</sup> eight patients were rated as excellent, three good, three fair and three poor (Table 1). The overall rating was good and the overall score averaged 16 (ranged from 12 to 18) points. No general complication was reported, the associated fractures healed in the accepted position and the injured sciatic nerve cured.

We have noticed a relationship between the patients' ages and severity of the trauma on one hand and the outcomes on the other hand. Five patients with an average age of 4.4 years (range from 3-6 years) had hip dislocation due to minor trauma achieved excellent

outcomes as well signs of AVN were not detected during the follow-up period. Similarly, a female patient 6-years old, although had dislocation due to severe trauma, however, has an excellent result with no AVN. Conversely, the patients who developed AVN their ages averaged 33 years (range: 19 to 55 years), had exposed to severe trauma and the post-reduction aspiration of the hip joints revealed hemarthrosis.

## DISCUSSION

Factors influencing outcomes of traumatic hip dislocation include reduction time, severity of trauma, patients' ages and direction of dislocation. Although these factors have been thoroughly investigated, any of them was not assigned as the causative for the development of the AVN. Does the increased intracapsular pressure is the foremost factor?

Diagnosis of traumatic hip dislocation is easy, many authors and we likewise have noticed missed cases. Prominence of the associated injuries or insignificance of the trauma really leads to delay of the diagnosis<sup>[6,7]</sup>. Although delayed reduction has been regularly linked to incidence of AVN, definition of negligence period is not clear in the literature<sup>[1,9]</sup>. Experimentally, AVN was produced in the capital femoral epiphysis of immature dogs after increasing the intracapsular pressure for six hours and in the adult dogs for 12 h<sup>[18,19]</sup>. Consequently, dislocation is considered neglected when the reduction was not achieved before 12 h of injury. In the present study, all cases were reduced at an average 2.5 d, only 35% of the cases developed AVN (Table 1). Sapkas *et al*<sup>[10]</sup> have considered the reduction time is not a critical factor in the appearance of AVN.

Minor trauma can dislocate the hip in children (Figure 1), likewise at any age in the presence of the biological predisposing factors<sup>[2-5]</sup>. Thus, it is not mostly



**Figure 1** Plain radiographs of the pelvis both hip joints for a 4-year-old boy; the right hip joint was dislocated after minor trauma. A: Notice the neck-shaft angle; B: A radiograph was taken one week after closed reduction shows the stable reduction; C: A radiograph was taken after three years of reduction shows no signs of avascular necrosis.



**Figure 2** Plain radiographs of the pelvis both hip joints for a 27-year-old male, was admitted to hospital as a polytraumatized patient, the right hip dislocation was reduced two days after injury. A: The right hip dislocated posteriorly; B: Stable reduction by the second month; C: A radiograph was taken 16 years after reduction shows avascular necrosis of the femoral head and degenerative changes of the right hip joint.

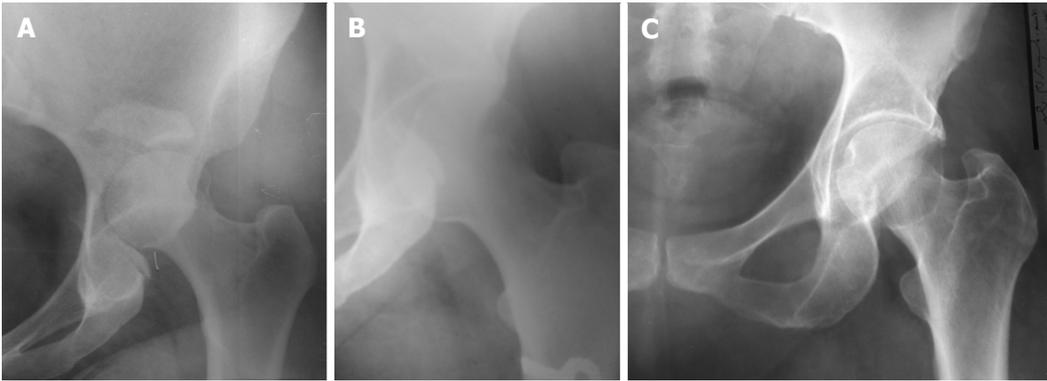
associated with other injuries<sup>[6-8]</sup>. However, severe trauma at least associated with a hemarthrosis. Laorr *et al*<sup>[11]</sup>, investigated 18 patients with traumatic hip dislocation and found hemarthrosis in all cases. This explains why many authors have linked severity of trauma to the incidence of AVN<sup>[7,10,20]</sup>. In the present study, we detected hemarthrosis in six, synovial fluid in four, and negative aspiration in seven hip joints. Additionally, the hips that were dislocated due to minor trauma have normal femoral heads, while most of those had dislocations due to severe trauma developed AVN during the follow-up period (Figures 1 and 2). However, the dislocations that associated with acetabular (Figure 3) or femoral shaft fractures have not developed AVN (cases No. 6, 13, 14 and 15 in Table 1). The associated femoral fractures, likely resulted from a substantial force sufficient for laceration of the hip capsule additionally<sup>[1]</sup>. Any of acetabular fracture or capsular laceration allowed for leakage of the hemarthrosis, and therefore, the intracapsular pressure has not increased.

The patient's age can predict the outcomes through the severity of trauma on the one hand and the age-related changes of the femoral head circulation on the other hand. At age under 5 years, the acetabulum is primarily soft pliable cartilage as well as there is a generalized ligamentous laxity, therefore the minor trauma can dislocate the hip joint<sup>[2,6]</sup>. Additionally, it

has been reported that the variations in the age-related sequelae of the traumatic hip dislocation have been in part attributed to the age-related changes in the hip circulation<sup>[2,8,12,21]</sup>.

At the fourth year of age, the femoral head is supplied through a retinacular arterial system, which consists of multiple arteries. With age, the multiple small vessels of the young coalesce to a limited number of larger vessels. Thus, damage to a single blood vessel can have serious consequences<sup>[2]</sup>. Most authors suggest that the posterosuperior branch of the medial circumflex artery is the most likely site of vascular damage<sup>[10,21,22]</sup>. Nevertheless, such vessels have a more ability to accommodate the extreme posterior displacement of the femoral head<sup>[23]</sup>. This explains why many authors have reported the continuation of femoral head circulation after reduction of pure hip dislocation<sup>[8,22]</sup>.

Direction of hip dislocation plays an important role in the development of AVN<sup>[8]</sup>. Generally, pure anterior dislocations have a better long-term prognosis than posterior dislocations<sup>[1,20]</sup>. In anterior dislocations, the capsule is disrupted anteriorly and inferiorly while in posterior dislocations the capsular tear either inferoposterior or directly posterior, depending on the amount of flexion present<sup>[1]</sup>. As the posterosuperior vessels is the most likely site of vascular damage<sup>[10,21,22]</sup>, the posteriorly dislocated femoral head compress



**Figure 3** Plain radiographs of right hip joint for a 42-year-old female, was diagnosed two days after a motor car accident. A: A posterior dislocation of the right hip with acetabular fractures; B: A radiograph was taken two weeks after closed reduction shows stable reduction; C: A radiograph was taken seven years after reduction shows no signs of avascular necrosis in the head of right femur.

these vessels against the posterior acetabular rim and interrupt the femoral head circulation<sup>[22]</sup>. Position of the limb prior to reduction also plays a role in the development of AVN<sup>[13]</sup>. In posterior dislocations, the leg is flexed, adducted, and internally rotated while in anterior dislocations, the leg is externally rotated with varying amounts of flexion and abduction<sup>[1]</sup>. So, the deformity in anterior dislocation increases capacity of the hip capsule to accommodate pressure more than that in posterior dislocation<sup>[13-15]</sup>. Moreover, recognizable limb deformity in anterior dislocation renders negligence is less likely.

Hip joint is enclosed by a thick fibrous capsule<sup>[2]</sup>. Therefore, the trauma that has sufficient severity to dislocate the inherently stable joint, constantly results in hemarthrosis, which increases the intracapsular pressure to a level sufficient to tamponade of the retinacular blood vessels<sup>[2,11,12]</sup>. This was proved experimentally in two separate studies, as they produced AVN when the intracapsular pressure of the hip was increased for six or twelve hours<sup>[18,19]</sup>. Likewise, the tight repair of the hip capsule after surgical dislocation led to a drop in the perfusion of the femoral head<sup>[20,22]</sup>. Given that, the development of AVN must depend essentially upon the steadiness of interruption of blood flow<sup>[21]</sup>. Hence, the hemarthrosis that was detected at an average 13.2 d after injury will offer the circumstance sufficient for the development of avascular AVN even after prompt reduction<sup>[11,12]</sup>.

Post reduction management plays a role in the development of AVN. Most surgeons recommend a period of traction until the patient's initial pain has subsided. However, this position increases the intracapsular pressure<sup>[13-15,20,21]</sup>. Therefore, the best recommendations for post-reduction treatment are avoidance of strict immobilization and allow full weight bearing once the patient can control his leg in space<sup>[1,11-13]</sup>. Aspiration of the hip, if it has hemarthrosis, should be repeated during the first day and in the next days as long as the joint effusion persists.

The present study has many limitations: In part, the included data were retrospectively collected from a

heterogeneous group of patients and in another part, lacked the use of the diagnostic tools as measuring of intracapsular pressure and MRI. However, heterogeneity provided an opportunity for studying of different age groups and different types of trauma, albeit in a small number of patients. Availability of patients for a considerable period of follow-up offered the data that warranted the building of the logical opinion.

We believe that the factors as hemarthrosis, the position of the limb during the pre-reduction period particularly in posterior dislocation and traction in post-reduction period can increase the intracapsular pressure to a level sufficient for occlusion of intracapsular blood vessels. Delayed reduction accentuates influence of increased intracapsular pressure in favour of the development of AVN.

## ARTICLE HIGHLIGHTS

### Research background

In February 1993, a 3-years old boy present with the secondary inability to walk after fall during running since four days. Hip dislocation was detected and reduced immediately. In June 1995, a male 33-years-old had present with multiple traumas due to a motor car accident and a hip dislocation that was missed for three days. By the sixth-month post reduction, the second patient developed avascular necrosis (AVN). In the same week, I called the first patient for follow-up and radiological examination that revealed normal hips. At this moment I wondered, why the second patient developed AVN despite the delayed reduction was the common denominator? In subsequent years I started a study titled "Fixation of intracapsular femoral neck fractures: Effect of trans-osseous capsular decompression" (published). Therefore, the importance of the intracapsular pressure has resurfaced. Again I wondered, what the relationship between the age and the severity of the trauma regarding the hip dislocation? As well, what the influence of hemarthrosis on the development of AVN?

### Research motivation

This study was conducted for answering of the inquiries that can be summarized in, "when we expect the development of the AVN after hip dislocation and how to avoid the predisposing factors".

### Research objectives

The objective of this study was the detection of the factor(s) that can accentuate hazardous of delayed reduction. We assumed increased intracapsular pressure is the concerned factor. Realizing this hypothesis will open the way for avoidance the complications resulted from hip joint effusion either due to

trauma or disease.

### Research methods

This is an observational retrospective study depend on the analysis of patients records and reviewing of the literature in realizing of its objectives.

### Research results

We have noticed a relationship between the patients' ages and severity of the trauma regarding the incidence of the hip dislocation, as well the severity of trauma and development of AVN.

### Research conclusions

Increased intracapsular pressure can be a result of the combined effect of hip dislocation and traction of the limb in the post-reduction period. Complications of hip diseases that associated with hip effusion as infections or Perthes disease can be diminished through reduction of intracapsular pressure. The prompt reduction is not enough to avoid the development of the AVN. The interferences as traction of the limb for immobilization can increase the intracapsular pressure of hip joint. Influence of the intracapsular pressure varies according to the patient's age. I suggest a prospective study using the advanced instruments for prediction of the development of AVN. The associated acetabular fractures allowed leakage of the hemarthrosis as well fracture of femoral shaft possibly lacerated the hip capsule and in both cases, we could not detect fluid through aspiration. The recommendations for post-reduction treatment are the aspiration of the hemarthrosis, avoidance of strict immobilization and allow full weight bearing once the patient can control his leg in space.

### Research perspectives

Despite the heterogeneity of the patients, however, it provided an opportunity for studying of different age groups and different types of trauma, albeit in a small number of patients. The future research should be directed toward the reduction of the complications of the diseases that associated with increased of the intracapsular pressure. The best method for the future research is a prospective randomized controlled study.

## REFERENCES

- 1 **Tornetta P 3rd**, Mostafavi HR. Hip Dislocation: Current Treatment Regimens. *J Am Acad Orthop Surg* 1997; **5**: 27-36 [PMID: 10797205 DOI: 10.5435/00124635-199701000-00004]
- 2 **Blasier RD**, Hughes LO. Fractures and traumatic dislocations of the hip in children. In: Beaty JH, Kasser JR, eds. *Fractures in Children*, 5th ed. Philadelphia, PA: Lippincott Williams and Wilkins, 2001; **21**: 913-940
- 3 **Hermanson M**, Häggglund G, Riad J, Wagner P. Head-shaft angle is a risk factor for hip displacement in children with cerebral palsy. *Acta Orthop* 2015; **86**: 229-232 [PMID: 25428756 DOI: 10.3109/17453674.2014.991628]
- 4 **Upadhyay SS**, Moulton A, Burwell RG. Biological factors predisposing to traumatic posterior dislocation of the hip. A selection process in the mechanism of injury. *J Bone Joint Surg Br* 1985; **67**: 232-236 [PMID: 3884614 DOI: 10.1007/s00264-005-0056-9]
- 5 **Mirovsky Y**, Fischer S, Hendel D, Halperin N. Traumatic anterior dislocation of the hip joint with fracture of the acetabulum: a case report. *J Trauma* 1988; **28**: 1597-1599 [PMID: 3184226 DOI: 10.1007/s11751-008-0033-0]
- 6 **Zrig M**, Mnif H, Koubaa M, Abid A. Traumatic hip dislocation in children. *Acta Orthop Belg* 2009; **75**: 328-333 [PMID: 19681318]
- 7 **Officerski CM**. Traumatic dislocation of the hip in children. *J Bone Joint Surg Br* 1981; **63-B**: 194-197 [PMID: 7217141]

- 8 **Durakbaşa O**, Okan N, Canbora K, Görgeç M. [Factors affecting the results of treatment in traumatic dislocation of the hip]. *Acta Orthop Traumatol Turc* 2005; **39**: 133-141 [PMID: 15925936]
- 9 **Hougaard K**, Thomsen PB. Traumatic posterior dislocation of the hip--prognostic factors influencing the incidence of avascular necrosis of the femoral head. *Arch Orthop Trauma Surg* 1986; **106**: 32-35 [PMID: 3566493 DOI: 10.1007/BF00435649]
- 10 **Sapkas G**, Pantazopoulos T, Karanikas E, Hartofilakidis-Garofalidis G. Effect of hip dislocation on the blood supply to the femoral head. An experimental study in rabbits. *Acta Orthop Scand* 1983; **54**: 204-209 [PMID: 6845995 DOI: 10.3109/17453678308996557]
- 11 **Laorr A**, Greenspan A, Anderson MW, Moehring HD, McKinley T. Traumatic hip dislocation: early MRI findings. *Skeletal Radiol* 1995; **24**: 239-245 [PMID: 7644933 DOI: 10.1007/BF00198406]
- 12 **Rieger H**, Pennig D, Klein W, Grünert J. Traumatic dislocation of the hip in young children. *Arch Orthop Trauma Surg* 1991; **110**: 114-117 [PMID: 2015133 DOI: 10.1007/BF00393886]
- 13 **Massoud EIE**. Fixation of intracapsular femoral neck fractures: Effect of trans-osseous capsular decompression. *Dicle Med J* 2010; **37**: 89-96 [DOI 10.5798/diclemedj.09.09.2010.02]
- 14 **Soto-Hall R**, Johnson LH, Johnson RA. Variations in the intra-articular pressure of the hip joint in injury and disease, a probable factor in avascular necrosis. *J Bone Joint Surg Am* 1964; **46**: 509-516 [PMID: 14131429 DOI: 10.2106/00004623-196446030-00004]
- 15 **Strömqvist B**, Nilsson LT, Egund N, Thorngren KG, Wingstrand H. Intracapsular pressures in undisplaced fractures of the femoral neck. *J Bone Joint Surg Br* 1988; **70**: 192-194 [PMID: 3346286]
- 16 **Thompson VP**, Epstein HC. Traumatic dislocation of the hip; a survey of two hundred and four cases covering a period of twenty-one years. *J Bone Joint Surg Am* 1951; **33-A**: 746-778; passim [PMID: 14850515]
- 17 **Matta JM**. Fractures of the acetabulum: accuracy of reduction and clinical results in patients managed operatively within three weeks after the injury. *J Bone Joint Surg Am* 1996; **78**: 1632-1645 [PMID: 8934477 DOI: 10.1055/s-0030-1267077]
- 18 **Henard DC**, Calandruccio RA. Experimental production of roentgenographic and histological changes in the capital femoral epiphysis following abduction, extension, and internal rotation of the hip. *Surg Forum* 1971; **22**: 442-444 [PMID: 5121432]
- 19 **Woodhouse CF**. Dynamic influences of vascular occlusion affecting the development of avascular necrosis of the femoral head. *Clin Orthop Relat Res* 1964; **32**: 119-129 [PMID: 5889049]
- 20 **Ganz R**, Gill TJ, Gautier E, Ganz K, Krügel N, Berlemann U. Surgical dislocation of the adult hip a technique with full access to the femoral head and acetabulum without the risk of avascular necrosis. *J Bone Joint Surg Br* 2001; **83**: 1119-1124 [PMID: 11764423 DOI: 10.1302/0301-620X.83B8.11964]
- 21 **Tucker FR**. Arterial supply to the femoral head and its clinical importance. *J Bone Joint Surg Br* 1949; **31B**: 82-93 [PMID: 18124373]
- 22 **Nötzli HP**, Siebenrock KA, Hempling A, Ramseier LE, Ganz R. Perfusion of the femoral head during surgical dislocation of the hip. Monitoring by laser Doppler flowmetry. *J Bone Joint Surg Br* 2002; **84**: 300-304 [PMID: 11922376 DOI: 10.1302/0301-620X.84B2.12146]
- 23 **Grose AW**, Gardner MJ, Sussmann PS, Helfet DL, Lorich DG. The surgical anatomy of the blood supply to the femoral head: description of the anastomosis between the medial femoral circumflex and inferior gluteal arteries at the hip. *J Bone Joint Surg Br* 2008; **90**: 1298-1303 [PMID: 18827238 DOI: 10.1302/0301-620X.90B10.20983]

P- Reviewer: Mavrogenis AF S- Editor: Cui LJ L- Editor: A  
E- Editor: Li D



## Clinical Practice Study

**Establishing minimum clinically important difference values for the Patient-Reported Outcomes Measurement Information System Physical Function, hip disability and osteoarthritis outcome score for joint reconstruction, and knee injury and osteoarthritis outcome score for joint reconstruction in orthopaedics**

Man Hung, Jerry Bounsanga, Maren W Voss, Charles L Saltzman

Man Hung, Jerry Bounsanga, Maren W Voss, Charles L Saltzman, Department of Orthopaedic Surgery Operations, University of Utah, Salt Lake City, UT 84108, United States

Man Hung, Division of Public Health, University of Utah, Salt Lake City, UT 84108, United States

Man Hung, Population Health Research Foundation, University of Utah, Salt Lake City, UT 84112, United States

ORCID number: Man Hung (0000-0003-2827-3740); Jerry Bounsanga (000-0001-6852-4650); Maren W Voss (0000-0002-9054-7389); Charles L Saltzman (0000-0003-2877-2339).

**Author contributions:** Hung M was instrumental in study design, data collection, data processing, data analysis, interpretation, study oversight, literature review, manuscript writing and editing; Bounsanga J was instrumental in data processing, data analysis, manuscript writing and editing; Voss MW was instrumental in literature review, data analysis, manuscript writing and editing; Saltzman CL was instrumental in study design, data collection, interpretation and manuscript editing.

**Supported by** National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health, No. U01AR067138. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

**Institutional review board statement:** Institutional review board approval/waiver was obtained through the University of Utah, IRB #00053404.

**Informed consent statement:** Study participants completed

PRO measures as part of the standard of care in treatment.

**Conflict-of-interest statement:** The authors have no conflicts of interest to disclose.

**Data sharing statement:** The dataset analyzed during the current study is not publicly available due to HIPAA regulations but may be available from the University of Utah if the requestor has obtained proper IRB approval from the University of Utah and its Enterprise Data Warehouse.

**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:** Man Hung, PhD, Associate Professor, Department of Orthopaedic Surgery Operations, University of Utah, 590 Wakara Way, Salt Lake City, UT 84108, United States. [man.hung@hsc.utah.edu](mailto:man.hung@hsc.utah.edu)  
Telephone: +1-801-5875372  
Fax: +1-801-5875411

**Received:** January 4, 2018

**Peer-review started:** January 4, 2018

**First decision:** January 23, 2018

**Revised:** January 30, 2018

**Accepted:** February 6, 2018

**Article in press:** February 6, 2018

## Abstract

### AIM

To establish minimum clinically important difference (MCID) for measurements in an orthopaedic patient population with joint disorders.

### METHODS

Adult patients aged 18 years and older seeking care for joint conditions at an orthopaedic clinic took the Patient-Reported Outcomes Measurement Information System Physical Function (PROMIS<sup>®</sup> PF) computerized adaptive test (CAT), hip disability and osteoarthritis outcome score for joint reconstruction (HOOS JR), and the knee injury and osteoarthritis outcome score for joint reconstruction (KOOS JR) from February 2014 to April 2017. MCIDs were calculated using anchor-based and distribution-based methods. Patient reports of meaningful change in function since their first clinic encounter were used as an anchor.

### RESULTS

There were 2226 patients who participated with a mean age of 61.16 (SD = 12.84) years, 41.6% male, and 89.7% Caucasian. Mean change ranged from 7.29 to 8.41 for the PROMIS<sup>®</sup> PF CAT, from 14.81 to 19.68 for the HOOS JR, and from 14.51 to 18.85 for the KOOS JR. ROC cut-offs ranged from 1.97-8.18 for the PF CAT, 6.33-43.36 for the HOOS JR, and 2.21-8.16 for the KOOS JR. Distribution-based methods estimated MCID values ranging from 2.45 to 21.55 for the PROMIS<sup>®</sup> PF CAT; from 3.90 to 43.61 for the HOOS JR, and from 3.98 to 40.67 for the KOOS JR. The median MCID value in the range was similar to the mean change score for each measure and was 7.9 for the PF CAT, 18.0 for the HOOS JR, and 15.1 for the KOOS JR.

### CONCLUSION

This is the first comprehensive study providing a wide range of MCIDs for the PROMIS<sup>®</sup> PF, HOOS JR, and KOOS JR in orthopaedic patients with joint ailments.

**Key words:** Hhip disability and osteoarthritis outcome score for joint reconstruction; Patient-Reported Outcomes Measurement Information System Physical Function; Knee injury and osteoarthritis outcome score for joint reconstruction; Minimum clinically important difference; Joint; Physical function; Minimum detectable change; Arthroplasty; Orthopaedics; Clinical outcomes

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Personal value judgments should be used to apply these minimum clinically important difference (MCID) values to treatment planning and in guiding patient expectations of change. We recommend applying low values of MCIDs for screening purposes

and median values as a more conservative cut-off for evaluating longitudinal change.

Hung M, Bounsanga J, Voss MW, Saltzman CL. Establishing minimum clinically important difference values for the Patient-Reported Outcomes Measurement Information System Physical Function, hip disability and osteoarthritis outcome score for joint reconstruction, and knee injury and osteoarthritis outcome score for joint reconstruction in orthopaedics. *World J Orthop* 2018; 9(3): 41-49 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i3/41.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i3.41>

## INTRODUCTION

The National Institutes of Health sponsored an initiative to develop a Patient-Reported Outcomes Measurement Information System (PROMIS<sup>®</sup>)<sup>[1]</sup> using item response theory (IRT) methods. These methods have been recommended for use in the evaluation of arthroplasty outcomes because of their unique measurement properties<sup>[2]</sup>. Computerized adaptive testing (CAT) using IRT minimizes respondent burden without sacrificing instrument precision<sup>[3,4]</sup>. The PROMIS<sup>®</sup> Physical Function (PF) CAT assesses physical function in five domains but is not directly targeted at joint function. Yet the useful measurement and administration qualities of the PROMIS<sup>®</sup> PF CAT make it a valuable addition to patient-reported outcomes (PRO) assessments in joint reconstruction<sup>[5,6]</sup>. Aside from minimizing burden, top quality PRO instruments also offer reliable and valid scores that are easy to interpret<sup>[7]</sup>.

Recent attention in PRO development has focused in on the interpretability of scores, particularly in terms of how meaningful the outcomes are to patients<sup>[8]</sup>. Change in function is an important clinical outcome, thus PROs should be able to detect change in patient function. In interpreting change, the minimum clinically important difference (MCID) reflects the smallest amount of meaningful change<sup>[9]</sup>. "MCIDs are patient derived scores that reflect changes in a clinical intervention that are meaningful for the patient"<sup>[10]</sup>. Meaningful change is important, as it can serve as a benchmark of treatment effect, and it is critical in decision making. Whether or not a treatment produces a statistically significant outcome is less informative than whether it produces meaningful change, as an inflated sample size can yield statistical significance without clinical relevance<sup>[11,12]</sup>.

Multiple methods have been developed for determining MCID values and there is little agreement on the best standard to apply<sup>[10]</sup>. Distribution-based approaches rely on statistical methods and probability sampling. They describe how much change falls beyond random levels of variation. They rely on distributions of scores and how much the scores vary between patients in reaching a magnitude of change that is beyond chance fluctuation<sup>[13]</sup>. But distribution methods cannot

tell us whether the amount of change is meaningful from the clinician's or the patient's perspective<sup>[8]</sup>. An alternative approach is to use anchor-based methods which relates the change in patient scores to some other measure of health outcomes<sup>[13]</sup>.

Determining the MCID of the PROMIS<sup>®</sup> PF is an important step to understand the meaning of the scores. Collecting the longitudinal data necessary to analyze meaningful change takes time. Because the PROMIS<sup>®</sup> development began quite recently in 2004<sup>[1]</sup>, there have been very few studies estimating MCIDs for PROMIS<sup>®</sup> measures and little is known about MCID values in the orthopaedic adult reconstruction population<sup>[14]</sup>. Initial MCID development for PROMIS<sup>®</sup> instruments has begun in specific patient populations such as pediatrics<sup>[15]</sup> or cancer patients<sup>[16]</sup> but studies are lacking in orthopaedic patients.

Other PROs have been developed that are specific to the domain of joint function and it is helpful to consider the measurement properties of these newer instruments side by side. The knee injury and osteoarthritis outcome score for joint reconstruction (KOOS JR) and the hip disability and osteoarthritis outcome score for joint reconstruction (HOOS JR) are two joint specific instruments recently introduced in the arthroplasty arena<sup>[17-20]</sup>. Both instruments have been approved by the Centers for Medicaid and Medicare Services for use in joint replacement registries<sup>[21-24]</sup>. The HOOS and KOOS were selected given their use in joint replacement registries in the United States, though other valid measures such as the Oxford hip or knee score are more common in European registries and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) has a longer-term use for more general assessments of osteoarthritis<sup>[21]</sup>. Prior research has demonstrated that the HOOS and KOOS measures are sensitive to change<sup>[25]</sup>; however, we are unaware of any studies that develop MCIDs for these instruments<sup>[26]</sup>. The purpose of this study was to determine the MCIDs of the PROMIS<sup>®</sup> PF CAT, the HOOS JR, and the KOOS JR in an orthopaedic population with lower-extremity joint conditions.

## MATERIALS AND METHODS

### *Patient sample*

After receiving approval from the University of Utah Institutional Review Board, we analyzed data from an adult reconstruction population at a single academic medical center. All patients, aged 18 and older with pathology of the hip and knee were eligible for inclusion. As part of the standard of care, patients were provided with internet enabled hand-held tablets to answer demographic and PRO instruments which are linked to the electronic health record system *via* mEval. Questionnaires were either completed at clinic check-in or within 7-d prior to their visit *via* email. Follow-up data were obtained in the same manner at future clinic visits. No informed consent was obtained as all PRO

measurement was conducted as a part of customary standard of care. For this study, these visits were organized into four follow-up periods based upon the first recorded score within the database (baseline initial assessment): (1) 3-mo follow-up (80 to 100 d after initial assessment); (2) > 3-mo follow-up (90 d or more after initial assessment); 6-mo follow-up (170 to 190 d after initial assessment); and (3) > 6-mo follow-up (180 d or more after initial assessment). These follow-up periods were selected based upon recommendations within the literature<sup>[27-37]</sup>. It should be noted that the baseline score may not necessarily correlate with a specific intervention. Nonetheless, this method still allows for the monitoring of change over time.

A major goal of MCID determination is to allow for meaningful interpretation of scores for clinical decision-making, in addition to sample size calculation for investigating treatment effectiveness. As there is essentially no evidence that MCID values are dependent on the severity of disease conditions, length of follow-ups, or specific patient groups<sup>[38-40]</sup>, it is appropriate for this study to establish MCIDs among orthopaedic patients with a full range of joint impairments and varying follow-up time points. The present evaluation of MCID values was conducted in a general joint clinic population, among surgical and non-surgical patient samples regardless of specific treatment or intervention. Since MCID development were not meant to be treatment specific<sup>[40]</sup>, MCID values derived from this study can be applied to adult reconstruction patients with all types of surgical and non-surgical interventions.

### *Patient-reported outcomes*

The PROMIS<sup>®</sup> PF CAT, v1.2, draws from a 121-item test bank that contains both upper extremity and lower extremity functional items. The PROMIS<sup>®</sup> PF CAT algorithms were established by PROMIS<sup>®</sup> developers<sup>[41]</sup>, and the instrument was scored using T-scores, a standardized metric that has a mean of 50 and a standard deviation of 10<sup>[5]</sup>. Higher scores on the PROMIS<sup>®</sup> PF CAT indicate higher physical function.

**HOOS JR:** The HOOS JR is a 6-item measure assessing function and pain<sup>[22]</sup> with psychometric properties similar to the full HOOS<sup>[42]</sup>. The HOOS JR was scored on a 0 - 100 scale with larger numbers indicating higher hip function.

**KOOS JR:** The KOOS JR is a 7-item measure assessing function and pain<sup>[24]</sup>. The KOOS JR is scored on a 0-100 scale with larger numbers indicating higher levels of knee function.

### *Statistical analysis*

Descriptive statistics regarding patient characteristics and demographics were calculated. Mean change scores for the patients were evaluated for each time-period. Change scores were calculated as the follow-up score minus the baseline score on each measure, and

**Table 1** Demographics of patients (*n* = 2226)

Patient characteristics	<i>n</i>	Percent	Mean (SD)	Range
Age (yr)			61.16 (12.84)	18-93
Gender				
Male	927	41.6		
Female	1299	58.4		
Race				
White or Caucasian	1997	89.7		
Black or African American	1.2			
Asian	20	0.9		
American Indian and Alaska Native	32	1.4		
Native Hawaiian or Pacific Islander	11	0.5		
Other	113	5.1		
Unknown/missing	26	1.2		
Ethnicity				
Hispanic	114	5.1		
Non-Hispanic	2075	93.2		
Missing	37	1.7		

recorded as the absolute value difference between the scores. They were calculated for each of the follow-up periods described above including 3-mo, > 3 mo, 6-mo, and > 6 mo time-points.

The anchor-based methods applied patients' perspective to the question: "Compared to your FIRST EVALUATION at the University Orthopaedic Center: how would you describe your physical function now?" (much worse, worse, slightly worse, no change, slightly improved, improved, much improved) as a determinant of meaningful change. No change equates to a 0 value; the negative ratings are from -3 to -1 and positive ratings are from 1 to 3. When change is anchored to the patient perception or report of deterioration or improvement, it can be interpreted as a meaningful (or noticeable) level of change<sup>[9]</sup>. Patients with a  $\pm 2$  or  $\pm 3$  point change (much worse, worse, improved, much improved) were included in each analysis of change, a method used to distinguish noticeable change from no-change<sup>[43,44]</sup>. Patients reporting no change or only slight change were considered together as the no-change group. We combined the improved and deteriorated conditions using absolute values of the change scores to distinguish change from stable symptomology<sup>[45]</sup>.

The distribution-based methods included calculations based on the standard deviation (SD) and on the minimum detectable change (MDC). The SD approach used the 1/2 SD and 1/3 SD as variation-based estimates of MCID. The MDC is based on the standard error of measurement (SEM) of the follow-up scores and is the smallest score change that likely reflects a true change in condition. We calculated MDC at three confidence levels: 90%, 95% and 99%. The formulas for calculating the MDC are:  $MDC_{@90\%} = 1.65 * 2^{1/2} * SEM$ ;  $MDC_{@95\%} = 1.96 * 2^{1/2} * SEM$ ;  $MDC_{@99\%} = 2.56 * 2^{1/2} * SEM$ . The SEM equals to  $SD * (1-r)^{1/2}$ , where *r* is the reliability represented by Cronbach alpha and SD is

the standard deviation of the follow-up scores.

We fitted the receiver operating curve (ROC) to measure the best cut-off points to maximize sensitivity and specificity of the instruments. The cut-off was calculated as (sensitivity + specificity) - 1, based on Youden's J value<sup>[46]</sup>. Sensitivity is the proportion of correct identification of patients who showed changes, and specificity is the proportion of correct identification of patients showing no meaningful change. All statistical analyses were performed using SPSS 24.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.)<sup>[47]</sup>, and R 3.30 (R Development Core Team, Vienna, AT: R Foundation for Statistical Computing)<sup>[48]</sup>.

## RESULTS

### Demographics

A total of 2226 patients were included in the study. Mean age of participants was 61.16 years (SD = 12.84), with a range of 18-93 years. Most participants in the study were White or Caucasian (89.7%) and Non-Hispanic (93.2%). Detailed demographics can be found in Table 1.

### Anchor-based methods

**Mean change:** Mean change scores varied at each follow-up period. In terms of patients experiencing change, the highest mean change scores were observed at the 6-mo follow-up for the PF CAT (8.41), HOOS JR (19.68), and KOOS JR (18.85). The lowest mean change scores for patients experiencing change was at the 3-mo follow-up for all three measures. For the PF CAT mean change at 3-mo was 7.60 points, for the HOOS JR it was 14.81 points, and for the KOOS JR. It was 14.51 points. The median MCID value from the complete range of all two anchor-based methods and five distribution-based methods analyzed at all four time-points was similar to the mean change score for each measure and was 7.9 for the PF CAT, 18.0 for the HOOS JR, and 15.1 for the KOOS JR (Figure 1).

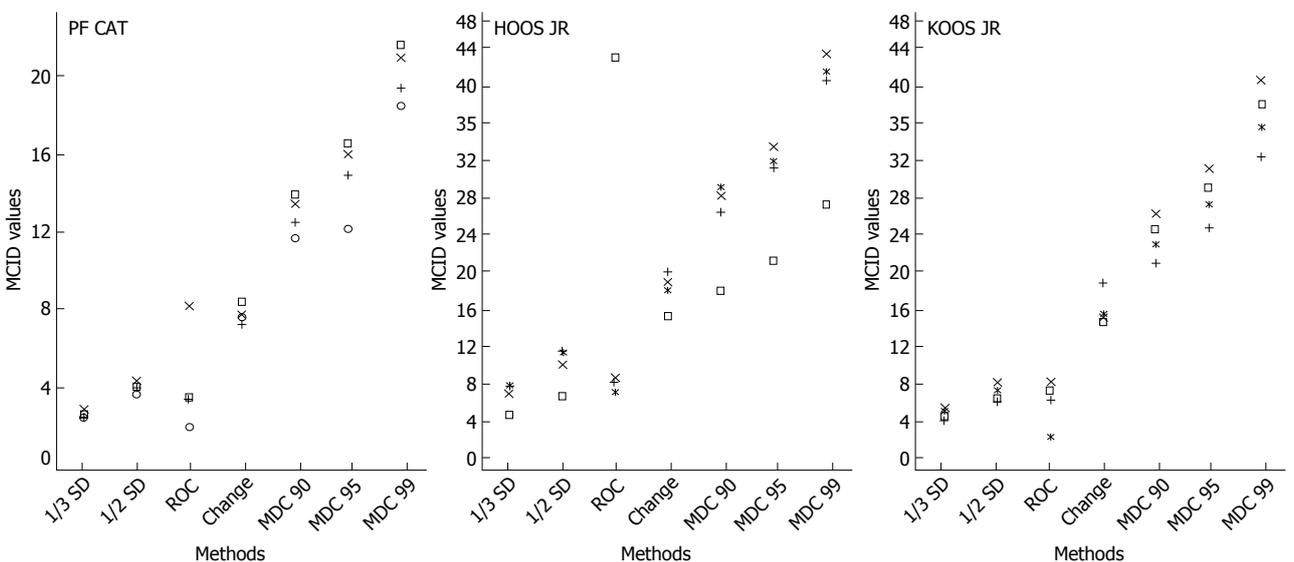
**ROC curve:** The ROC area under the curve was used to identify the optimal cut-off point between meaningful and non-meaningful change, by calculating the point at which the sum of false positive and false negative identifications are the fewest<sup>[49]</sup>. The highest ROC MCID value for the PF CAT was 8.18 at > 6-mo follow-up. For the HOOS JR the highest value was 43.36 observed at the 3-mo follow-up with a small sample size (*n* = 24). For the KOOS JR, the highest MCID value was 8.16 at > 3-mo follow-up. Detailed mean change and ROC cut-off values for the PF CAT, HOOS JR. and KOOS JR. can be found in Table 2.

### Distribution-based methods

**1/2 standard deviation of each of the function and pain scores:** The PF CAT (4.35) had the highest 1/2 SD value at the > 6-mo follow-up whereas the HOOS

**Table 2** Anchor-based methods for minimum clinically important difference determination of the PROMIS PF CAT, HOOS JR and KOOS JR

Instrument	<i>n</i>	No change (SD)	<i>n</i>	Mean change (SD)	ROC cut-off
3-mo from baseline follow-up					
PF CAT	54	6.95 (6.70)	88	7.60 (4.98)	1.97
HOOS JR	6	22.81 (10.10)	24	14.81 (12.45)	43.36
KOOS JR	14	10.49 (10.00)	37	14.51 (9.76)	7.24
> 3-mo from baseline follow-up					
PF CAT	366	6.02 (5.40)	577	7.29 (7.31)	3.44
HOOS JR	48	14.34 (15.23)	110	18.49 (12.53)	8.07
KOOS JR	96	12.71 (12.62)	151	14.82 (12.56)	8.16
6-mo from baseline follow-up					
PF CAT	21	4.36 (4.32)	34	8.41 (6.12)	3.52
HOOS JR	6	6.62 (5.87)	5	19.68 (18.65)	7.45
KOOS JR	12	13.49 (11.07)	14	18.85 (12.82)	6.12
> 6-mo from baseline follow-up					
PF CAT	192	6.44 (5.83)	421	7.69 (6.75)	8.18
HOOS JR	76	12.58 (11.61)	57	17.57 (13.92)	6.33
KOOS JR	81	12.45 (10.77)	64	15.47 (13.38)	2.21



**Figure 1** Multi-method minimum clinically important difference score ranges for PROMIS PF CAT, HOOS JR, and KOOS JR.

JR (10.96) had the highest 1/2 SD value at the 6-mo follow-up. The highest 1/2 SD value for the KOOS JR was 8.02 at the > 3-mo follow-up. At the 3-mo follow-up, PF CAT and HOOS JR had the lowest 1/2 SD values of 3.68 and 5.86. The KOOS JR had the lowest 1/2 SD value of 5.96 at the 6-mo follow-up.

**1/3 standard deviation of each of the function and pain scores:** The highest 1/3 SD value for the PF CAT (2.90) was observed at the > 6-mo follow-up whereas the HOOS JR (7.30) showed the highest 1/3 SD value at the 6-mo follow-up. The KOOS JR had the highest 1/3 SD value of 5.34 at the > 3-mo follow-up but the lowest 1/3 SD value of 3.98 at the 6-mo follow-up. The lowest 1/3 SD values for both the PF CAT (2.45) and HOOS JR (3.90) were observed at the 3-mo follow-up.

**Minimum detectable change (MDC) @90%, @95%, @99%:** The MDC was highest for the PF CAT

(MDC<sub>90%</sub> = 13.89, MDC<sub>95%</sub> = 16.50, MDC<sub>99%</sub> = 21.55) at the 6-mo follow-up. At the > 6-mo follow-up, the MDC was highest for the HOOS JR (MDC<sub>90%</sub> = 28.86, MDC<sub>99%</sub> = 41.67) and highest at > 3-mo HOOS JR (MDC<sub>95%</sub> = 31.90). The highest MDC for the KOOS JR (MDC<sub>90%</sub> = 26.21, MDC<sub>95%</sub> = 31.14, MDC<sub>99%</sub> = 40.67) was observed at the > 3-mo follow-up (Table 3).

## DISCUSSION

Determining the values of MCID for PRO measures enhances the interpretability and utility of the instruments. Determining score changes which reflect meaningful change requires understanding the patient perception of improvement or worsening. Anchor-based methods of determining an MCID tie the change scores to the patient reports of change and supplement the distribution-based methods which focus on precision in scores from a statistical standpoint. The current

**Table 3** Distribution-based methods for minimum clinically important difference determination of the PROMIS PF CAT, HOOS JR and KOOS JR

Instrument	n	SD		MDC		
		1/2	1/3	90%	95%	99%
3-mo from baseline follow-up						
PF CAT	663	3.68	2.45	11.64	14.14	18.47
HOOS JR	99	5.86	3.9	17.54	20.84	27.22
KOOS JR	129	6.52	4.35	24.49	29.09	37.99
> 3-mo from baseline follow-up						
PF CAT	2133	4.02	2.68	12.47	14.82	19.35
HOOS JR	245	9.33	6.22	28.11	33.39	43.61
KOOS JR	365	8.02	5.34	26.21	31.14	40.67
6-mo from baseline follow-up						
PF CAT	264	3.93	2.62	13.89	16.5	21.55
HOOS JR	31	10.96	7.3	26.36	31.31	40.89
KOOS JR	55	5.96	3.98	20.84	24.75	32.33
> 6-mo from baseline follow-up						
PF CAT	1520	4.35	2.9	13.46	15.98	20.88
HOOS JR	112	10.73	7.15	28.86	31.9	41.67
KOOS JR	154	7.12	4.75	22.91	27.22	35.55

MDC: Minimum detectable change.

comprehensive assessment of MCID values utilized multiple methods of anchor-based and distribution-based estimation.

The PROMIS® PF CAT mean change scores in this population of orthopaedic joint patients ranged from 7.29 to 8.41 depending on follow-up points. The ROC area under the curve ranged from 1.97 to 8.18. Distribution-based methods ranged using the SD method from a low of 2.45 (1/3 SD) to 4.35 (1/2 SD). The values using the MDC approach produced much larger values from 11.64 (MDC<sub>90%</sub>) to 21.55 (MDC<sub>99%</sub>). MCID values vary depending on the type of patient population (e.g., orthopaedic, cancer, pediatric) being evaluated, but overall the MCID values identified with the MDC approach in this study are much higher than the 2-3 point MCID of the PROMIS® mobility subscale identified in a pediatric population<sup>[15]</sup> or the 4-6 point PROMIS® PF CAT MCID values identified in a cancer population<sup>[16]</sup>.

The larger MCID values in this study could have been obtained for a number of reasons. The values could be population specific, reflecting an underlying difference in functional gain between the orthopaedic adult patient population and the pediatric and cancer patient populations previously studied. However, the most likely explanation is that the MCID value obtained is a reflection of the method used for calculation. Unlike other studies that commonly use just one approach to estimate MCID values, the current study used multiple approaches and multiple time points to arrive at twenty-eight MCID values per instrument, allowing better triangulation of results. This study found a great deal of consistency across the follow-up time-points for any one particular method of calculating MCIDs (Tables 2 and 3), suggesting that the methods were responsible for the variation of the MCID values and that the length of follow-ups was mostly irrelevant. It is important to recognize that this study incorporated a wide array of

cut-off standards, ranging from lenient to extremely strict. Since MDC<sub>95%</sub> and MDC<sub>99%</sub> are extremely strict cut-off standards, it is not surprising that these MCID values are high. None of the research reviewed as background for this study calculated MCIDs using such strict criteria<sup>[15,16]</sup>. The lowest MCID values derived from this study may be appropriate for screening purposes, but the median value (Figure 1) may be a better estimate of true and meaningful change when applying a conservative standard for evaluating treatment effects or for respondent analyses<sup>[50]</sup>. The more stringent cut-off standard derived MCID values reported in this study provide more definite assurance that important change has occurred.

The mean change for the HOOS JR ranged from 14.81 to 19.68. The ROC area under the curve ranged from 6.33 to 43.36. The 43.36 value appeared to be an outlier and is not considered a reliable estimate. The SD values ranged from 3.90 (1/3 SD) to 10.96 (1/2 SD). The MDC method of detecting change yielded a range of MCIDs of 17.54 (MDC<sub>90%</sub>) to 43.61 (MDC<sub>99%</sub>). These SD values are consistent with previous research identifying an MCID of 9.1 (1/2 SD method) for the HOOS in an arthroplasty population<sup>[51]</sup>. The median of the HOOS JR MCIDs was 18.0 and may be an appropriate conservative estimate for evaluating treatment effects.

For the KOOS JR, the mean change ranged from 14.51 to 18.85. The ROC maximized MCID values ranged from 2.21 to 8.16. The SD values ranged from 3.98 (1/3 SD) to 8.02 (1/2 SD). The MDC method of detecting change yielded a range of MCIDs from 20.84 (MDC<sub>90%</sub>) to 40.67 (MDC<sub>99%</sub>). The MDC<sub>90%</sub> values reported here are actually lower than previous research on the KOOS JR which produced a range for improved individuals from 28.3 to 35.5<sup>[52]</sup>. The median KOOS JR MCID was 15.1 in this patient population.

The findings demonstrate that the method used

to estimate MCIDs has a large impact on MCID value determination. The KOOS JR, for example, had a 2 point to 40 point difference in MCID depending on the method used. There is not yet consensus on a standardized approach for establishing MCID<sup>[10]</sup>. The lack of agreement between MCID values reported in this study, depending on the method used, is consistent with findings in the literature<sup>[53]</sup>. There have been recommendations that MCID determination should be standardized, but the best methods have not been agreed upon<sup>[38]</sup>. Until a more standardized method is established, the comprehensive range of MCIDs presented in this study provided much deeper insights than many existing studies. This comprehensive presentation enables patients, clinicians, care-givers and decision makers to be well-positioned in making their judgment call as to which MCID value(s) they should select based on how lenient or strict a standard they would like to set for their patients. It is tempting for clinicians to oversimplify and search for a single fixed MCID value, yet a single MCID value is often unstable<sup>[8]</sup>. A range of MCID values such as those presented in this study should indeed be considered by clinicians and health care practitioners.

The study may be limited by the type of patients who self-selected to return for follow-up visits, which is a common phenomenon across all orthopaedic and other clinics. Patients returning for longer-term follow-up were generally those experiencing more severe conditions and thus may not reflect the full range of improvement in condition. However, this should not be of much concern, as these patients returning for follow-ups were representative of the ones treated regularly in clinics, rendering the results of this study even more practical for standard orthopaedic practice. MCID value determination is generally not dependent on the severity of condition, thus the shorter-term or longer-term follow-up periods would not have impacted the MCID values, as evidenced from the empirical results of this study. In addition, not every patient in this study completed the outcome measures pre-treatment, thus some change scores may reflect a baseline time-point that was post-intervention. Yet these evaluations still produced meaningful change since longitudinal change over time was the main focus, not necessarily change from a specific time point to another specific time point.

One additional limitation comes from the use of anchor-based questions to determine clinically relevant change. An anchor-based question with a global rating of change measure is subject to recall bias, with some research indicating that reports of change may be more related to the current health status than real change from baseline<sup>[10]</sup>. Different anchor questions may produce different results as well. Distribution methods also have limitations as they derive MCIDs based on the variance of the data, which might be difficult to interpret. Since all methods have strengths and limitations, it was thus our intention for this study to be comprehensive in nature to cover a variety of approaches, allowing

readers to make informed decisions in selecting MCID values based on their personal value judgments as to which target MCID is worthwhile to pursue. Lastly, the demographic characteristics of this sample may not be representative of those in the United States and may affect MCID scores. Future research should investigate MCIDs in a more diverse demographic sample. It should also establish MCIDs linking baseline scores using Rasch methodology to provide deeper insights.

Overall, this study utilized rigorous methodologies to develop a wide range of MCID values for the PROMIS® PF, HOOS JR, and KOOS JR in an orthopaedic sample of patients with joint disorders. As there is no such concept as a correct or incorrect MCID, individual value judgments are necessary to apply MCIDs to treatment planning and in guiding patient expectations of treatment change.

## ARTICLE HIGHLIGHTS

### Research background

Newly developed patient-reported outcomes have many advantages, but require further studies, including establishing minimum clinically important difference (MCID) values. Determining the MCID for the Patient-Reported Outcomes Measurement Information System Physical Function (PROMIS® PF) will be useful for orthopaedic clinical practice and it is helpful to understand the MCID in the context of previously used measures like the hip disability and osteoarthritis outcome score for joint reconstruction (HOOS JR), and the knee injury and osteoarthritis outcome score for joint reconstruction (KOOS JR). Anchor-based and distribution-based methods can both be used to determine MCID.

### Research motivation

New instruments require studies to inform their score interpretation. Because of the lack of consensus on MCID methods, a comprehensive approach was taken, using both anchor- and distribution-based methods at multiple levels of precision and multiple follow-up time points. Cross verification of MCID values using powerful triangulation methods allow researchers and clinicians to understand the complexity of MCID evaluation and conscientiously select the most appropriate one for themselves.

### Research objectives

To determine MCIDs for the PROMIS PF, HOOS JR and KOOS JR in a general joint orthopaedic patient population applying comprehensive methods.

### Research methods

Consecutively enrolled patients aged 18 and older from a large academic orthopaedic joint clinic completed PROs at their first clinic visit and at follow-up points from 3-mo to 6-mo and beyond. These patients also completed an anchor question that queried how much their physical function had improved since their first clinic visit. They were grouped into change and no-change categories. Anchor-based analyses looked at mean change scores and the receiver operating curve to maximize the best cut-off based on sensitivity and specificity. Distribution-based analyses looked at the standard deviation, and minimum detectable change.

### Research results

There were 2226 patients who participated with a mean age of 61.16 (SD = 12.84) years, 41.6% male, and 89.7% Caucasian. Mean change ranged from 7.29 to 8.41 for the PROMIS® PF CAT; from 14.81 to 19.68 for the HOOS JR; and from 14.51 to 18.85 for the KOOS JR. ROC cut-offs ranged from 1.97-8.18 for the PF CAT, 6.33-43.36 for the HOOS JR, and 2.21-8.16 for the KOOS JR. Distribution-based methods estimated MCID values ranging from 2.45 to 21.55 for the PROMIS® PF CAT; from 3.90 to 43.61 for the HOOS JR; and from 3.98 to 40.67 for the KOOS JR. The median MCID value in the range was similar to

the mean change score for each measure and was 7.9 for the PF CAT, 18.0 for the HOOS JR, and 15.1 for the KOOS JR.

### Research conclusions

Overall this study identified a large range of MCIDs for the PROMIS® PF, HOOS JR, and KOOS JR in an orthopaedic sample of patients with joint ailments. This range reflects the comprehensive strategies applied to determine MCIDs at varying levels of precision and cut off standards. The range of MCIDs presented in this study can be incorporated into decision making to guide treatment recommendations, compute sample size for research studies and clinical trials, and conduct respondent analyses.

### Research perspectives

Decisions on which MCID value to select or which MCID value is useful should be based on an individual's personal value and belief. Future research direction should focus on investigation of MCIDs with a more diverse demographic sample and to link MCIDs with baseline scores using Rasch-based methods.

## REFERENCES

- 1 Cella D, Yount S, Rothrock N, Gershon R, Cook K, Reeve B, Ader D, Fries JF, Bruce B, Rose M; PROMIS Cooperative Group. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. *Med Care* 2007; **45**: S3-S11 [PMID: 17443116 DOI: 10.1097/01.mlr.0000258615.42478.55]
- 2 Hossain FS, Konan S, Patel S, Rodriguez-Merchan EC, Haddad FS. The assessment of outcome after total knee arthroplasty: are we there yet? *Bone Joint J* 2015; **97-B**: 3-9 [PMID: 25568406 DOI: 10.1302/0301-620x.97b1.34434]
- 3 Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, Amtmann D, Bode R, Buysse D, Choi S, Cook K, Devellis R, DeWalt D, Fries JF, Gershon R, Hahn EA, Lai JS, Pilkonis P, Revicki D, Rose M, Weinfurt K, Hays R; PROMIS Cooperative Group. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol* 2010; **63**: 1179-1194 [PMID: 20685078 DOI: 10.1016/j.jclinepi.2010.04.011]
- 4 Hung M, Nickisch F, Beals TC, Greene T, Clegg DO, Saltzman CL. New paradigm for patient-reported outcomes assessment in foot & ankle research: computerized adaptive testing. *Foot Ankle Int* 2012; **33**: 621-626 [PMID: 22995227 DOI: 10.3113/fai.2012.0621]
- 5 Rose M, Bjorner JB, Gandek B, Bruce B, Fries JF, Ware JE. The PROMIS Physical Function Item Bank Was Calibrated to a Standardized Metric and Shown to Improve Measurement Efficiency. *J Clin Epidemiol* 2014; **67**: 516-526 [PMID: 24698295 DOI: 10.1016/j.jclinepi.2013.10.024]
- 6 Fries JF, Witter J, Rose M, Cella D, Khanna D, Morgan-DeWitt E. Item response theory, computerized adaptive testing, and PROMIS: assessment of physical function. *J Rheumatol* 2014; **41**: 153-158 [PMID: 24241485 DOI: 10.3899/jrheum.130813]
- 7 Deutsch L, Smith L, Gage B, Kelleher C, Garfinkel D. Patient-reported outcomes in performance measurement: commissioned paper on PRO-based performance measures for healthcare accountable entities. Proceedings of the Washington, DC: National Quality Forum; 2012
- 8 Wright A, Hannon J, Hegedus EJ, Kavchak AE. Clinimetrics corner: a closer look at the minimal clinically important difference (MCID). *J Man Manip Ther* 2012; **20**: 160-166 [PMID: 23904756 DOI: 10.1179/2042618612y.0000000001]
- 9 Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertain the minimal clinically important difference. *Control Clin Trials* 1989; **10**: 407-415 [PMID: 2691207]
- 10 Cook CE. Clinimetrics Corner: The Minimal Clinically Important Change Score (MCID): A Necessary Pretense. *J Man Manip Ther* 2008; **16**: E82-E83 [PMID: 19771185 DOI: 10.1179/jmt.2008.16.4.82E]
- 11 Turner D, Schünemann HJ, Griffith LE, Beaton DE, Griffiths AM, Critch JN, Guyatt GH. The minimal detectable change cannot reliably replace the minimal important difference. *J Clin Epidemiol* 2010; **63**: 28-36 [PMID: 19800198 DOI: 10.1016/j.jclinepi.2009.01.024]
- 12 Hung M, Bounsanga J, Voss MW. Interpretation of correlations in clinical research. *Postgrad Med* 2017; **129**: 902-906 [PMID: 28936887 DOI: 10.1080/00325481.2017.1383820]
- 13 McGlothlin AE, Lewis RJ. Minimal clinically important difference: defining what really matters to patients. *JAMA* 2014; **312**: 1342-1343 [PMID: 25268441 DOI: 10.1001/jama.2014.13128]
- 14 White DK, Master H. Patient Reported Measures of Physical Function in Knee Osteoarthritis. *Rheum Dis Clin North Am* 2016; **42**: 239-252 [PMID: 27133487 DOI: 10.1016/j.rdc.2016.01.005]
- 15 Thissen D, Liu Y, Magnus B, Quinn H, Gipson DS, Dampier C, Huang IC, Hinds PS, Selewski DT, Reeve BB, Gross HE, DeWalt DA. Estimating minimally important difference (MID) in PROMIS pediatric measures using the scale-judgment method. *Qual Life Res* 2016; **25**: 13-23 [PMID: 26118768 DOI: 10.1007/s11136-015-1058-8]
- 16 Yost KJ, Eton DT, Garcia SF, Cella D. Minimally important differences were estimated for six Patient-Reported Outcomes Measurement Information System-Cancer scales in advanced-stage cancer patients. *J Clin Epidemiol* 2011; **64**: 507-516 [PMID: 21447427 DOI: 10.1016/j.jclinepi.2010.11.018]
- 17 Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998; **28**: 88-96 [PMID: 9699158 DOI: 10.2519/jospt.1998.28.2.88]
- 18 Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score (KOOS) - validation and comparison to the WOMAC in total knee replacement. *Health Qual Life Outcomes* 2003; **1**: 17 [PMID: 12801417 DOI: 10.1186/1477-7525-1-17]
- 19 Thorborg K, Roos EM, Bartels EM, Petersen J, Hölmich P. Validity, reliability and responsiveness of patient-reported outcome questionnaires when assessing hip and groin disability: a systematic review. *Br J Sports Med* 2010; **44**: 1186-1196 [PMID: 19666629 DOI: 10.1136/bjsm.2009.060889]
- 20 Nilsson AK, Lohmander LS, Klässbo M, Roos EM. Hip disability and osteoarthritis outcome score (HOOS)--validity and responsiveness in total hip replacement. *BMC Musculoskelet Disord* 2003; **4**: 10 [PMID: 12777182 DOI: 10.1186/1471-2474-4-10]
- 21 Ayers DC, Franklin PD. Joint replacement registries in the United States: a new paradigm. *J Bone Joint Surg Am* 2014; **96**: 1567-1569 [PMID: 25232081 DOI: 10.2106/jbjs.n.00641]
- 22 Lyman S, Lee YY, Franklin PD, Li W, Mayman DJ, Padgett DE. Validation of the HOOS, JR: A Short-form Hip Replacement Survey. *Clin Orthop Relat Res* 2016; **474**: 1472-1482 [PMID: 26926772 DOI: 10.1007/s11999-016-4718-2]
- 23 Tait MA, Dredge C, Barnes CL. Preoperative Patient Education for Hip and Knee Arthroplasty: Financial Benefit? *J Surg Orthop Adv* 2015; **24**: 246-251 [PMID: 26731389]
- 24 Lyman S, Lee YY, Franklin PD, Li W, Cross MB, Padgett DE. Validation of the KOOS, JR: A Short-form Knee Arthroplasty Outcomes Survey. *Clin Orthop Relat Res* 2016; **474**: 1461-1471 [PMID: 26926773 DOI: 10.1007/s11999-016-4719-1]
- 25 Hung M, Saltzman CL, Greene T, Voss MW, Bounsanga J, Gu Y, Anderson MB, Peters CL, Gililand J, Pelt CE. Evaluating instrument responsiveness in joint function: The HOOS JR, the KOOS JR, and the PROMIS PF CAT. *J Orthop Res* 2017; Epub ahead of print [PMID: 28921658 DOI: 10.1002/jor.23739]
- 26 Paradowski PT, Kęska R, Witoński D. Validation of the Polish version of the Knee injury and Osteoarthritis Outcome Score (KOOS) in patients with osteoarthritis undergoing total knee replacement. *BMJ Open* 2015; **5**: e006947 [PMID: 26141301 DOI: 10.1136/bmjopen-2014-006947]
- 27 Paatelma M, Kilpikoski S, Simonen R, Heinonen A, Alen M, Videman T. Orthopaedic manual therapy, McKenzie method or advice only for low back pain in working adults: a randomized

- controlled trial with one year follow-up. *J Rehabil Med* 2008; **40**: 858-863 [PMID: 19242624 DOI: 10.2340/16501977-0262]
- 28 **Uchiyama S**, Imaeda T, Toh S, Kusunose K, Sawaizumi T, Wada T, Okinaga S, Nishida J, Omokawa S; Clinical Outcomes Committee of the Japanese Orthopaedic Association; Impairment Evaluation Committee of the Japanese Society for Surgery of the Hand. Comparison of responsiveness of the Japanese Society for Surgery of the Hand version of the carpal tunnel syndrome instrument to surgical treatment with DASH, SF-36, and physical findings. *J Orthop Sci* 2007; **12**: 249-253 [PMID: 17530376 DOI: 10.1007/s00776-007-1128-z]
- 29 **Carmont MR**, Silbernagel KG, Nilsson-Helander K, Meidan O, Karlsson J, Maffulli N. Cross cultural adaptation of the Achilles tendon Total Rupture Score with reliability, validity and responsiveness evaluation. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 1356-1360 [PMID: 22847247 DOI: 10.1007/s00167-012-2146-8]
- 30 **Landauer F**, Wimmer C, Behensky H. Estimating the final outcome of brace treatment for idiopathic thoracic scoliosis at 6-month follow-up. *Pediatr Rehabil* 2003; **6**: 201-207 [PMID: 14713586 DOI: 10.1080/13638490310001636817]
- 31 **Little DG**, MacDonald D. The use of the percentage change in Oswestry Disability Index score as an outcome measure in lumbar spinal surgery. *Spine* (Phila Pa 1976) 1994; **19**: 2139-2143 [PMID: 7809744]
- 32 **Cornell CN**, Levine D, O'Doherty J, Lyden J. Unipolar versus bipolar hemiarthroplasty for the treatment of femoral neck fractures in the elderly. *Clin Orthop Relat Res* 1998; **(348)**: 67-71 [PMID: 9553535]
- 33 **Kotsis SV**, Chung KC. Responsiveness of the Michigan Hand Outcomes Questionnaire and the Disabilities of the Arm, Shoulder and Hand questionnaire in carpal tunnel surgery. *J Hand Surg Am* 2005; **30**: 81-86 [PMID: 15680560 DOI: 10.1016/j.jhssa.2004.10.006]
- 34 **MacDermid JC**, Richards RS, Donner A, Bellamy N, Roth JH. Responsiveness of the short form-36, disability of the arm, shoulder, and hand questionnaire, patient-rated wrist evaluation, and physical impairment measurements in evaluating recovery after a distal radius fracture. *J Hand Surg Am* 2000; **25**: 330-340 [PMID: 10722826 DOI: 10.1053/jhsu.2000.jhsu25a0330]
- 35 **Ibrahim T**, Beiri A, Azzabi M, Best AJ, Taylor GJ, Menon DK. Reliability and validity of the subjective component of the American Orthopaedic Foot and Ankle Society clinical rating scales. *J Foot Ankle Surg* 2007; **46**: 65-74 [PMID: 17331864 DOI: 10.1053/j.jfas.2006.12.002]
- 36 **Segal NA**, Glass NA, Teran-Yengle P, Singh B, Wallace RB, Yack HJ. Intensive Gait Training for Older Adults with Symptomatic Knee Osteoarthritis. *Am J Phys Med Rehabil* 2015; **94**: 848-858 [PMID: 25768068 DOI: 10.1097/PHM.0000000000000264]
- 37 **Gregory J**, Harwood D, Gochanour E, Sherman S, Romeo A. Clinical outcomes of revision biceps tenodesis. *Int J Shoulder Surg* 2012; **6**: 45 [PMID: 22787333 DOI: 10.4103/0973-6042.96993]
- 38 **Terwee CB**, Roorda LD, Dekker J, Bierma-Zeinstra SM, Peat G, Jordan KP, Croft P, de Vet HC. Mind the MIC: large variation among populations and methods. *J Clin Epidemiol* 2010; **63**: 524-534 [PMID: 19926446 DOI: 10.1016/j.jclinepi.2009.08.010]
- 39 **Ostelo RW**, Deyo RA, Stratford P, Waddell G, Croft P, Von Korf M, Bouter LM, de Vet HC. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine* (Phila Pa 1976) 2008; **33**: 90-94 [PMID: 18165753 DOI: 10.1097/BRS.0b013e31815e3a10]
- 40 **Jones PW**, Beeh KM, Chapman KR, Decramer M, Mahler DA, Wedzicha JA. Minimal clinically important differences in pharmacological trials. *Am J Respir Crit Care Med* 2014; **189**: 250-255 [PMID: 24383418 DOI: 10.1164/rccm.201310-1863PP]
- 41 **Gershon RC**, Rothrock N, Hanrahan R, Bass M, Cella D. The Use of PROMIS and Assessment Center to Deliver Patient-Reported Outcome Measures in Clinical Research. *J Appl Meas* 2010; **11**: 304-314 [PMID: 20847477]
- 42 **Davis AM**, Perruccio AV, Canizares M, Hawker GA, Roos EM, Maillefert JF, Lohmander LS. Comparative, validity and responsiveness of the HOOS-PS and KOOS-PS to the WOMAC physical function subscale in total joint replacement for osteoarthritis. *Osteoarthritis Cartilage* 2009; **17**: 843-847 [PMID: 19215728 DOI: 10.1016/j.joca.2009.01.005]
- 43 **Polson K**, Reid D, McNair PJ, Larmer P. Responsiveness, minimal importance difference and minimal detectable change scores of the shortened disability arm shoulder hand (QuickDASH) questionnaire. *Man Ther* 2010; **15**: 404-407 [PMID: 20434942 DOI: 10.1016/j.math.2010.03.008]
- 44 **Franchignoni F**, Vercelli S, Giordano A, Sartorio F, Bravini E, Ferriero G. Minimal clinically important difference of the disabilities of the arm, shoulder and hand outcome measure (DASH) and its shortened version (QuickDASH). *J Orthop Sports Phys Ther* 2014; **44**: 30-39 [PMID: 24175606 DOI: 10.2519/jospt.2014.4893]
- 45 **Juniper EF**, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res* 1996; **5**: 35-46 [PMID: 8901365]
- 46 **Youden WJ**. Index for rating diagnostic tests. *Cancer* 1950; **3**: 32-35 [PMID: 15405679]
- 47 **IBM Corp.** SPSS Statistics for Windows. Armonk, New York: IBM Corp., 2015
- 48 **R Development Core Team.** R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2010
- 49 **de Vet HC**, Ostelo RW, Terwee CB, van der Roer N, Knol DL, Beckerman H, Boers M, Bouter LM. Minimally important change determined by a visual method integrating an anchor-based and a distribution-based approach. *Qual Life Res* 2007; **16**: 131-142 [PMID: 17033901 DOI: 10.1007/s11136-006-9109-9]
- 50 **Man-Son-Hing M**, Laupacis A, O'Rourke K, Molnar FJ, Mahon J, Chan KB, Wells G. Determination of the clinical importance of study results. *J Gen Intern Med* 2002; **17**: 469-476 [PMID: 12133163]
- 51 **Berliner JL**, Brodke DJ, Chan V, SooHoo NF, Bozic KJ. John Charnley Award: Preoperative Patient-reported Outcome Measures Predict Clinically Meaningful Improvement in Function After THA. *Clin Orthop Relat Res* 2016; **474**: 321-329 [PMID: 26201420 DOI: 10.1007/s11999-015-4350-6]
- 52 **Singh JA**, Luo R, Landon GC, Suarez-Almazor M. Reliability and Clinically Important Improvement Thresholds for Osteoarthritis Pain and Function scales: A Multicenter study. *J Rheumatol* 2014; **41**: 509-515 [PMID: 24429183 DOI: 10.3899/jrheum.130609]
- 53 **Beaton DE**, van Eerd D, Smith P, van der Velde G, Cullen K, Kennedy CA, Hogg-Johnson S. Minimal change is sensitive, less specific to recovery: a diagnostic testing approach to interpretability. *J Clin Epidemiol* 2011; **64**: 487-496 [PMID: 21109396 DOI: 10.1016/j.jclinepi.2010.07.012]

**P- Reviewer:** Drosos GI, Malik H **S- Editor:** Cui LJ **L- Editor:** A  
**E- Editor:** Li D



## Clinical Practice Study

**Use of ketamine sedation for the management of displaced paediatric forearm fractures**

Anatole Vilhelm Wiik, Poonam Patel, Joanna Bovis, Adele Cowper, Philip Socrates Pastides, Alison Hulme, Stuart Evans, Charles Stewart

Anatole Vilhelm Wiik, Department of Surgery and Cancer, Charing Cross Hospital, London W6 8RF, United Kingdom

Poonam Patel, Adele Cowper, Charles Stewart, Department of Paediatric Emergency, Chelsea and Westminster Hospital, London SW10 9NH, United Kingdom

Joanna Bovis, Philip Socrates Pastides, Alison Hulme, Stuart Evans, Department of Trauma and Orthopaedics, Chelsea Westminster Hospital, London SW10 9NH, United Kingdom

ORCID number: Anatole Vilhelm Wiik (0000-0003-0937-7675); Poonam Patel (0000-0002-1729-2973); Joanna Bovis (0000-0002-1377-0595); Adele Cowper (0000-0002-3274-9898); Philip Socrates Pastides (0000-0002-0982-9603); Alison Hulme (0000-0002-4619-1506); Stuart Evans (0000-0002-1873-0752); Charles Stewart (0000-0002-9649-5233).

**Author contributions:** Wiik AV and Stewart C designed the study; Wiik AV and Stewart C collected the data; Wiik AV, Patel P, Bovis J and Cowper A analysed the results; Wiik AV, Patel P, Bovis J, Cowper A, Pastides PS, Hulme A, Evans S and Stewart C interpreted and wrote the report.

**Institutional review board statement:** This was a registered service improvement project at Chelsea Westminster hospital audit department (QIP LA-353). Ethical approval was not sought nor required as it was part of a service evaluation project for the paediatric emergency department at Chelsea Westminster hospital.

**Informed consent statement:** Informed consent was obtained prior to any treatment from the parent or guardian.

**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.

**Data sharing statement:** Dataset available 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/>

Manuscript source: Invited manuscript

Correspondence to: Anatole Vilhelm Wiik, BSc, MBBS, MD, Doctor, Lecturer, Department of Surgery and Cancer, Charing Cross Hospital, Fulham Place Road, London W6 8RF, United Kingdom. [a.wiik@imperial.ac.uk](mailto:a.wiik@imperial.ac.uk)  
Telephone: +44-20-33130970  
Fax: +44-20-33115218

Received: November 3, 2017

Peer-review started: November 4, 2017

First decision: December 27, 2017

Revised: January 4, 2018

Accepted: February 4, 2018

Article in press: February 5, 2018

Published online: March 18, 2018

## Abstract

### AIM

To determine if ketamine sedation is a safe and cost effective way of treating displaced paediatric radial and ulna fractures in the emergency department.

### METHODS

Following an agreed interdepartmental protocol, fractures of the radius and ulna (moderately to severely displaced) in children between the age of 2 and 16 years old, presenting within a specified 4 mo period, were manipulated in our paediatric emergency department. Verbal and written consent was obtained prior to procedural sedation to ensure parents were informed and satisfied to have ketamine. A single attempt at manipulation was performed. Pre and post

manipulation radiographs were requested and assessed to ensure adequacy of reduction. Parental satisfaction surveys were collected after the procedure to assess the perceived quality of treatment. After closed reduction and cast immobilisation, patients were then followed-up in the paediatric outpatient fracture clinic and functional outcomes measured prospectively. A cost analysis compared to more formal manipulation under a general anaesthetic was also undertaken.

## RESULTS

During the 4 mo period of study, 10 closed, moderate to severely displaced fractures were identified and treated in the paediatric emergency department using our ketamine sedation protocol. These included fractures of the growth plate (3), fractures of both radius and ulna (6) and a single isolated proximal radius fracture. The mean time from administration of ketamine until completion of the moulded plaster was 20 min. The mean time interval from sedation to full recovery was 74 min. We had no cases of unacceptable fracture reduction and no patients required any further manipulation, either in fracture clinic or under a more formal general anaesthetic. There were no serious adverse events in relation to the use of ketamine. Parents, patients and clinicians reported extremely favourable outcomes using this technique. Furthermore, compared to using a manipulation under general anaesthesia, each case performed under ketamine sedation was associated with a saving of £1470, the overall study saving being £14700.

## CONCLUSION

Ketamine procedural sedation in the paediatric population is a safe and cost effective method for the treatment of displaced fractures of the radius and ulna, with high parent satisfaction rates.

**Key words:** Paediatrics; Forearm fractures; Displaced fractures; Ketamine; Salter Harris; Procedural sedation

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Displaced paediatric forearm fractures can be safely and effectively treated in the emergency department with ketamine procedural sedation.

Wiik AV, Patel P, Bovis J, Cowper A, Pastides PS, Hulme A, Evans S, Stewart C. Use of ketamine sedation for the management of displaced paediatric forearm fractures. *World J Orthop* 2018; 9(3): 50-57 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i3/50.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i3.50>

## INTRODUCTION

Fractures of the radius and ulna account for 18% to 40% of all fractures in children<sup>[1,2]</sup>. They are the most common childhood fracture presenting to the paediatric

emergency department (ED), with population studies suggesting that the incidence is on the rise throughout the world<sup>[3,4]</sup>. The majority are treated in the ED with closed reduction and immobilisation in a cast or a splint<sup>[5,6]</sup>. An arc of rotation of 100 degrees, split evenly between pronation and supination is accepted as normal<sup>[7]</sup>. The goal of treatment is to restore appropriate length and alignment so normal forearm rotation can return after healing<sup>[8]</sup>. Simple closed reduction and temporary stable immobilisation is the standard of care sought for these fractures as they generally heal well and surgical fixation doesn't come without risk<sup>[9]</sup>. The provision of closed reduction can be problematic as there are variations in treatment practice as result of hospital resources, local policy and experience<sup>[10,11]</sup>. Despite this, a safe and optimal level of analgesia should be achieved before manipulation to avoid unnecessary distress to the child and to ensure a favourable outcome<sup>[12]</sup>. Simple analgesia such as paracetamol and non-steroidal anti-inflammatory drugs, along with intra-nasal opiates and nitrous oxide may be sufficient and have been shown to be an effective treatment in the ED<sup>[13]</sup>. However formal ED procedural sedation is an attractive alternative as it offers a greater opportunity to deliver the optimal fracture reduction and cast application<sup>[11]</sup>. Sedation in the ED is particularly helpful if the fracture pattern is unstable and requires complex traction manoeuvres to achieve adequate correction<sup>[14]</sup>. Providing complete treatment in the ED and avoiding theatres would negate the economic and psychosocial impact on the child and family if they were admitted into hospital<sup>[15,16]</sup>. It also has been shown to be more cost-effective to society, which is important in times of economic austerity<sup>[17]</sup>.

There are a variety of classes of procedural sedation drugs used in the United Kingdom<sup>[18]</sup>. The most popular include opioids, benzodiazepines, propofol and ketamine<sup>[18]</sup>. Ketamine is the only drug that does not routinely interfere with protective airway reflexes and spontaneous respiration<sup>[18]</sup>. Ketamine is also the most complete agent as it produces amnesia, anxiolysis and profound analgesia<sup>[19]</sup>. This drug was first used in humans in the 1960<sup>[20]</sup>. It was used extensively in the Vietnam war in the 1970s for surgical anaesthesia due to its good safety profile<sup>[21]</sup>. Its widespread application in paediatric procedural sedation was developed in the 1990s following the work of Green *et al*<sup>[22,23]</sup>. Over the last three decades it has become one of the most widely used sedative agents in the ED<sup>[24,25]</sup>. It acts as a dissociative agent that non-competitively blocks NDMA receptors<sup>[20]</sup>. Traditionally the dose required is 1-2 mg/kg, administered *via* slow intravenous infusion and can be combined with opioids and benzodiazepines<sup>[24]</sup>.

The aim of this clinical practice study was to determine if ketamine is a safe and cost effective way of treating displaced fractures of the radius and ulna in children.

## MATERIALS AND METHODS

From May to September 2017, we prospectively evaluated



Patient label

Paediatric Procedural Sedation using Ketamine

Date \_\_\_\_\_ Time \_\_\_\_\_ Procedure planned \_\_\_\_\_

Exclusion criteria (risk evaluation) (1)*	ASA greater than 2 (excludes all unstable systemic illness)	Previous adverse reaction to an anaesthetic
	Age under 18 m	Psychosis, ADHD
	Any airway abnormality	Bowel obstruction
	Acute systemic illness, <i>i.e.</i> , sepsis	Abnormal conscious state/risk of raised intracranial pressure
PPS information sheet(2)* discussed with patient/parents		
Fasting	2 h (all intake) yes no (in emergency situations the duty consultant can elect to give ketamine without prior fasting)	
Informed consent obtained yes no	Medication(s) prescribed drawn up	
Staffing identified proceduralist Sedationist Nurse Anaesthetist informed (bleep 0400)		
Time out	Verification of patient, family members, staff and PPS equipment (3)*	
During Procedure	PPS to be performed in a quiet environment. Baseline observations taken immediately prior to procedure (BP, RR, HR, SpO2) and every 5 min (except BP) until the patient has returned to baseline (4)*	
Post procedure	Patient returned to baseline activity and verbalisation	
	Observations within normal limits	
	Tolerating oral liquids	
	Post procedural care discussed with family (using the information leaflet)	
Clinical staff		
Print name _____	Signature _____	Role in PPS _____
Print name _____	Signature _____	Role in PPS _____
Print name _____	Signature _____	Role in PPS _____

Figure 1 Paediatric Procedural Sedation using Ketamine.

a new ketamine protocol (Figure 1) for paediatric ED procedural sedation at Chelsea and Westminster Hospital (CWH). All eligible children with significantly displaced or unstable fractures of the radius and ulna who presented to CWH ED during daylight weekday hours that needed closed reduction and moulded casting were included. The service improvement project was registered locally (QIP# LA353) to follow good clinical governance practice guidelines.

**Treatment protocol**

Following triage all children presenting to CWH ED with a suspected fracture of the radius and ulna undergo orthogonal anterior-posterior and lateral radiography. The radiographs are then screened by an ED doctor or triage nurse; if significant malalignment is identified the on-call orthopaedic registrar is notified. If the fracture is deemed suitable for manipulation using sedation the orthopaedic registrar and paediatric ED specialist explain the procedure to the child and parent/legal guardian. Counselling is given prior to obtaining written consent to ensure that the family is happy with the proposed sedation plan. They are advised that other treatment options are available if they wish. The inclusion criteria is any child below the age of 16 years with a significantly displaced or unstable fracture of the radius and/or ulna. Plain radiographs are demonstrated

as examples of the nature of these fractures. Exclusion criteria included open fractures, ASA greater than 2, under 18 mo of age, any airway abnormality, acute systemic illness, previous adverse anaesthetic reactions, raised intracranial pressure, and/or bowel obstruction.

Informed written consent is taken and final neurovascular assessment is documented. The weight of the child is measured before he or she is taken to a quiet room for ketamine sedation and closed reduction. The parent/legal guardian is given the option to stay with the child for support and comfort. The team consists of a paediatrician, a specialist ED trainee/consultant with ketamine sedation experience, and an orthopaedic registrar. Blood pressure, pulse, respiratory rate and oxygen saturation are monitored and recorded. An alert is sent to an anaesthetic consultant that the procedure is about to start in case of serious adverse event (SAE) occurs. A sedation checklist is completed.

To start 1 mg/kg of ketamine is given through a peripheral intravenous cannula normally in the antecubital fossa or dorsum of the hand of the contralateral upper limb. After a period of 3 min the child's vitals are rechecked. If the child appears to be sedated a gentle manipulation is attempted. If they are not adequately sedated, a top-up of 0.5 mg/kg is administered. Manipulation is performed; when the position is deemed to be satisfactory a stockinette is placed over the arm followed

by a thin layer of wool and a complete well moulded cast utilizing three point fixation. The level of the fracture determines the decision whether or not to extend the cast above the elbow.

Generally the child begins to wake after 20 min and is monitored until fully verbalising with normal observations. Radiographs are performed to ensure a satisfactory reduction and compared to the pre-injury images; these are presented at trauma meeting the following morning.

### Follow-up

Patients are seen in a paediatric fracture clinic 1 and 2 wk after manipulation when further radiographs are performed. If alignment is maintained the child is reviewed 3-6 wk later for removal of cast and repeat radiographs. A comprehensive examination is performed at this stage particularly looking for any obvious deformity, range of motion and for clinical evidence of fracture union. If union is felt to be insufficient a cast may be re-applied or splint provided. The child is reviewed 4-6 wk later for a final check. At the point of cast removal advice is given to avoid contact sport for a period deemed appropriate to allow for the bone to strengthen in accordance to Wolff's law<sup>[26]</sup>.

### Statistical analysis

All patient data was anonymised. All hospital medical record numbers were retained in the paediatric ED database. Patient demographics, site and nature of injury, time of procedure, sedation or reduction outcomes were documented. Consent forms were kept in the patient files. Pre and post reduction radiographs were taken from our departmental picture archiving and communication systems (PACS). Absolute angulation measurements were taken from the lateral radiographs using angle measuring tool (SECTRA) and measured by AW and PP. A repeated measure *t*-test was utilised to detect if a difference was made. A significance level was set to  $\alpha = 0.005$  due to small numbers. The results were then compared to the best available evidence regarding acceptable reduction parameters for different fracture levels of the forearm<sup>[7]</sup>. Parental satisfaction was assessed using a validated satisfaction score<sup>[27]</sup>.

## RESULTS

### Demographics

A total of 10 closed unilateral forearm fractures were included in the 4 mo time period. All ten were due to indirect trauma, the majority being due to a fall on an outstretched hand. There were 8 boys and 2 girls. The mean age was 8 years (range 2.2-14.5). There were 6 fractures on the left side and 4 fractures on the right side. There were no cases of compartment syndrome or neurovascular compromise. All children had successful procedural sedation. Two children required topping up to 1.5 mg/kg to achieve appropriate analgesia and sedation. There were no serious adverse events. Vomiting was

the most common adverse event, seen in 3 children. All were treated definitively at time of injury and required no further manipulation. No patients were lost to follow-up and all patients reported excellent functional outcomes at discharge as guided by Price *et al*<sup>[28]</sup>. Figures 2-4 (A-D) demonstrate the variety of fracture types and fracture reduction result.

### Radiographic results

There were three Salter Harris II fractures of the distal radius, four fractures of the distal third of the radius and/or ulna, two fractures of the mid-shaft of the radius and/or ulna and one fracture of proximal third of the radius. The mean dorsal angulation prior to reduction was 45 degrees (range 17-80). The mean angulation after reduction was 6 degrees (0-15) an improvement that reached statistical significance ( $P < 0.001$ ). Following reduction all fractures were within the parameters recommended by Noonan and Price as acceptable<sup>[7]</sup>. One patient had an over correction going from a 45 degrees dorsal angulation to 15 degrees of volar angulation, however there was no functional deficit at discharge.

### Length of stay

The mean time from fracture diagnosis to sedation administration was 181 min (range 129-234). The mean time to completion of cast application was 20 min (range 7-35). The mean time from sedation to full recovery was 74 min (range 45-120). The mean interval between pre-reduction and post-reduction radiographs was 198 min (range 91-370 min). The mean length of stay in the ED department from arrival to discharge was 311 min (range 213-446).

### Cost analysis of ketamine vs general anaesthesia in theatres

In our trust the health resource group (HRG) code for general anaesthesia in paediatric theatres is £1620 per child. The cost for procedural sedation with ketamine in the paediatric ED was £150 per child. The cost of hospital inpatient admission was not calculated to give a fair comparison. The cost saving is £1470 per child without the addition of cost for admission and loss of earning to the parent/legal guardian if they had to stay with the child. The minimum total financial savings for these 10 children was £14700.

### Parental satisfaction questionnaire

The validated sedation satisfaction score was out of 10, with 0 being not at all and 10 being very satisfied<sup>[27]</sup>. The mean satisfaction score for all questions was 9.6. The individual scores for each item is seen in Table 1. A score of 10 was the most common result for each questionnaire item.

## DISCUSSION

The use of ketamine for procedural sedation in the ED



Figures 2 Lateral and anteroposterior radiographs of a Salter Harris II distal radius fracture before (A, B) and after reduction (C, D).



Figures 3 Lateral and anteroposterior radiographs of a midshaft radius and ulna fracture before (A, B) and after reduction (C, D).

in the developed world is gaining popularity<sup>[19,24]</sup>. In the past few years there is a growing body of evidence supporting its use for successful procedural sedation with a good safety and efficacy profile<sup>[29,30]</sup>. Serious

adverse events are low with the largest prospective cohort study to date reporting a 1.1% risk with no deaths in 6295 children. Vomiting (5.2%) and oxygen desaturation (5.6%) were the most common adverse



Figures 4 Lateral and anteroposterior radiographs of a distal radius and ulna fracture before (A, B) and after reduction (C, D).

**Table 1 Parental satisfaction scores**

Questionnaire item	Mean	Range	Percent answering "10"
Preparation and instruction given	9.86	9-10	85.7
The care given by nurse pre-procedure	9.43	8-10	71.4
The care given by doctor pre-procedure	9.86	9-10	85.7
The suitability of environment	9.57	8-10	71.4
The experience of the child	8.57	3-10	71.4
The care given by the nurse post-procedure	10	10	100
The care given by doctor post-procedure	9.86	9-10	85.7
Overall parent satisfaction	9.71	9-10	71.4

event found in this multi-centre study<sup>[24]</sup>. With that risk being further reduced if no other sedatives, such as propofol or fentanyl, were used in conjunction. Earlier works by Green *et al*<sup>[31]</sup>, support these findings as they found 3.9% of children having respiratory adverse events and 8.4% having vomiting. Furthermore they found that co-administering drugs (anticholinergics and benzodiazepines), which were to reduce the risk, in fact made them worse<sup>[31]</sup>.

In our small study, we found no serious adverse events but three children had vomiting. High parental satisfaction scores in this pilot study demonstrate its acceptance amongst the families whose children had procedural sedation. All children had definitive reduction and stabilisation which resulted in an excellent functional outcome. This is contrary to a recent study comparing ketamine vs propofol for closed reduction of paediatric both bone forearm fractures which found 35% and 48% unacceptable alignment respectively at 4 wk<sup>[32]</sup>. However

their institution used a splint unlike ours which used a completed moulded cast to maintain reduction. An explanation which they admittedly acknowledge<sup>[32]</sup>. This finding is supported by another recent study that found only 8.8% children had displaced to an unacceptable standard if a moulded cast was used<sup>[13]</sup>. An outcome which is impressive considering only Entonox and intranasal diamorphine was used for reduction analgesia<sup>[13]</sup>. Nevertheless our result reinforces the finding that ketamine can give effective pain relief and sedation to allow thorough manipulation that resulted in fractures that were reduced and immobilised appropriately. The only major disadvantage we found with ketamine in our paediatric ED was the length of stay which was longer than normal. It was 5 h and 11 min which is beyond our National Health Service 4-h target. A target which was met using Entonox and intranasal diamorphine with a mean time of 3 h and 51 min<sup>[13]</sup>. Still it is a parameter which can be improved as the greatest cause of lost

time is administrative. Our mean result of 181 min to sedation from diagnosis of fracture could improve once this protocol becomes established as routine.

Like many studies, this study has limitations. Due to the range of forearm fracture types along with small numbers, we are unable to give clear fracture displacement cut-off guidelines to which should be safely managed in the ED. However a recent international multi-centre study survey sought to evaluate and establish the clinical practice of reducing paediatric forearm fractures<sup>[11]</sup>. The results of 111 paediatric ED physicians at 12 tertiary children hospitals found that ketamine was the most commonly (88%) and most frequently (55%) used procedural sedation agent followed by intranasal fentanyl and Entonox. The survey found that most ED physicians would tolerate a “no reduction required policy” for distal forearm fractures up to 20 degrees and 10 degrees for children less than 5 and 10 years old, respectively. It also indicated that majority of ED physicians would prefer fractures with obvious clinical deformity to be managed by the orthopaedic team in theatre due to lack of experience. The survey study also did not define a cut-off which was deemed unacceptable to be treated in the ED. However closely interpreting their survey results, the authors inferred from a clinical vignette with a 25 degree angulated fracture that 74% of physicians would treat that injury in the ED with procedural sedation. In our study we successfully treated fractures with a mean angulation of 45°. Another larger (100 children) study definitively treated 90% of forearm fractures with a mean of 28° of dorsal angulation in the ED with Entonox and intranasal diamorphine<sup>[13]</sup>. Our and the latter study, both utilised an interdepartmental protocol by which the ED physician gave the sedation and an orthopaedic doctor with fracture reduction experience managed the forearm. This may account for the success in both practical studies and the hesitancy found in the survey study of ED physicians to manipulate deformed fractures. Nonetheless the authors of this paper feel that most paediatric forearm fractures, irrespective of deformity angulation, can be treated in the ED as long as they feel that the fracture pattern is reducible and can be maintained for the duration of its healing.

Other weaknesses acknowledged include, the small number of patients and a lack of comparative procedural sedation agents, but as it was an audit of quality of improvement, the study had to be completed in a reasonable time for a single agent. However our prospective study design meant that we had good data uptake, capturing a variety of outcomes which validates its use in clinical practice. It also ensured a clear protocol, which meant that all children got the same method and delivery of care which makes analysis more robust in terms of reproducibility in everyday practice. Lastly our study demonstrated the success that can be achieved with a team effort using a variety of specialties and skillsets to deliver a service which at heart is at the benefit of the child and the family.

In conclusion, ketamine sedation for children is safe and cost-effective for treating displaced fractures of the radius and ulna, it is associated with a high level of satisfaction.

## ARTICLE HIGHLIGHTS

### Research background

Children forearm fractures account for up to 40% of fractures that present to the emergency department (ED), majority which could be managed there.

### Research motivation

This study improved the quality of care given to children with deformed forearm fractures in the ED.

### Research objectives

The main aim of this quality improvement project was to determine if ketamine sedation is a safe and cost-effective way of treating deformed paediatric forearm fractures in the ED.

### Research methods

Over a set 4 mo period we prospectively evaluated a new ketamine protocol for paediatric ED procedural sedation. All eligible children with significantly displaced or unstable fractures of the radius and ulna that presented during daylight weekday hours that needed closed reduction and moulded casting were included.

### Research results

A total of 10 forearm fractures with a mean 45° angulation deformity were definitively treated in the ED with ketamine procedural sedation. The cost saving was £1470 for each child compared if the patient was taken to theatre. Overall mean parental satisfaction was 9.6 out of 10.

### Research conclusions

Ketamine procedural sedation in the paediatric population is a safe and cost effective method for the treatment of displaced forearm fractures.

### Research perspectives

Majority of paediatric forearm fracture, irrespective of displacement, can be treated in the ED as long as the fracture pattern is reducible and can be maintained safely in a moulded cast for the duration of its healing.

## REFERENCES

- 1 **Naranje SM**, Erali RA, Warner WC Jr, Sawyer JR, Kelly DM. Epidemiology of Pediatric Fractures Presenting to Emergency Departments in the United States. *J Pediatr Orthop* 2016; **36**: e45-e48 [PMID: 26177059 DOI: 10.1097/BPO.0000000000000595]
- 2 **Rennie L**, Court-Brown CM, Mok JY, Beattie TF. The epidemiology of fractures in children. *Injury* 2007; **38**: 913-922 [PMID: 17628559 DOI: 10.1016/j.injury.2007.01.036]
- 3 **Mäyränpää MK**, Mäkitie O, Kallio PE. Decreasing incidence and changing pattern of childhood fractures: A population-based study. *J Bone Miner Res* 2010; **25**: 2752-2759 [PMID: 20564246 DOI: 10.1002/jbmr.155]
- 4 **Galano GJ**, Vitale MA, Kessler MW, Hyman JE, Vitale MG. The most frequent traumatic orthopaedic injuries from a national pediatric inpatient population. *J Pediatr Orthop* 2005; **25**: 39-44 [PMID: 15614057]
- 5 **Sinikumpu JJ**, Victorzon S, Antila E, Pokka T, Serlo W. Nonoperatively treated forearm shaft fractures in children show good long-term recovery. *Acta Orthop* 2014; **85**: 620-625 [PMID: 25238437 DOI: 10.3109/17453674.2014.961867]
- 6 **Jones K**, Weiner DS. The management of forearm fractures in children: a plea for conservatism. *J Pediatr Orthop* 1999; **19**:

- 811-815 [PMID: 10573354 DOI: 10.1097/01241398-199911000-00021]
- 7 Noonan KJ, Price CT. Forearm and distal radius fractures in children. *J Am Acad Orthop Surg* 1998; **6**: 146-156 [PMID: 9689186 DOI: 10.5435/00124635-199805000-00002]
  - 8 Pace JL. Pediatric and Adolescent Forearm Fractures: Current Controversies and Treatment Recommendations. *J Am Acad Orthop Surg* 2016; **24**: 780-788 [PMID: 27755262 DOI: 10.5435/JAAOS-D-15-00151]
  - 9 Franklin CC, Robinson J, Noonan K, Flynn JM. Evidence-based medicine: management of pediatric forearm fractures. *J Pediatr Orthop* 2012; **32** Suppl 2: S131-S134 [PMID: 22890452 DOI: 10.1097/BPO.0b013e318259543b]
  - 10 Meyer S, Grundmann U, Gottschling S, Kleinschmidt S, Gortner L. Sedation and analgesia for brief diagnostic and therapeutic procedures in children. *Eur J Pediatr* 2007; **166**: 291-302 [PMID: 17205245 DOI: 10.1007/s00431-006-0356-0]
  - 11 Schofield S, Schutz J, Babl FE; Paediatric Research in Emergency Departments International Collaborative (PREDICT). Procedural sedation and analgesia for reduction of distal forearm fractures in the paediatric emergency department: a clinical survey. *Emerg Med Australas* 2013; **25**: 241-247 [PMID: 23759045 DOI: 10.1111/1742-6723.12074]
  - 12 Drendel AL, Kelly BT, Ali S. Pain assessment for children: overcoming challenges and optimizing care. *Pediatr Emerg Care* 2011; **27**: 773-781 [PMID: 21822093 DOI: 10.1097/PEC.0b013e31822877f7]
  - 13 Kurien T, Price KR, Pearson RG, Dieppe C, Hunter JB. Manipulation and reduction of paediatric fractures of the distal radius and forearm using intranasal diamorphine and 50% oxygen and nitrous oxide in the emergency department: a 2.5-year study. *Bone Joint J* 2016; **98-B**: 131-136 [PMID: 26733526 DOI: 10.1302/0301-620X.98B1.36118]
  - 14 McCarty EC, Mencio GA, Walker LA, Green NE. Ketamine sedation for the reduction of children's fractures in the emergency department. *J Bone Joint Surg Am* 2000; **82-A**: 912-918 [PMID: 10901305 DOI: 10.2106/00004623-200007000-00002]
  - 15 Ben-Amitay G, Kosov I, Reiss A, Toren P, Yoran-Hegesh R, Kotler M, Mozes T. Is elective surgery traumatic for children and their parents? *J Paediatr Child Health* 2006; **42**: 618-624 [PMID: 16972969 DOI: 10.1111/j.1440-1754.2006.00938.x]
  - 16 Stargatt R, Davidson AJ, Huang GH, Czarnecki C, Gibson MA, Stewart SA, Jansen K. A cohort study of the incidence and risk factors for negative behavior changes in children after general anesthesia. *Paediatr Anaesth* 2006; **16**: 846-859 [PMID: 16884468 DOI: 10.1111/j.1460-9592.2006.01869.x]
  - 17 Jordan RW, Aquilina A, Westacott DJ, Cooke S. A comparison of ketamine sedation and general anaesthesia for manipulation of paediatric forearm fractures. *Acta Orthop Belg* 2016; **82**: 836-842 [PMID: 29182126]
  - 18 Atkinson P, French J, Nice CA. Procedural sedation and analgesia for adults in the emergency department. *BMJ* 2014; **348**: g2965 [PMID: 24812113 DOI: 10.1136/bmj.g2965]
  - 19 Tobias JD, Leder M. Procedural sedation: A review of sedative agents, monitoring, and management of complications. *Saudi J Anaesth* 2011; **5**: 395-410 [PMID: 22144928 DOI: 10.4103/1658-354X.87270]
  - 20 Kost S, Roy A. Procedural sedation and analgesia in the pediatric emergency department: A review of sedative pharmacology. *Clinical Pediatric Emergency Medicine* 2010; **11**: 233-243 [DOI: 10.1016/j.cpem.2010.08.002]
  - 21 Domino EF. Taming the ketamine tiger. 1965. *Anesthesiology* 2010; **113**: 678-684 [PMID: 20693870 DOI: 10.1097/ALN.0b013e3181ed09a2]
  - 22 Green SM. The safety of ketamine for emergency department pediatric sedation. *J Oral Maxillofac Surg* 1995; **53**: 1232-1233 [PMID: 7562186 DOI: 10.1016/0278-2391(95)90654-1]
  - 23 Green SM, Rothrock SG, Harris T, Hopkins GA, Garrett W, Sherwin T. Intravenous ketamine for pediatric sedation in the emergency department: safety profile with 156 cases. *Acad Emerg Med* 1998; **5**: 971-976 [PMID: 9862587 DOI: 10.1111/j.1553-2712.1998.tb02773.x]
  - 24 Bhatt M, Johnson DW, Chan J, Taljaard M, Barrowman N, Farion KJ, Ali S, Beno S, Dixon A, McTimoney CM, Dubrovsky AS, Sourial N, Roback MG; Sedation Safety Study Group of Pediatric Emergency Research Canada (PERC). Risk Factors for Adverse Events in Emergency Department Procedural Sedation for Children. *JAMA Pediatr* 2017; **171**: 957-964 [PMID: 28828486 DOI: 10.1001/jamapediatrics.2017.2135]
  - 25 Sacchetti A, Stander E, Ferguson N, Maniar G, Valko P. Pediatric Procedural Sedation in the Community Emergency Department: results from the ProSCED registry. *Pediatr Emerg Care* 2007; **23**: 218-222 [PMID: 17438433 DOI: 10.1097/PEC.0b013e31803e176c]
  - 26 Wolff J. The classic: on the inner architecture of bones and its importance for bone growth. 1870. *Clin Orthop Relat Res* 2010; **468**: 1056-1065 [PMID: 20162387 DOI: 10.1007/s11999-010-1239-2]
  - 27 Lew VK, Lalwani K, Palermo TM. Factors affecting parental satisfaction following pediatric procedural sedation. *J Clin Anesth* 2010; **22**: 29-34 [PMID: 20206848 DOI: 10.1016/j.jclinane.2009.02.012]
  - 28 Price CT, Scott DS, Kurzner ME, Flynn JC. Malunited forearm fractures in children. *J Pediatr Orthop* 1990; **10**: 705-712 [PMID: 2250053 DOI: 10.1097/01241398-199011000-00001]
  - 29 Vardy JM, Dignon N, Mukherjee N, Saffi DM, Balachandran G, Taylor S. Audit of the safety and effectiveness of ketamine for procedural sedation in the emergency department. *Emerg Med J* 2008; **25**: 579-582 [PMID: 18723707 DOI: 10.1136/emj.2007.056200]
  - 30 Kidd LR, Lyons SC, Lloyd G. Paediatric procedural sedation using ketamine in a UK emergency department: a 7 year review of practice. *Br J Anaesth* 2016; **116**: 518-523 [PMID: 26893406 DOI: 10.1093/bja/aev555]
  - 31 Green SM, Roback MG, Krauss B, Brown L, McGlone RG, Agrawal D, McKee M, Weiss M, Pitetti RD, Hostetler MA, Wathen JE, Treston G, Garcia Pena BM, Gerber AC, Losek JD; Emergency Department Ketamine Meta-Analysis Study Group. Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. *Ann Emerg Med* 2009; **54**: 158-168.e1-4 [PMID: 19201064 DOI: 10.1016/j.annemergmed.2008.12.011]
  - 32 Morrison T, Carender C, Kilbane B, Liu RW. Procedural Sedation With Ketamine Versus Propofol for Closed Reduction of Pediatric Both Bone Forearm Fractures. *Orthopedics* 2017; **40**: 288-294 [PMID: 28877328 DOI: 10.3928/01477447-20170824-01]

P- Reviewer: Liu JY S- Editor: Wang JL L- Editor: A  
E- Editor: Li D



## Retraction note to four articles published in *World Journal of Orthopaedics*

Quanjun Cui

Quanjun Cui, Editor-in-Chief of *World Journal of Orthopaedics*, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

ORCID number: Quanjun Cui (0000-0003-4285-4488).

Author contributions: Cui Q wrote this retraction note.

Conflict-of-interest statement: No potential conflicts of interest relevant to this article were reported.

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: Quanjun Cui, MD, Professor, Vice Chair for Research, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, 400 Ray C Hunt Dr, Charlottesville, VA 22908, United States. [qc4q@hscmail.mcc.virginia.edu](mailto:qc4q@hscmail.mcc.virginia.edu)  
Telephone: +1-434-2430266  
Fax: +1-434-2430242

Received: February 24, 2018

Revised: March 1, 2018

Accepted: March 7, 2018

Article in press: March 7, 2018

Published online: March 18, 2018

© The Author(s) 2018. Published by Baishideng Publishing Group Inc. All rights reserved.

Cui Q. Retraction note to four articles published in *World Journal of Orthopaedics*. *World J Orthop* 2018; 9(3): 58-59 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i3/58.htm>  
DOI: <http://dx.doi.org/10.5312/wjo.v9.i3.58>

### RETRACTION NOTE

Retraction Note to four articles published in *World Journal of Orthopaedics*: (1) Iwamoto J, Sato Y, Takeda T, Matsumoto H. Return to sports activity by athletes after treatment of spondylolysis. *World J Orthop* 2010; 1(1):26-30 PMID: 22474624 DOI: 10.5312/wjo.v1.i1.26; (2) Iwamoto J, Sato Y, Takeda T, Matsumoto H. Effectiveness of exercise for osteoarthritis of the knee: A review of the literature. *World J Orthop* 2011; 2(5):37-42 PMID: 22474634 DOI: 10.5312/wjo.v2.i5.37; (3) Iwamoto J, Sato Y, Takeda T, Matsumoto H. Analysis of stress fractures in athletes based on our clinical experience. *World J Orthop* 2011; 2(1):7-12 PMID: 22474626 DOI: 10.5312/wjo.v2.i1.7; and (4) Iwamoto J, Takada T, Sato Y, Matsumoto H. Effect of risedronate on speed of sound in postmenopausal women with osteoporosis. *World J Orthop* 2013; 4(4): 316-322 PMID: 24147269 DOI: 10.5312/wjo.v4.i4.316.

These articles<sup>[1-4]</sup> have been retracted at the request of the Editors-in-Chief as misconduct over authorship of the paper was detected and confirmed.

The Editors-in-Chief recently received communications concerning about the misconduct over the authorship and the integrity of the study. Editorial Office has conducted an investigation and has contacted the authors concerning the allegation. Evidence obtained by the Editorial Office including authors' statements confirmed the misconduct by the authors. One of the conditions of submission of a paper for publication in the journal is that authors declare that all authors must meet authorship criteria. As such these articles represent an abuse of the scientific publishing system. The Editors-in-Chief take a very strong view on this matter and apologies are offered to readers of the journal that this was not detected during the submission process.

### REFERENCES

- 1 Iwamoto J, Sato Y, Takeda T, Matsumoto H. Return to sports

- activity by athletes after treatment of spondylolysis. *World J Orthop* 2010; **1**: 26-30 [PMID: 22474624 DOI: 10.5312/wjo.v1.i1.26]
- 2 **Iwamoto J**, Sato Y, Takeda T, Matsumoto H. Effectiveness of exercise for osteoarthritis of the knee: A review of the literature. *World J Orthop* 2011; **2**: 37-42 [PMID: 22474634 DOI: 10.5312/wjo.v2.i5.37]
- 3 **Iwamoto J**, Sato Y, Takeda T, Matsumoto H. Analysis of stress fractures in athletes based on our clinical experience. *World J Orthop* 2011; **2**: 7-12 [PMID: 22474626 DOI: 10.5312/wjo.v2.i1.7]
- 4 **Iwamoto J**, Sato Y, Takeda T, Matsumoto H. Effect of risedronate on speed of sound in postmenopausal women with osteoporosis. *World J Orthop* 2013; **4**: 316-322 [PMID: 24147269 DOI: 10.5312/wjo.v4.i4.316]

**S- Editor:** Cui LJ **L- Editor:** A **E- Editor:** Li RF





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 April 18; 9(4): 60-71



**W****J****O**

# World Journal of Orthopedics

**Contents**

Monthly Volume 9 Number 4 April 18, 2018

**MINIREVIEWS**

- 60 Why total knees fail-A modern perspective review  
*Lum ZC, Shieh AK, Dorr LD*

**ORIGINAL ARTICLE****Basic Study**

- 65 Snapping elbow-A guide to diagnosis and treatment  
*Bjerre JJ, Finn Johannsen E, Rathcke M, Krogsgaard MR*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Wing-Hoi Cheung, BSc, PhD, Associate Professor, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong, Hong Kong, China

**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 Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central and Scopus.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Li-Jun Cui*  
**Proofing Editorial Office Director:** *Ya-Juan Ma*

**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, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com>

[www.wjgnet.com/2218-5836/editorialboard.htm](http://www.wjgnet.com/2218-5836/editorialboard.htm)

**EDITORIAL OFFICE**  
 Xiu-Xia Song, Director  
*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 April 18, 2018

**COPYRIGHT**  
 © 2018 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.f6publishing.com>

## Why total knees fail-A modern perspective review

Zachary C Lum, Alvin K Shieh, Lawrence D Dorr

Zachary C Lum, Alvin K Shieh, Department of Orthopaedic Surgery, Davis Medical Center, University of California, Sacramento, CA 95817, United States

Lawrence D Dorr, Department of Orthopaedic Surgery, Keck Medical Center of University of Southern California, Los Angeles, CA 90033, United States

ORCID number: Zachary C Lum (0000-0002-5871-8539); Alvin K Shieh (0000-0002-3087-7124); Lawrence D Dorr (0000-0002-9664-2416).

Author contributions: All authors contributed to the manuscript.

Conflict-of-interest statement: No potential conflicts of interest relevant to this article were reported.

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: Zachary C Lum, MD, Surgeon, Department of Orthopaedic Surgery, Davis Medical Center, University of California, 4860 Y Street, Suite 3800, Sacramento, CA 95817, United States. [zacharylum@gmail.com](mailto:zacharylum@gmail.com)  
Telephone: +1-916-7342807

Received: January 4, 2018

Peer-review started: January 5, 2018

First decision: January 31, 2018

Revised: March 6, 2018

Accepted: April 1, 2018

Article in press: April 1, 2018

Published online: April 18, 2018

arthroplasty (TKA) failures included aseptic loosening, instability and malalignment. As polyethylene production improved, modes of failure from polyethylene wear and subsequent osteolysis became less prevalent. Newer longitudinal studies report that infection has become the primary acute cause of failure with loosening and instability remaining as the overall greatest reasons for revision. Clinical database and worldwide national registries confirm these reports. With an increasing amount of TKA operations performed in the United States, and with focus on value-based healthcare, it is imperative to understand why total knees fail.

**Key words:** Total knee arthroplasty failure mechanism; Total knee arthroplasty failure mode; Revision total knee arthroplasty; Periprosthetic joint infection; Aseptic loosening total knee; Total knee arthroplasty instability

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** With increasing number of revision total knee arthroplasty (TKAs) being performed, tighter control on healthcare costs and value based care may occur. Surgeons are tasked with the responsibility to avoid risk factors for revision TKA. Newer longitudinal studies report that infection has become the primary acute cause of failure with loosening and instability remaining as the overall greatest reasons for revision. The surgeon must be aware of the risk factors and preventative measures for these failure modes, including preoperative management, surgical techniques and enhanced materials.

Lum ZC, Shieh AK, Dorr LD. Why total knees fail-A modern perspective review. *World J Orthop* 2018; 9(4): 60-64 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i4/60.htm>  
DOI: <http://dx.doi.org/10.5312/wjo.v9.i4.60>

### Abstract

Historically, the most common mechanism of total knee

### INTRODUCTION

With more total knee arthroplasty (TKA) operations

being performed and patients' lifespan increasing, there is an ever-growing number with this operation in the United States. Based upon 2010 data, an estimated 4.7 million individuals (3.0 million females, 1.7 million males) are living in the United States with a total knee. Additionally as the average age for TKA is becoming younger and living longer, the total number of revisions performed increases. By 2020, it is estimated 1.3 million TKAs will be performed along with 127000 revisions<sup>[1]</sup>. Also, with focus on value-based healthcare, and government bundled payment initiatives, it is imperative to understand why total knees fail<sup>[2]</sup>.

## HISTORICAL PERSPECTIVE

In 1982, Rand *et al*<sup>[3]</sup> reported 227 knees undergoing revision in the Mayo Clinic registry data from 1970 to 1980. Within those revisions, average time from initial arthroplasty to failure was 2.7 years with loosening (34.9%) being the major cause for TKA failure. Instability and malalignment were second and third at 16.7% and 14.8%, respectively. Component malposition, periprosthetic fracture and patellofemoral complications were all around 5%. Periprosthetic joint infections were reported to be exceedingly rare at 0.2% (but this will become the leading cause of revision). The dominance of loosening was likely because of high use of the older hinge prosthesis designs such as the Guepar that resulted in increased interface stresses and loosening.

In 1988, Moreland described the etiology of total knee failures, and loosening and instability were still the leading causes with secondary reasons being infection, extensor mechanism disruption, arthrofibrosis, periprosthetic fracture and complex regional pain syndrome<sup>[4]</sup>. Loose implants were caused by inappropriate bony resection, poor ligamentous balancing, cement technique, patient factors such as high activity level, implant constraint level, and osteolysis. Instability had the characteristics of varus/valgus malalignment, imbalance of the flexion-extension gap, anteroposterior laxity and patellofemoral subluxation/dislocation. Moreland concluded a majority of failure mechanisms is under the surgeon's technical control.

In 2001, Fehring *et al*<sup>[5]</sup> reported early (< 5 year) failure mechanisms between 1986 and 1999. Their most common identified etiology for failure in 279 knees was now infection at 38%. Aseptic loosening of cemented implants had plummeted to 3% with lack of cementless TKA ingrowth at 13%, and polyethylene wear/osteolysis which causes loosening at 7%. Instability was still high at 26% with patellofemoral failures (usually instability) being 8%. Five percent had miscellaneous problems such as arthrofibrosis, malalignment, or periprosthetic fracture. They also concluded some of these causes could be improved by surgical technique and perioperative care. They proposed that infection prevention could be reduced by addressing wound healing problems (such as albumin > 3.5 g/L, preoperative total lymphocyte count (TLC) > 1500 cells/mm<sup>3</sup>, and transferrin level > 200),

reducing traffic in the operating room (OR), appropriate sterile technique and managing the operating room air environment. Their emphasis was that early failures could be controlled to improve implant longevity.

Sharkey *et al*<sup>[6]</sup> won the 2002 Knee Society award paper for their review of TKA failures. They categorized their 212 TKA failures into early (< 2 years) and late (> 2 years). Early failures most commonly were infection in 25% of knees, instability (21%), arthrofibrosis (17%) and loosening (16%). Late failure groups were similar in numerical order to the overall cohort, reporting polyethylene wear (44%), loosening (34%) and instability (22%) as the major 3 causes. Overall, the most common failure mechanisms in decreasing order were estimated at 27% polyethylene wear, 25% component loosening, 21% instability and 17% infection. These authors also concluded that attention to surgical technique and postoperative care by the surgeon was very important but because multiple failure mechanisms were often seen in one case, some of the failure mechanisms could be addressed by design and material improvement.

In 2006, Mulhall *et al*<sup>[7]</sup> reported on overall, early (< 2 years) and late (> 2 years) TKA failure mechanisms in 318 patients. Overall the majority of revisions were after 2 years and thus mechanical issues were primarily the cause. Early revisions (31% of patients) were primarily due to infection (25%), with ultimate outcomes worse than the outcomes of knees with revision for aseptic loosening. Revisions after 2 years (69% of their patients), were mechanical with instability (29%), polyethylene wear (25%) and component loosening (41%). They also concluded that patient factors such as diabetic control, and technical factors such implant design could be modifiable between early and late failures to improve patient outcomes.

The summary of these longitudinal studies is that infection has become the primary acute cause of failure with loosening and instability remaining as the overall greatest reasons for revision (Table 1). The researchers' conclusions are that most failures can be avoided by improvements in technique and design.

## SHIFT TO NEWER POLYETHYLENE MANUFACTURING PROCESSES

Design improvement has impacted failure mechanisms. As polyethylene production improved, modes of failure from polyethylene wear and subsequent osteolysis became less prevalent. Hossain *et al*<sup>[8]</sup> studied revisions of 349 knees between 1999 and 2008. Infection had become the most common reason for revision overall, both in early (< 2 years) and in late (> 2 years) failures. Aseptic loosening was second most common, followed by polyethylene wear.

Hossain *et al*<sup>[8]</sup> and Schroer *et al*<sup>[9]</sup> performed multi-center analysis of etiology for 844 revision TKAs between 2010 and 2011. They found aseptic loosening (31.2%), instability (18.7%) and infection (16.2%) as the 3 major overall causes with early failures continuing to

**Table 1 Clinical studies by failure mechanism (%)**

Ref.	Knees	Loosening	Infection	Instability	Malalignment	Poly/Lysis	Other
Rand <i>et al</i> <sup>[3]</sup>	227	34.9	0.2	16.7	14.8	-	5
Moreland <i>et al</i> <sup>[4]</sup>		MC		2 <sup>nd</sup> MC			
Fehring <i>et al</i> <sup>[5]</sup>	279	3%	38	26	5	7	5
Sharkey <i>et al</i> <sup>[6]</sup>	212	17/34	25/7.8	21/22	12/12	12/44	
Mulhall <i>et al</i> <sup>[7]</sup>	318	41	25/7	29	9	6/25	
Hossain <i>et al</i> <sup>[8]</sup>	349	3/12	12/21	4/3	4/3	1/12	
Schroer <i>et al</i> <sup>[9]</sup> and Lombardi <i>et al</i> <sup>[10]</sup>	844	19/31	23/16	25/19	8/7	1/10	2/1
Sharkey <i>et al</i> <sup>[11]</sup>	781	22/40	38/28	12/8	3/2	2/4	
Delanois <i>et al</i> <sup>[13]</sup>	337597	20.3	20.4	7.5		2.6	12
Kasahara <i>et al</i> <sup>[18]</sup>	147	40	24	9		9	18
Koh <i>et al</i> <sup>[19]</sup>	634	33	38	7	1	15	8

Overall percentages listed above may be approximates. Percentages may not be mutually exclusive<sup>[6,8-10]</sup>. Sharkey *et al*<sup>[6]</sup> table: First number is early (< 2 year) failures, second number is late failures; Hossain *et al*<sup>[8]</sup>: First number is early (< 2 year) failures, second is late failures; Schroer and Lombardi *et al*<sup>[9-10]</sup>: First number is early (< 2 year) failures, second is overall failures.

be infection (23%) and instability (25%). Secondary causes included polyethylene wear (10%), arthrofibrosis (6.9%) and malalignment (6.6%) with stiff knees being predominantly an early cause for revision among these. Polyethylene wear represented less than 1% of revisions performed under 5 years, but remained common in revision failures greater than 15 years in knees with older polyethylene which confirmed benefit of newer polyethylene improvements. Aseptic loosening was the only failure mechanism consistent in all time intervals<sup>[10]</sup>.

Sharkey *et al*<sup>[11]</sup> provided a 10-year update on their experience of performing 781 revisions of 10,003 total procedures (7.8% revision rate). They too saw a dramatic decrease from 25% to 3.5% in the rate of polyethylene wear as the cause of revision. Early (< 2 years) failures were 37.6% of all failures with infection most common, and more than half (51.4%) of the 62.4% late (> 2 years) revisions were aseptic loosening.

## CLINICAL DATA VS LARGE DATA

While most published results of total knee revisions came from single-center or regional multi-center data, larger and more diverse cohorts have become possible with the advent of nationwide databases. In the United States, the Nationwide Inpatient Sample (NIS) database, developed in 1988 and revamped in 2012, provides a random sampling of approximately 20% of all United States hospital discharges and encompasses smaller community hospitals as well as larger urban academic centers. Using this registry, Bozic *et al*<sup>[12]</sup> reported on 60355 TKA revision procedures performed between 2005 and 2006 across the United States. They found the most common cause of revision knee arthroplasty was infection at 25.2%, implant loosening at 16.1%, and implant failure or breakage at 9.7%. While noting the limitations of large administrative data, they reported their findings were similar to other studies that found infection to be the greatest contributing factor to at least early failure mechanisms.

Delanois *et al*<sup>[13]</sup> provided an updated look at the revision rate in the United States using the same NIS database from 2009 through 2013 and reaffirmed that the two leading causes of revision TKA were infection and aseptic loosening at 20.4% and 20.3%, respectively. Both NIS-based papers reported on higher revision rates in the South with upwards of one-third of all revision performed in southern states. Although demographic data was provided, with well over 70% of all revision occurring in Caucasians, no analysis was performed to identify regional differences in failure mechanisms. All-component revision was the most common operation with a total healthcare cost averaging more than \$75000.

## WORLD EXPERIENCES

The use of nationwide registries began in 1975 with the Swedish Knee Arthroplasty Register (SKAR) through the efforts of Goran Bauer<sup>[14]</sup>. Since then, other countries have followed their example, including Finland (1980), Norway (1987), Denmark (1995), South Korea (1989), New Zealand (1998), England and Wales (2003), and Japan (2010) (Table 2).

The initial success of the registries prompted the creation of the Nordic Arthroplasty Register Association, a compilation of arthroplasty databases from Sweden, Denmark, and Norway who shared similar demographics, healthcare and socioeconomic systems, and were in close proximity to each other. Subsequently Niimaki in 2015 combined five worldwide registries: Australia, New Zealand, Norway, Sweden, and England and Wales<sup>[15]</sup>. The leading indication for revision in each country was aseptic loosening (range 22.8%-29.7%). Pain was the second leading indication for revision in Norway and New Zealand (27.4% and 22.0% respectively), while infection was the second most common cause in the three remaining countries (20.6%-21.7%). However, Niimaki identifies inconsistencies in the categorization of failure mechanisms amongst the registries that clouds the ability to interpret the results. For example, pain and malalignment are not categories in the Swedish

**Table 2 Large data and registry data by total knee arthroplasty failure mechanism**

Ref.	Knees	Loosening, %	Infection, %	Instability, %	Poly/Lysis, %	Other, %
Bozic <i>et al</i> <sup>[12]</sup>	60435	16	25	7	8	
Delanois <i>et al</i> <sup>[13]</sup>	337597	20.3	20.4	7.5	2.6	12
Sadoghi <i>et al</i> <sup>[23]</sup>	36307	30	15	6	8	
Australia 2003-2012 <sup>[24]</sup>	31698	30	22	6	2	
England/Wales 2011-2012 <sup>[25]</sup>	5135	35	23	14	20	
New Zealand 1999-2011 <sup>[26]</sup>	4603	37	24	7	n/a	
Norway 1994-2009 <sup>[27]</sup>	3445	24	13	10	5	
Sweden 2001-2010 <sup>[28]</sup>	3375	26	23	13	5	

Overall percentages are listed above.

registry whereas polyethylene wear is not an option in the United Kingdom registry. He therefore suggests that standardizing the registries can help in compiling data to draw more compelling conclusions. Nevertheless, the data consistently supports aseptic loosening as the most common indication for revision TKA at similar rates to those found in the United States. Siqueira *et al*<sup>[16]</sup> reviewed TKA failure modes outside the United States by combining both large clinical studies and national joint registry results. They concluded 1994-2012 national databases and reported aseptic loosening as the most common reason for failure, with infection being second.. Clinical studies reported by large tertiary referral centers also reported aseptic loosening as being the most common overall reason for revision, while early failures were due to infection. The data from Europe, although not consistently reported, confirms that the emphasis on failure needs to be focused on infection early and overall on aseptic loosening.

The performance of TKA is quickly rising in Asia, where over half the world's population resides, and it is especially prevalent in women, who have an 8-fold increased rate of primary TKAs compared to men<sup>[17]</sup>. Kasahara *et al*<sup>[18]</sup> recently reported on a multicenter experience of five arthroplasty referral centers in Japan with 140 TKA revision from 2006-2011. Overall revision rate was 3.3% with aseptic loosening as the leading cause at 40% followed by infection at 24%. Koh *et al*<sup>[19]</sup> from South Korea, published a retrospective review of 634 revisions at 19 centers from 2008-2012, representing an estimated 10% of all procedures performed in the country. Overall revision rate was 3.0% with infection (38%) as the leading cause followed by aseptic loosening (33%) and wear (13%). Similar to other reports, they separated failures as early (< 2 years) versus late (> 2 years); infection dominated as the leading cause of early failure (77%) but it was only 23% of all late failures with aseptic loosening (44%) the most common as it is throughout the world. Wear was only an indication for revision in the late failure group and comprised 18%. With limited long-term registry data, it remains unclear whether the failure patterns of knee replacement differ between the Western and Eastern Hemispheres, but it seems that Asia is more similar to the United States with infection the early

cause while Aseptic loosening dominates all time periods in Europe.

## CURRENT CHALLENGES

As total knee arthroplasty increases in demand and prevalence, the number of revision total knee operations increase as well. Kurtz *et al*<sup>[2]</sup> predicted the number of revision TKAs performed in the United States by 2030 would be greater than 250000 operations. Hamilton *et al*<sup>[20]</sup> reviewed risk factors for revision TKA which includes obesity, young age and comorbid conditions as the most common in both the United States as well as other countries.

Altogether, patients across the world with total knee arthroplasties face similar challenges today. Aseptic loosening/instability and infection are the primary causes of failure. Countries with higher rates of unicompartmental or bicompartmental arthroplasties increasingly cite pain as an indication for revision, though that remains highly dependent on the patient, the surgeon, and the reporting mechanism. As surgical implants continue to evolve, surgical techniques to achieve long-term fixation and careful attention to infection prevention remain the most challenging obstacles to achieve excellent long-term outcomes.

As the understanding of how total knees fail, orthopedic research has focused on improving the technology and surgical technique as well as in depth study of infection. There is a large volume of research dedicated towards lowering infection risk factors such as patient optimization, efficient surgery, maintaining ideal intraoperative conditions, and decreasing postoperative complications<sup>[21]</sup>. Surgical technique has focused on understanding patient anatomy, and personalizing leg alignment and component position. Bellemans *et al*<sup>[22]</sup> evaluated anatomic and mechanical axis in 250 asymptomatic adults. They reported that 32% of males and 17% of females had a natural mechanical axis of 3 degrees varus or greater. A common etiology of instability is malrotation of the femoral component relative to the tibia. Meticulous attention to surgical technique is critical as instrumentation is unable to adjust for this rotation. Personalization of a patient's normal anatomy and ligament balancing may be helpful to lower revision rates

and patient satisfaction.

## CONCLUSION

With increasing number of revision TKAs being performed, tighter control on healthcare costs and value based care may occur. Surgeons are tasked with the responsibility to avoid risk factors for revision TKA. Newer longitudinal studies report that infection has become the primary acute cause of failure with loosening and instability remaining as the overall greatest reasons for revision. Knowledge of total knee arthroplasty failure mechanisms allows the arthroplasty surgeon to be aware of individual risk factors, and to strategize management for each patient to optimize their care.

## REFERENCES

- 1 **Maradit Kremers H**, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, Jiranek WA, Berry DJ. Prevalence of Total Hip and Knee Replacement in the United States. *J Bone Joint Surg Am* 2015; **97**: 1386-1397 [PMID: 26333733 DOI: 10.2106/JBJS.N.01141]
- 2 **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]
- 3 **Rand JA**, Bryan RS. Revision after total knee arthroplasty. *Orthop Clin North Am* 1982; **13**: 201-212 [PMID: 7063192]
- 4 **Moreland JR**. Mechanisms of failure in total knee arthroplasty. *Clin Orthop Relat Res* 1988; (**226**): 49-64 [PMID: 3335107]
- 5 **Fehring TK**, Odum S, Griffin WL, Mason JB, Nadaud M. Early failures in total knee arthroplasty. *Clin Orthop Relat Res* 2001; (**392**): 315-318 [PMID: 11716402]
- 6 **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]
- 7 **Mulhall KJ**, Ghomrawi HM, Scully S, Callaghan JJ, Saleh KJ. Current etiologies and modes of failure in total knee arthroplasty revision. *Clin Orthop Relat Res* 2006; **446**: 45-50 [PMID: 16672871 DOI: 10.1097/01.blo.0000214421.21712.62]
- 8 **Hossain F**, Patel S, Haddad FS. Midterm assessment of causes and results of revision total knee arthroplasty. *Clin Orthop Relat Res* 2010; **468**: 1221-1228 [PMID: 20058112 DOI: 10.1007/s11999-009-1204-0]
- 9 **Schroer WC**, Berend KR, Lombardi AV, Barnes CL, Bolognesi MP, Berend ME, Ritter MA, Nunley RM. Why are total knees failing today? Etiology of total knee revision in 2010 and 2011. *J Arthroplasty* 2013; **28**: 116-119 [PMID: 23954423 DOI: 10.1016/j.arth.2013.04.056]
- 10 **Lombardi AV Jr**, Berend KR, Adams JB. Why knee replacements fail in 2013: patient, surgeon, or implant? *Bone Joint J* 2014; **96-B**: 101-104 [PMID: 25381419 DOI: 10.1302/0301-620X.96B11.34350]
- 11 **Sharkey PF**, Lichstein PM, Shen C, Tokarski AT, Parvizi J. Why are total knee arthroplasties failing today--has anything changed after 10 years? *J Arthroplasty* 2014; **29**: 1774-1778 [PMID: 25007726 DOI: 10.1016/j.arth.2013.07.024]
- 12 **Bozic KJ**, Kurtz SM, Lau E, Ong K, Chiu V, Vail TP, Rubash HE, Berry DJ. The epidemiology of revision total knee arthroplasty in the United States. *Clin Orthop Relat Res* 2010; **468**: 45-51 [PMID: 19554385 DOI: 10.1007/s11999-009-0945-0]
- 13 **Delanois RE**, Mistry JB, Gwam CU, Mohamed NS, Choksi US, Mont MA. Current Epidemiology of Revision Total Knee Arthroplasty in the United States. *J Arthroplasty* 2017; **32**: 2663-2668 [PMID: 28456561 DOI: 10.1016/j.arth.2017.03.066]
- 14 **Robertsson O**, Lewold S, Knutson K, Lidgren L. The Swedish Knee Arthroplasty Project. *Acta Orthop Scand* 2000; **71**: 7-18 [PMID: 10743986 DOI: 10.1080/00016470052943829]
- 15 **Niinimäki TT**. The reasons for knee arthroplasty revisions are incomparable in the different arthroplasty registries. *Knee* 2015; **22**: 142-144 [PMID: 25596073 DOI: 10.1016/j.knee.2014.12.007]
- 16 **Siqueira MB**, Klika AK, Higuera CA, Barsoum WK. Modes of failure of total knee arthroplasty: registries and realities. *J Knee Surg* 2015; **28**: 127-138 [PMID: 25419836 DOI: 10.1055/s-0034-1396014]
- 17 **Kim HA**, Kim S, Seo YI, Choi HJ, Seong SC, Song YW, Hunter D, Zhang Y. The epidemiology of total knee replacement in South Korea: national registry data. *Rheumatology (Oxford)* 2008; **47**: 88-91 [PMID: 18077497 DOI: 10.1093/rheumatology/kem308]
- 18 **Kasahara Y**, Majima T, Kimura S, Nishiike O, Uchida J. What are the causes of revision total knee arthroplasty in Japan? *Clin Orthop Relat Res* 2013; **471**: 1533-1538 [PMID: 23385774 DOI: 10.1007/s11999-013-2820-2]
- 19 **Koh JJ**, Cho WS, Choi NY, Kim TK; Kleos Korea Research Group. Causes, risk factors, and trends in failures after TKA in Korea over the past 5 years: a multicenter study. *Clin Orthop Relat Res* 2014; **472**: 316-326 [PMID: 23982406 DOI: 10.1007/s11999-013-3252-8]
- 20 **Hamilton DF**, Howie CR, Burnett R, Simpson AH, Patton JT. Dealing with the predicted increase in demand for revision total knee arthroplasty: challenges, risks and opportunities. *Bone Joint J* 2015; **97-B**: 723-728 [PMID: 26033049 DOI: 10.1302/0301-620X.97B6.35185]
- 21 **Parvizi J**, Gehrke T; International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. *J Arthroplasty* 2014; **29**: 1331 [PMID: 24768547 DOI: 10.1016/j.arth.2014.03.009]
- 22 **Bellemans J**, Colyn W, Vandenneucker H, Victor J. The Chitranjan Ranawat award: is neutral mechanical alignment normal for all patients? The concept of constitutional varus. *Clin Orthop Relat Res* 2012; **470**: 45-53 [PMID: 21656315 DOI: 10.1007/s11999-011-1936-5]
- 23 **Sadoghi P**, Liebensteiner M, Agreiter M, Leithner A, Böhler N, Labek G. Revision surgery after total joint arthroplasty: a complication-based analysis using worldwide arthroplasty registers. *J Arthroplasty* 2013; **28**: 1329-1332 [PMID: 23602418 DOI: 10.1016/j.arth.2013.01.012]
- 24 **Australian Orthopaedic Association (AOA)**. National Joint Replacement Registry (NJRR) Hip and Knee Arthroplasty Annual Report 2012. Available from: URL: <https://aoanjrr.sahmri.com/documents/10180/60142/Annual%20Report%202012?version=1.3&t=1361226543157>
- 25 **National Joint Registry (NJR) for England and Wales 9th Annual Report 2012**. Available from: URL: [http://www.njrcentre.org.uk/njrcentre/Portals/0/Documents/England/Reports/9th\\_annual\\_report/NJR%209th%20Annual%20Report%202012.pdf](http://www.njrcentre.org.uk/njrcentre/Portals/0/Documents/England/Reports/9th_annual_report/NJR%209th%20Annual%20Report%202012.pdf)
- 26 **New Zealand Orthopaedic Association the New Zealand Joint Registry Thirteen Year Report 2012**. Available from: URL: <http://www.cdhb.govt.nz/NJR/reports/A2D65CA3.pdf>
- 27 **The Norwegian Arthroplasty Register (NAR) Report June 2010**. Available from: URL: [http://nrlwebihelsenet/eng/Report\\_2010.pdf](http://nrlwebihelsenet/eng/Report_2010.pdf)
- 28 **The Swedish Knee Arthroplasty Register (SKAR) Annual Report 2012**. Available from: URL: [http://www.kneenkose/english/online/uploaded/Files/117\\_SKAR2012\\_Engl\\_10.pdf](http://www.kneenkose/english/online/uploaded/Files/117_SKAR2012_Engl_10.pdf)

P- Reviewer: Cui QJ, Liu JY, Unver B, Wu CC S- Editor: Wang XJ

L- Editor: A E- Editor: Li D



## Basic Study

**Snapping elbow-A guide to diagnosis and treatment**

Jonathan Jetsmark Bjerre, Finn Elkjær Johannsen, Martin Rathcke, Michael Rindom Krogsgaard

Jonathan Jetsmark Bjerre, Martin Rathcke, Michael Rindom Krogsgaard, Section for Sportstraumatology M51, Bispebjerg-Frederiksberg Hospital, Copenhagen NV DK-2400, Denmark

Finn Elkjær Johannsen, Institute for Sportsmedicine M81, Bispebjerg-Frederiksberg Hospital, Copenhagen NV DK-2400, Denmark

ORCID number: Jonathan Jetsmark Bjerre (0000-0002-6477-3219); Finn Elkjær Johannsen (0000-0002-3732-6229); Martin Rathcke (0000-0002-5629-7371); Michael Rindom Krogsgaard (0000-0002-9976-4865).

**Author contributions:** Rathcke M and Krogsgaard MR designed the study; Johannsen FE and Rathcke M recorded the case stories; Bjerre JJ did the literature analyses; Bjerre JJ and Krogsgaard MR wrote the paper.

**Institutional review board statement:** The project was considered a register research project by Danish Committee System on Health Research Ethics.

**Conflict-of-interest statement:** None of the authors have any proprietary interests in the materials described in the article.

**Data sharing statement:** Not applicable.

**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:** Michael Rindom Krogsgaard, MD, PhD, Professor, Surgeon, Section for Sportstraumatology M51, Bispebjerg-Frederiksberg Hospital, Bispebjerg Bakke 23, Copenhagen NV DK-2400, Denmark. [michael.rindom.krogsgaard@regionh.dk](mailto:michael.rindom.krogsgaard@regionh.dk)  
Telephone: +45-31226817

Received: November 11, 2017

Peer-review started: November 11, 2017

First decision: December 11, 2017

Revised: December 21, 2017

Accepted: March 1, 2018

Article in press: March 2, 2018

Published online: April 18, 2018

**Abstract****AIM**

To develop practical guidelines for diagnosis and treatment of the painful snapping elbow syndrome (SE).

**METHODS**

Clinical studies were searched in the databases PubMed and Scopus for the phrases "SE", "snapping triceps", "snapping ulnar nerve" and "snapping annular ligament". A total of 36 relevant studies were identified. From these we extracted information about number of patients, diagnostic methods, patho-anatomical findings, treatments and outcomes. Practical guidelines for diagnosis and treatment of SE were developed based on analysis of the data. We present two illustrative patient cases-one with intra-articular pathology and one with extra-articular pathology.

**RESULTS**

Snapping is audible, palpable and often visible. It has a lateral (intra-articular) or medial (extra-articular) pathology. Snapping over the medial humeral epicondyle is caused by dislocation of the ulnar nerve or a part of the triceps tendon, and is demonstrated by dynamic ultrasonography. Treatment is by open surgery. Lateral snapping over the radial head has an intra-articular pathology: A synovial plica, a torn annular ligament or a meniscus-like remnant from the foetal elbow. Pathology can be visualized by conventional arthrography, magnetic resonance (MR) arthrography, high resolution magnetic resonance imaging (MRI) and arthroscopy, while conventional MRI and radiographs often turn out normal. Treatment is by arthroscopic or eventual open resection. Early surgical intervention is recommended as

the snapping can damage the ulnar nerve (medial) or the intra-articular cartilage (lateral). If medial snapping only occurs during repeated or loaded extension/flexion of the elbow (in sports or work) it may be treated by reduction of these activities. Differential diagnoses are loose bodies (which can be visualized by radiographs) and postero-lateral instability (demonstrates by clinical examination). An algorithm for diagnosis and treatment is suggested.

### CONCLUSION

The primary step is establishment of laterality. From this follows relevant diagnostic measures and treatment as defined in this guideline.

**Key words:** Elbow; Arthroscopy; Surgery; Diagnosis; Ultrasonography; Snapping

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Elbow snapping is medial or lateral. Medial snapping is caused by dislocation of the ulnar nerve or a part of the triceps tendon, demonstrated clinically and by dynamic ultrasonography. Treatment is transposition of the nerve and/or resection of the snapping tendon. Lateral snapping is intra-articular by a synovial plica, a torn annular ligament or a meniscus-like remnant from the foetal elbow, demonstrated by arthrography, magnetic resonance arthrography, high resolution magnetic resonance imaging or arthroscopy. Treatment is arthroscopic resection. Early surgical intervention is recommended to reduce tissue damage. Medial snapping promoted by repeated, loaded activities might be treated by activity reduction.

Bjerre JJ, Finn Johannsen E, Rathcke M, Krogsgaard MR. Snapping elbow-A guide to diagnosis and treatment. *World J Orthop* 2018; 9(4): 65-71 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i4/65.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i4.65>

## INTRODUCTION

Snapping elbow (SE) is a rare condition, which can be confused with more common pathologies like an intra-articular free body, lateral epicondylitis or medial epicondylitis. Symptoms from SE occur during dynamic activities. Therefore, standard radiographs and magnetic resonance imaging (MRI) are often normal, leaving risk that the condition remains undiagnosed.

It is useful to distinguish between lateral and medial snapping, as pathology, diagnostic strategy and treatment are different in the two situations.

We suggest a practical guideline for diagnosis and treatment of SE, based on our own experience with three elbows in two patients and a review of the literature.

## MATERIALS AND METHODS

Literature was searched in Pubmed with four phrases: "SE" (resulting in 85 hits), "snapping triceps" (39 hits), "snapping ulnar nerve" (31 hits) and "snapping annular ligament" (9 hits). A similar search was performed in Scopus, and two additional, relevant articles were identified. We excluded papers that had no information about diagnostic strategy or treatment as well as articles in other languages than English or Scandinavian.

One article was not available online or from the author.

From the 36 remaining articles (Figure 1) information about number of patients, diagnostic method, patho-anatomical findings, treatments and outcomes was extracted.

We treated two cases with principally different reasons for snapping.

### Case reports 1

A 16-year-old boy with painful locking of the right elbow during 2-3 years. No trauma in history. Standard MR scanning and radiographs were normal. A sore clicking was found at the lateral epicondyle with 80°-90° of elbow flexion, and it was most painful with simultaneous pronation. He had similar but milder symptoms on the left side. Both elbows were stable and with normal range of motion.

Dynamic ultrasound raised suspicion of a tight, lateral part of the triceps tendon as the cause of snapping. However, extraarticular injection of 1 cc Carbocain plus 1 cc of Depomedrol® in this area did not relieve the symptoms.

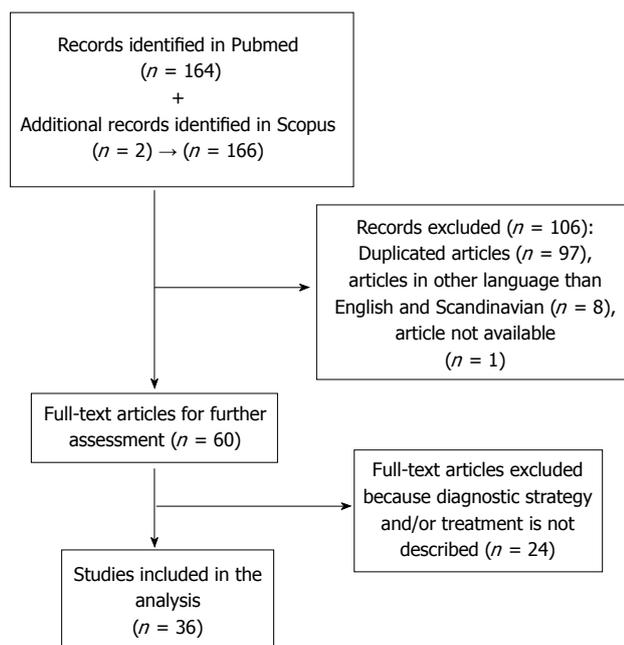
At arthroscopy an inter-positioned lunar plica antero-laterally (video 1) was resected, and a tight chord of capsule in relation to the plica was loosened.

Pain and snapping disappeared after the operation. A similar condition was treated by arthroscopy in the left elbow 6 wk later. At 3-years follow-up he felt a slight tenderness in the right elbow from time to time, but it was different from his preoperative pain and he had no snapping. The left elbow was symptom free.

### Case reports 2

A 16-year-old boy with painful medial elbow clicking bilaterally for over a year, in particular during heavy resistance training of the triceps muscle. The snapping was mildly painful, but he had post-exercise pain that forced him to reduce the training load. Popping of the triceps muscle over the medial epicondyle at 110° of flexion was suspected by clinical examination (video 2). There were no neurological symptoms and a negative Tinel's test in relation to the ulnar nerve. Dynamic sonography visualized the popping tissue (video 3), but it was not possible to distinguish if this originated from the ulnar nerve or a part of the triceps tendon. The elbow appeared otherwise normal.

Open surgery showed that snapping was caused by



**Figure 1** From the 36 remaining articles information about number of patients, diagnostic method, patho-anatomical findings, treatments and outcomes was extracted.

dislocation of the ulnar nerve (video 4). The sulcus was therefore deepened 3 mm, the nerve was repositioned, and a part of the medial triceps tendon was transpositioned to form a cover over the sulcus. This resolved the snapping condition, and the patient was able to exercise normally between two and five months postoperatively. Then a feeling of instability of the nerve during heavy resistance training occurred, but it was pain free. One year after the operation he stopped regular training and had no symptoms. This was still the case at 3-years follow-up. Both patients declared, that they were satisfied with the treatment, and with their present experience they would agree to be operated for SE again, if necessary.

## RESULTS

The identified clinical reports of SE are summarized in the tables. They are divided into lateral, intra-articular cases (Table 1) and medial, extra-articular cases (Table 2) of SE. There are 105 cases of lateral snapping with a mean age of 39.7 years (range 11-66) and 42 cases of medial snapping with a mean age of 28.7 years (range 9-65). In some patients SE was presumably triggered by athletic performance (throwing and tennis typical for lateral snapping, and weightlifting, decathlon and dumbbell exercises for medial snapping). However, the majority of cases could not be connected to sports.

This review does not allow to make an estimate of the incidence of SE, but based on the reported cases, the different pathologies can be ranked with intraarticular plica as the most common, followed by medially snapping triceps (rare), snapping ulnar nerve (rare), snapping annular ligament (very rare)

and extremely rare pathologies: snapping medial antebrachial cutaneous nerve, intraarticular meniscus and laterally snapping triceps.

### ***Intra-articular, lateral snapping***

Intra-articular snapping is caused by annular ligament pathology, lateral meniscal remnants or hypertrophic synovial plicae<sup>[1-12]</sup>. Clicking due to dynamic impingement of these soft tissues is difficult to demonstrate with static MRI.

Three reports describe snapping caused by anomalous meniscal remnants<sup>[5,7]</sup>. Standard MRI did not reveal the pathology, but it was demonstrated by MRI- and radiographic arthrography, respectively.

In one report a plica was demonstrated by radiographic arthrography and MRI as a protruding shadow<sup>[11]</sup>. Contrast MRI was used to diagnose three cases of a snapping plica<sup>[10]</sup>. In one case conventional MRI raised suspicion of a small, pathological structure, which was diagnosed as a plica by high-resolution MRI<sup>[13]</sup>.

By conventional MRI it was in most cases not possible to visualize lateral SE pathology, and diagnoses were established with MR-arthrography, high resolution MRI or radiographic arthrography. With arthroscopy the intra-articular snapping pathology can be visualized and treated in the same procedure by resection of the snapping tissue.

Arthroscopic resection of plicae or meniscus-like tissues was standard treatment, except in three cases of open resection. Reported results were good with either method (Table 1), as elbow function normalized in the majority of cases.

One patient who had postero-lateral rotatory elbow instability did not improve, but the snapping might have been caused by instability and not by intra-articular pathology<sup>[2]</sup>.

### ***Extra-articular, medial snapping***

Subluxation of either the ulnar nerve or a medial part of the triceps tendon, or of both can cause extra-articular snapping of the elbow<sup>[15-26]</sup>. In many cases it can be recognized by thorough physical examination. The ulnar nerve snaps in the interval 70-90 degrees of flexion, and the triceps around 115 degrees. These snaps are usually visible and audible<sup>[27]</sup>. By dynamic ultrasound and dynamic MRI<sup>[28]</sup> the snapping tissue can be visualized, but interpretation of the anatomical structures is not always conclusive, as described in our case 2<sup>[20,27,28]</sup>. Dislocation of the snapping structure is not visible on standard MRI with the elbow extended, but with the elbow flexed dislocation can often be demonstrated<sup>[29]</sup>.

A snapping triceps can be treated by either resection<sup>[19,22-23,25,30-34]</sup> or by suture of the snapping part to the main tendon<sup>[18,25]</sup>. Medial epicondylectomy was used in one case<sup>[19]</sup>. Ulnar nerve dislocation was treated by anterior transposition<sup>[16,26,35]</sup> or fixation of the nerve in the deepened cubital tunnel<sup>[35]</sup>.

**Table 1 Literature reports on intra-articular snapping elbow**

Report and year	No. of patients	Snapping Pathology	Diagnostic procedure	Treatment	Results
Akagi <i>et al</i> <sup>[1]</sup> , 1998	One	Snapping plica	Arthrogram, arthroscopy	Open arthrotomy	Complete recovery
Antuna <i>et al</i> <sup>[2]</sup> , 2001	Fourteen	Snapping plica	MRI, arthroscopic examination	Arthroscopic resection	Ten complete recoveries, two partial recoveries, two failures
Aoki <i>et al</i> <sup>[3]</sup> , 2003	Two	Snapping annular ligament	Arthroscopic examination	One had arthroscopic resection	One complete recovery after resection
Chai <i>et al</i> <sup>[4]</sup> , 2004	One	Snapping annular ligament	Ultrasonography	Arthroscopic resection	Relief of snapping
Fukase <i>et al</i> <sup>[13]</sup> , 2005	One	Snapping plica	Special MRI <sup>1</sup>	Open resection	Complete recovery
Huang <i>et al</i> <sup>[5]</sup> , 2005	One	Snapping meniscus	MR-arthrography	Arthroscopic resection	Complete recovery
Huang <i>et al</i> <sup>[6]</sup> , 2005	One	Snapping annular ligament	MRI, arthroscopic examination	Arthroscopic resection	Relief of snapping, less pain
Kang <i>et al</i> <sup>[7]</sup> , 2010	Two	Snapping meniscus	MRI, arthrography	Arthroscopic resection	Complete recovery
Maruyama <i>et al</i> <sup>[8]</sup> , 2010	One	Snapping annular ligament	Arthroscopy	Arthroscopic release of the ligament	Complete recovery
Brahe Pedersen <i>et al</i> <sup>[9]</sup> , 2017	Sixtyfour	Hypertrophic synovial plica	Clinical examination and ultrasound	Arthroscopic resection	Significant improvement in Oxford Elbow score after 3 and 22 mo
Shinohara <i>et al</i> <sup>[14]</sup> , 2010	One	Tight fibrous structure	MRI, arthroscopy	Arthroscopic resection	Complete recovery
Steinert <i>et al</i> <sup>[10]</sup> , 2008	Three	Hypertrophic synovial plica	Contrast MRI (in two), arthroscopy	Arthroscopic resection	Complete recovery
Tateishi <i>et al</i> <sup>[11]</sup> , 2005	One	Snapping plica	MRI, arthrogram	Open resection	Complete recovery

<sup>1</sup>Special MRI was high-resolution magnetic resonance imaging of the elbow using microscopy coils. MRI: Magnetic resonance imaging; MR: Magnetic resonance.

One case series reported snapping of the medial antebrachial cutaneous nerve<sup>[35]</sup> that is medial to the medial humeral condyle (and not posterior as the ulnar nerve). There were no neurological symptoms reported from this nerve, and snapping was observed intra-operatively. In three of the four patients there was also snapping of triceps and the ulnar nerve. In retrospective review of the preoperative ultrasonography investigations, snapping of the medial antebrachial cutaneous nerve could be identified. In three patients the medial antebrachial cutaneous nerve was transpositioned and in one it was decompressed, while triceps- and ulnar nerve dislocation was also treated in three.

The most common symptoms were pain and painful snapping, and neurological symptoms from the ulnar nerve were rarely reported.

## DISCUSSION

It is useful to divide snapping of the elbow joint into lateral and medial snapping, as these are caused by different pathological conditions and can easily be distinguished clinically (Figure 2).

Generally, intra-articular snapping pathology cannot be demonstrated by conventional MRI, and MR-arthrography, high resolution MRI or radiographic arthrography is necessary<sup>[1,6,9,13]</sup>.

In a series with 14 patients treated for lateral, intra-articular plicas snapping over the radial head by arthroscopic resection<sup>[2]</sup>, ten patients were completely relieved of their symptoms, two still experienced mild pain and one was asymptomatic for 4 years, but then

experienced recurrence of symptoms. In one patient treatment failed, but he was subsequently diagnosed with postero-lateral instability as the possible cause of the snapping phenomenon. In the largest series reported<sup>[9]</sup> with 64 patients, there was a significant and clinically relevant increase in Oxford Elbow Score three and 22 mo after operation. Therefore, surgical treatment of the lateral SE is successful in the majority of cases, and it should preferably be performed arthroscopically, as this permits optimal visualization of the joint and minimize morbidity. Non-surgical treatment has not been described for lateral SE.

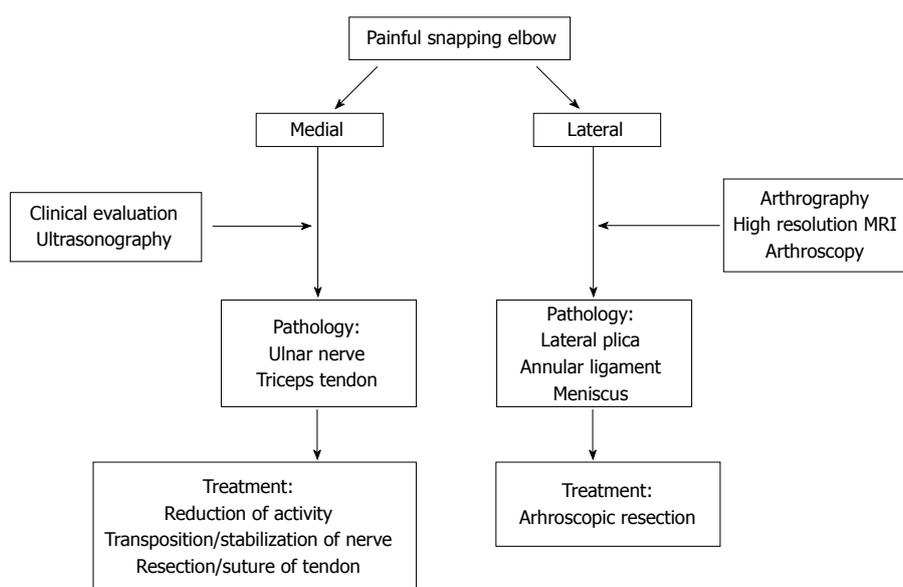
Dynamic ultrasonography is the best to visualize medial snapping, but it can be difficult to identify which anatomic structure that is snapping (as described in case 2)<sup>[20,25,27]</sup>. Fabrizio *et al*<sup>[36]</sup> reported a variation of the triceps brachii with a thin fourth muscular head inserting on the medial part of the olecranon as a cause of medial snapping. An accessory snapping triceps tendon can clinically be confused with snapping of the ulnar nerve, as the two structures are closely located at the medial epicondyle. Watts described this diagnostic pitfall in a report of three cases<sup>[34]</sup>, of which two primary had transposition of the ulnar nerve and one a fixation of the nerve in the ulnar sulcus. In all three cases snapping persisted, and the cause was identified as a discrete accessory tendon originating from the triceps. The authors concluded from their series that a subluxing ulnar nerve does not snap, and that medial snapping is always caused by anterior sliding of a strip of the triceps tendon during elbow flexion.

Snapping of a medial part of the triceps muscle is recognized as a reason for continuous snapping after

**Table 2** Reports of extra-articular snapping elbow

Report and year	No. of cases	Snapping pathology	Diagnostic procedure	Treatment	Results
Anand <i>et al</i> <sup>[16]</sup> , 2012	One	Snapping ulnar nerve	Open surgery	Transposition of nerve	Complete recovery, returned to elite sport
Cesmebasi <i>et al</i> <sup>[35]</sup> , 2015	Four	Snapping medial antebrachial cutaneous nerve (4), triceps (3) and ulnar nerve (3)	Open surgery/sonography	Open decompression, stabilization or transposition of nerves, resection of tendon	Improvement (mild persistent symptoms to complete recovery)
Chuang <i>et al</i> <sup>[17]</sup> , 2016	One	Snapping triceps and subluxing ulnar nerve	Dynamic sonography	NSAIDs and reduction in repetitive elbow flexion activities at work	Partial improvement
Dreyfuss <i>et al</i> <sup>[18]</sup> , 1978	Two	Snapping triceps	Open reinsertion of the snapping part of the triceps	Reinsertion of the snapping tendon	1 complete recovery, 1 partial
Haws <i>et al</i> <sup>[30]</sup> , 1995	One	Snapping triceps	Open exploration	Open resection of tendon	Complete recovery
Hayashi <i>et al</i> <sup>[19]</sup> , 1984	One	Snapping triceps	Physical examination, radiographs, open surgery	Medial epicondylectomy and division of tendon	Complete recovery
Jacobson <i>et al</i> <sup>[20]</sup> , 2001	Three	Snapping ulnar nerve, snapping triceps	Dynamic sonography	Open "surgical treatment for each abnormality"	Not reported
Lasecki <i>et al</i> <sup>[21]</sup> , 2014	One	Snapping triceps and ulnar nerve	MRI and dynamic sonography	Not reported	Not reported
Minami <i>et al</i> <sup>[31]</sup> , 1999	One	Snapping triceps	Not reported	Open tendon resection	Complete recovery
Reis <i>et al</i> <sup>[22]</sup> , 1980	One	Snapping triceps	Open surgery	Open tendon resection	Complete recovery
Rolfesen <sup>[23]</sup> , 1970	One	Snapping triceps	Open surgery	Open tendon resection	Complete recovery
Spinner <i>et al</i> <sup>[32]</sup> , 2001	One	Snapping triceps	Physical examination	Open tendon Excision	Complete recovery
Spinner <i>et al</i> <sup>[24]</sup> , 1999	Two	Snapping triceps	Physical examination, MRI	Reduction in weight lifting	Symptoms only appeared during weight lifting
Spinner <i>et al</i> <sup>[33]</sup> , 1999	One	Snapping triceps lateral	Palpation and MRI	Open tendon resection	Complete recovery
Spinner <i>et al</i> <sup>[25]</sup> , 2000	Fifteen	Snapping triceps after operation for snapping ulnar nerve	Physical examination, MRI	Lateral transposition or excision of tendon (nine patients), six refused surgery	Complete relief of snapping in surgically treated patients. No relief in non-operated
Watts <i>et al</i> <sup>[34]</sup> , 2009	Three	Snapping triceps	Open exploration	Excision (two), tendon division (one)	Complete recovery
Xarchas <i>et al</i> <sup>[26]</sup> , 2007	Three	Snapping ulnar nerve	Palpation	Anterior nerve transposition (two), NSAIDs and change of job as waitress (one)	Complete recovery after surgery. Not reported for non-surgery

NSAIDs: Non-steroidal anti-inflammatory drugs; MRI: Magnetic resonance imaging.



**Figure 2** Snapping of the elbow joint into lateral and medial snapping caused by different pathological conditions and can easily be distinguished clinically.

ulnar nerve transposition<sup>[22-23,25,30-32,34]</sup>. It is unclear in these cases if the snapping triceps was unrecognised during ulnar nerve surgery or if it was a complication to dissection of the tendon during release of the ulnar nerve. However, we and others present cases of medial snapping, treated successfully by ulnar nerve surgery<sup>[20,26]</sup>. Therefore, the triceps should always be inspected in flexion and extension of the elbow during surgery for ulnar nerve snapping.

It is unknown to which extent the medial antebrachial cutaneous nerve is involved in medial snapping, as there is only one case report of this nerve as snapping structure<sup>[35]</sup>. It is challenging to decide by ultrasonography which anatomical structure that causes medial snapping<sup>[35]</sup> and the final diagnosis is established during operation. All snapping pathologies should be addressed.

Medial snapping in persons with repeated or loaded activities involving elbow flexion and extension during work (e.g., a waitress, a postman) or sports (weightlifting, body building) can be treated by reduction of these activities<sup>[17,24,26]</sup>. In other cases, surgical intervention should preferably be early, as intra-articular pathologies can lead to damage of the cartilage, and snapping of the ulnar nerve can lead to neuropathy<sup>[12,25]</sup>.

Intra-articular loose bodies and postero-lateral elbow instability can cause locking, which may be interpreted as lateral snapping<sup>[2,12]</sup>. Radiographs and CT are useful to identify intra-articular loose bodies, while postero-lateral instability is a clinical diagnosis. Also, lateral snapping is sometimes treated as epicondylitis, which is not a snapping condition.

In conclusion, SE is clinically divided into intra-articular (lateral) and extra-articular (medial) cases, based on the location of snapping. Intra-articular pathology is best visualized with high-resolution MRI, MR arthrography or radiographic arthrography. Arthroscopic or open resection of the pathological tissue is successful in most cases. Extra-articular pathology is best diagnosed by dynamic ultrasonography and during surgery. Solitary snapping of the ulnar nerve is extremely rare, and a triceps associated snapping tendon should always be suspected. Treatment is by open surgery.

## ARTICLE HIGHLIGHTS

### Research background

Patients with snapping elbow (SE) are seen by orthopaedic surgeons, rheumatologists and physical therapists, but the diagnosis is rare.

### Research motivation

Most health care workers have no clinical experience with SE, as it is a rare condition. Therefore, there is a risk of misdiagnosis and delay of relevant treatment. Snapping can be visible, audible and palpable, but usual diagnostic measures can fail to demonstrate pathology.

### Research objectives

From a literature search combined with our own clinical experience we wanted to analyse what is known about SE, its diagnosis and its treatment. The main purpose was to present a guideline to identify the patho-anatomical cause of

SE, its general binary categorization and the best treatment of each pathology.

### Research methods

Literature was searched in PubMed and Scopus and key points in diagnosis and treatment were identified. Two typical cases are described.

### Research results

Our review indicates that SE should be clinically divided into lateral and medial, and that diagnosis and treatment is a logic consequence of this. Lateral, intra-articular pathology is best diagnosed with high-resolution MRI, MR-arthrography or radiographic arthrography. Surgical intervention is the treatment of choice and successful in the majority of the cases. Medial, extra-articular pathology is best diagnosed by dynamic ultrasonography and during surgery. It is most commonly caused by subluxation of a medial part of the triceps tendon or the ulnar nerve. Treatment is by open surgery, except in patients with repeated, loaded activities during flexion and extension (at work or during sports), in which case symptoms may resolve by reduction of this activity.

### Research conclusions

This guideline suggests a standardized approach to diagnosis and treatment of patients with SE. As early surgical intervention is recommended because the snapping can damage nerve (medial) or cartilage (lateral), this guideline is a tool for better patient care.

### Research perspectives

There are no randomized studies on treatment of SE, but the largest series of 64 cases is on lateral SE, meaning that randomized controlled studies could be performed regarding treatment of this pathology. The other pathologies are too rare. There are probably many undiagnosed cases, and studies on incidence would describe the magnitude of this health problem.

## REFERENCES

- 1 **Akagi M**, Nakamura T. Snapping elbow caused by the synovial fold in the radiohumeral joint. *J Shoulder Elbow Surg* 1998; **7**: 427-429 [PMID: 9752657 DOI: 10.1016/S1058-2746(98)90037-4]
- 2 **Antuna SA**, O'Driscoll SW. Snapping plicae associated with radiocapitellar chondromalacia. *Arthroscopy* 2001; **17**: 491-495 [PMID: 11337715 DOI: 10.1053/jars.2001.20096]
- 3 **Aoki M**, Okamura K, Yamashita T. Snapping annular ligament of the elbow joint in the throwing arms of young brothers. *Arthroscopy* 2003; **19**: E4-E7 [PMID: 14551563 DOI: 10.1016/S0749-8063(03)00741-2]
- 4 **Chai JW**, Kim S, Lim HK, Bae KJ. Ultrasonographic diagnosis of snapping annular ligament in the elbow. *Ultrasonography* 2015; **34**: 71-73 [PMID: 25327527 DOI: 10.14366/ulg.14032]
- 5 **Huang GS**, Lee CH, Lee HS, Chen CY. A meniscus causing painful snapping of the elbow joint: MR imaging with arthroscopic and histologic correlation. *Eur Radiol* 2005; **15**: 2411-2414 [PMID: 15717195 DOI: 10.1007/s00330-005-2685-1]
- 6 **Huang GS**, Lee CH, Lee HS, Chen CY. MRI, arthroscopy, and histologic observations of an annular ligament causing painful snapping of the elbow joint. *AJR Am J Roentgenol* 2005; **185**: 397-399 [PMID: 16037511 DOI: 10.2214/ajr.185.2.01850397]
- 7 **Kang ST**, Kim TH. Lateral sided snapping elbow caused by a meniscus: two case reports and literature review. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 840-844 [PMID: 20151108 DOI: 10.1007/s00167-010-1076-6]
- 8 **Maruyama M**, Takahara M, Kikuchi N, Ito K, Watanabe T, Ogino T. Snapping elbow with congenital radial head dislocation: case report. *J Hand Surg Am* 2010; **35**: 981-985 [PMID: 20456870 DOI: 10.1016/j.jhssa.2010.02.026]
- 9 **Brahe Pedersen J**, Kristensen PK, Mønsted P, Thillemann TM. Short-term results after arthroscopic resection of synovial plicae in the radiohumeral joint: a case series of 64 procedures. *SICOT J* 2017; **3**: 42 [PMID: 28589876 DOI: 10.1051/sicotj/2017021]
- 10 **Steinert AF**, Goebel S, Rucker A, Barthel T. Snapping elbow

- caused by hypertrophic synovial plica in the radiohumeral joint: a report of three cases and review of literature. *Arch Orthop Trauma Surg* 2010; **130**: 347-351 [PMID: 19089437 DOI: 10.1007/s00402-008-0798-0]
- 11 **Tateishi K**, Tsumura N, Matsumoto T, Fujioka H, Kokubu T, Kuroda R, Shiba R, Kurosaka M. Bilateral painful snapping elbows triggered by daily dumbbell exercises: a case report. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 487-490 [PMID: 16261350 DOI: 10.1007/s00167-005-0692-z]
  - 12 **Ruch DS**, Papadonikolakis A, Campolattaro RM. The posterolateral plica: a cause of refractory lateral elbow pain. *J Shoulder Elbow Surg* 2006; **15**: 367-370 [PMID: 16679240 DOI: 10.1016/j.jse.2005.08.013]
  - 13 **Fukase N**, Kokubu T, Fujioka H, Iwama Y, Fujii M, Kurosaka M. Usefulness of MRI for diagnosis of painful snapping elbow. *Skeletal Radiol* 2006; **35**: 797-800 [PMID: 15940486 DOI: 10.1007/s00256-005-0940-9]
  - 14 **Shinohara T**, Horii E, Tatebe M, Yamamoto M, Okui N, Hirata H. Painful snapping elbow in patients with congenital radioulnar synostosis: report of two cases. *J Hand Surg Am* 2010; **35**: 1336-1339 [PMID: 20684930 DOI: 10.1016/j.jhsa.2010.05.006]
  - 15 **Kang JH**, Joo BE, Kim KH, Park BK, Cha J, Kim DH. Ultrasonographic and Electrophysiological Evaluation of Ulnar Nerve Instability and Snapping of the Triceps Medial Head in Healthy Subjects. *Am J Phys Med Rehabil* 2017; **96**: e141-e146 [PMID: 28151762 DOI: 10.1097/PHM.0000000000000706]
  - 16 **Anand A**, Campion NJ, Chakraverty R, Pimpalnerkar A. Bilateral snapping ulnar nerve syndrome in a professional decathlete – a rare case report and a review of the literature. *Eur Orthop Traumatol* 2012; **3**: 263-266 [DOI: 10.1007/s12570-012-0111-0]
  - 17 **Chuang HJ**, Hsiao MY, Wu CH, Özçakar L. Dynamic Ultrasound Imaging for Ulnar Nerve Subluxation and Snapping Triceps Syndrome. *Am J Phys Med Rehabil* 2016; **95**: e113-e114 [PMID: 26945221 DOI: 10.1097/PHM.0000000000000466]
  - 18 **Dreyfuss U**, Kessler I. Snapping elbow due to dislocation of the medial head of the triceps. A report of two cases. *J Bone Joint Surg Br* 1978; **60**: 56-57 [PMID: 627579]
  - 19 **Hayashi Y**, Kojima T, Kohno T. A case of cubital tunnel syndrome caused by the snapping of the medial head of the triceps brachii muscle. *J Hand Surg Am* 1984; **9A**: 96-99 [PMID: 6693751 DOI: 10.1016/S0363-5023(84)80194-X]
  - 20 **Jacobson JA**, Jebson PJ, Jeffers AW, Fessell DP, Hayes CW. Ulnar nerve dislocation and snapping triceps syndrome: diagnosis with dynamic sonography--report of three cases. *Radiology* 2001; **220**: 601-605 [PMID: 11526255 DOI: 10.1148/radiol.2202001723]
  - 21 **Lasecki M**, Olchowcy C, Pawluś A, Zaleska-Dorobisz U. The Snapping Elbow Syndrome as a Reason for Chronic Elbow Neuralgia in a Tennis Player - MR, US and Sonoelastography Evaluation. *Pol J Radiol* 2014; **79**: 467-471 [PMID: 25525475 DOI: 10.12659/PJR.891393]
  - 22 **Reis ND**. Anomalous triceps tendon as a cause for snapping elbow and ulnar neuritis: a case report. *J Hand Surg Am* 1980; **5**: 361-362 [PMID: 7419878 DOI: 10.1016/S0363-5023(80)80176-6]
  - 23 **Rolfson L**. Snapping triceps tendon with ulnar neuritis. Report on a case. *Acta Orthop Scand* 1970; **41**: 74-76 [PMID: 5453901 DOI: 10.3109/17453677008991979]
  - 24 **Spinner RJ**, Wenger DE, Barry CJ, Goldner RD. Episodic snapping of the medial head of the triceps due to weightlifting. *J South Orthop Assoc* 1999; **8**: 288-292 [PMID: 12132803]
  - 25 **Spinner RJ**, O'Driscoll SW, Jupiter JB, Goldner RD. Unrecognized dislocation of the medial portion of the triceps: another cause of failed ulnar nerve transposition. *J Neurosurg* 2000; **92**: 52-57 [PMID: 10616082 DOI: 10.3171/jns.2000.92.1.0052]
  - 26 **Xarchas KC**, Psillakis I, Koukou O, Kazakos KJ, Ververidis A, Verettas DA. Ulnar nerve dislocation at the elbow: review of the literature and report of three cases. *Open Orthop J* 2007; **1**: 1-3 [PMID: 19461901 DOI: 10.2174/1874325000701010001]
  - 27 **Spinner RJ**, Goldner RD. Snapping of the medial head of the triceps: diagnosis and treatment. *Tech Hand Up Extrem Surg* 2002; **6**: 91-97 [PMID: 16520623 DOI: 10.1097/00130911-200206000-00008]
  - 28 **Guillin R**, Marchand AJ, Roux A, Niederberger E, Duvauferrier R. Imaging of snapping phenomena. *Br J Radiol* 2012; **85**: 1343-1353 [PMID: 22744321 DOI: 10.1259/bjr/52009417]
  - 29 **Spinner RJ**, Hayden FR Jr, Hipps CT, Goldner RD. Imaging the snapping triceps. *AJR Am J Roentgenol* 1996; **167**: 1550-1551 [PMID: 8956595 DOI: 10.2214/ajr.167.6.8956595]
  - 30 **Haws M**, Brown RE. Bilateral snapping triceps tendon after bilateral ulnar nerve transposition for ulnar nerve subluxation. *Ann Plast Surg* 1995; **34**: 550-551 [PMID: 7639496 DOI: 10.1097/00006637-199505000-00017]
  - 31 **Minami A**, Kato H, Iwasaki N. Snapping of Triceps Tendon After Anterior Nerve Transposition for Recurrent Subluxation of the Ulnar Nerve. *Hand Surg* 1999; **4**: 193-196 [PMID: 11089180 DOI: 10.1142/S0218810499000253]
  - 32 **Spinner RJ**, Gabel GT. Latrogenic snapping of the medial head of the triceps after ulnar nerve transposition. *J South Orthop Assoc* 2001; **10**: 236-240 [PMID: 12132823]
  - 33 **Spinner RJ**, Goldner RD, Fada RA, Sotereanos DG. Snapping of the triceps tendon over the lateral epicondyle. *J Hand Surg Am* 1999; **24**: 381-385 [PMID: 10194025 DOI: 10.1053/jhsu.1999.0381]
  - 34 **Watts AC**, McEachan J, Reid J, Rymaszewski L. The snapping elbow: a diagnostic pitfall. *J Shoulder Elbow Surg* 2009; **18**: e9-e10 [PMID: 18667338 DOI: 10.1016/j.jse.2008.03.010]
  - 35 **Cesmebasi A**, O'driscoll SW, Smith J, Skinner JA, Spinner RJ. The snapping medial antebraichial cutaneous nerve. *Clin Anat* 2015; **28**: 872-877 [PMID: 26212210 DOI: 10.1002/ca.22601]
  - 36 **Fabrizio PA**, Clemente FR. Variation in the triceps brachii muscle: a fourth muscular head. *Clin Anat* 1997; **10**: 259-263 [PMID: 9213044 DOI: 10.1002/(SICI)1098-2353(1997)10:4:3.CO;2-N]

**P- Reviewer:** Kodde IF, Papachristou GC, Sinha A **S- Editor:** Cui LJ

**L- Editor:** A **E- Editor:** Li D





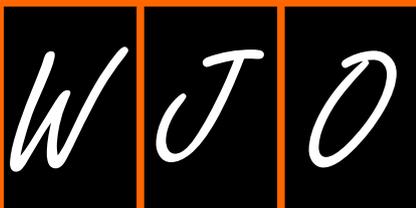
Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 May 18; 9(5): 72-77





**CASE REPORT**

- 72 Periosteal pseudotumor in complex total knee arthroplasty resembling a neoplastic process

*Chowdhry M, Dipane MV, McPherson EJ*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Florian Michael Baumann, MD, Associate Professor, Surgeon, Department of Trauma Surgery, Regensburg University Medical Center, Regensburg 93042, Germany

**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 Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central and Scopus.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Fang-Fang Ji*  
**Proofing Editorial Office Director:** *Ya-Juan Ma*

**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, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com>

[www.wjgnet.com/2218-5836/editorialboard.htm](http://www.wjgnet.com/2218-5836/editorialboard.htm)

**EDITORIAL OFFICE**  
 Ya-Juan Ma, Director  
*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 May 18, 2018

**COPYRIGHT**  
 © 2018 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.f6publishing.com>

## Periosteal pseudotumor in complex total knee arthroplasty resembling a neoplastic process

Madhav Chowdhry, Matthew V Dipane, Edward J McPherson

Madhav Chowdhry, Matthew V Dipane, Edward J McPherson, LA Orthopedic Institute, Los Angeles, CA 90057, United States

ORCID number: Madhav Chowdhry (0000-0003-0769-0326); Matthew V Dipane (0000-0001-5978-8662); Edward J McPherson (0000-0003-0327-4181).

**Author contributions:** All authors contributed equally to this paper in regards to conception and structure of this case report, data collection, literature review, drafting, critical revisions, and final approval of the final version.

**Informed consent statement:** A written informed consent was taken by the participant before the beginning of the study.

**Conflict-of-interest statement:** The authors of the study have no potential conflict of interest to declare.

**CARE Checklist (2013):** The authors have read the CARE Checklist (2013), and the manuscript was prepared and revised according to the CARE Checklist (2013).

**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:** Edward J McPherson, MD, FACS, Director, LA Orthopedic Institute, 2200 West Third Street, Suite 400, Los Angeles, CA 90057, United States. [edmcpherson@gmail.com](mailto:edmcpherson@gmail.com)  
Telephone: +1-213-2075660

Received: January 5, 2018

Peer-review started: January 6, 2018

First decision: January 23, 2018

Revised: January 30, 2018

Accepted: February 28, 2018

Article in press: February 28, 2018

Published online: May 18, 2018

### Abstract

This case report describes in detail an erosive distal diaphyseal pseudotumor that occurred 6 years after a complex endoprosthetic hinge total knee arthroplasty (TKA). A female patient had conversion of a knee fusion to an endoprosthetic hinge TKA at the age of 62. At her scheduled 6-year follow-up, she presented with mild distal thigh pain and radiographs showing a 6-7 cm erosive lytic diaphyseal lesion that looked very suspicious for a neoplastic process. An *en bloc* resection of the distal femur and femoral endoprosthesis was performed. Histologic review showed the mass to be a pseudotumor with the wear debris emanating from within the femoral canal due to distal stem loosening. We deduce that mechanized stem abrasion created microscopic titanium alloy particles that escaped *via* a small diaphyseal crack and stimulated an inflammatory response resulting in a periosteal erosive pseudotumor. The main lesson of this report is that, in the face of a joint replacement surgery of the knee, pseudotumor formation is a more likely diagnosis than a neoplastic process when encountering an expanding bony mass. Thus, a biopsy prior to *en bloc* resection, would be our recommended course of action any time a suspicious mass is encountered close to a TKA.

**Key words:** Pseudotumor; Total knee arthroplasty; Metallic wear debris; Loose implant

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Pseudotumor formation is a biologic response to microscopic metal particulate debris observed in metal-to-metal total hip bearings. It is considered non-

existent in total knee arthroplasty (TKA), where the bearing surface articulates metal-to-ultrahigh molecular weight polyethylene. This report describes a rare case of pseudotumor formation in an endoprosthesis hinge TKA, as a result of femoral stem loosening with metallic debris exiting through a small crack in the distal femoral diaphysis. This case reveals that pseudotumor formation should always be considered when evaluating an expanding mass around a TKA.

Chowdhry M, Dipane MV, McPherson EJ. Periosteal pseudotumor in complex total knee arthroplasty resembling a neoplastic process. *World J Orthop* 2018; 9(5): 72-77 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i5/72.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i5.72>

## INTRODUCTION

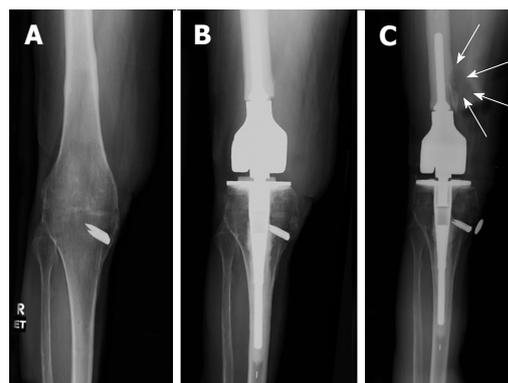
All orthopaedic devices when implanted into the human body have the potential to cause immunologic reaction. Most reactions occur as a result of particulate debris formation stemming from mechanical implant loosening, breakage, interface corrosion/fretting or articular bearing wear. In total joint arthroplasty, the dominant inflammatory reaction encountered is osteolysis/synovitis reaction<sup>[1,2]</sup>. This inflammatory response is a result of high molecular weight polyethylene (HMWPE) and/or poly-methyl-meth-acrylate (PMMA) particles that activate a macrophage-predominant reaction that, in the end, causes bone resorption and elicits a significant articular and, on occasion, periarticular synovitis<sup>[3]</sup>.

Another inflammatory reaction observed more recently in the last 2 decades is the pseudotumor phenomenon<sup>[4,5]</sup>. Its prevalence is almost exclusively associated with metal-to-metal articular total hip bearings<sup>[6]</sup>. The pseudotumor reaction is distinctly different than the classic HMWPE/PMMA induced osteolysis/synovitis reaction, as it is primarily a lymphocytic response to reactive metal debris. It is a non-neoplastic, sterile, solid and/or cystic lesion that frequently extends beyond the articular joint capsule<sup>[7]</sup>. Although macrophages are seen in the pseudotumor response, the primary cellular response is lymphocytic<sup>[8]</sup>.

As one would expect, pseudotumor formation in TKA is very rare as there are no knee systems that articulate metal-to-metal. In this report we describe a large pseudotumor that presented as a distal femoral-diaphyseal periosteal soft tissue tumor 6 years after insertion of an endoprosthesis hinge TKA. We present histologic review of the pseudotumor and forensically deduce the origin of the metal debris that resulted in this inflammatory soft tissue response.

## CASE REPORT

This unique case involves a 68-year-old female who was hit by a car as a pedestrian crossing the street and was



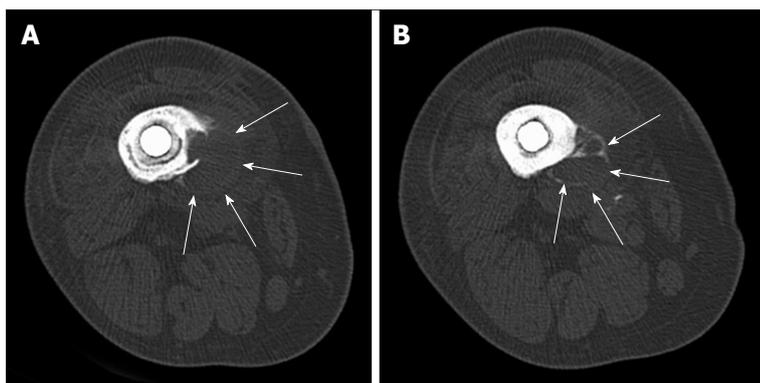
**Figure 1** AP radiograph of right knee reviewing life-cycle of right knee reconstruction. A: Pre-operative radiograph showing successful knee fusion. The area over the medial staple has a split thickness skin graft (STSG) of 5 cm x 7 cm. Patient ambulates with full weight bearing on the right leg. Localized osteopenia is present in the knee region; B: Four months post-operative radiograph of cemented endoprosthesis hinge total knee arthroplasty using a modified Zimmer Biomet RS (Reduced Size) OSS Knee system. Note particularly the placement of the joint line in the cephalad direction. This was purposefully done to avoid dissecting near the area of the tibia with the STSG. Also, note the relatively short cemented femoral stem; C: Radiograph at 6 years. Patient complains of mild pain for the past 5 months. Note the erosive lesion in the distal femoral diaphysis. White arrows outline the soft tissue mass surrounding the erosive lesion. Also note the radiolucent line in the distal femoral diaphysis. This suggests cement-bone separation, likely from repetitive cantilever bend.

dragged along for a distance. She was 35-year-old at the time of injury which resulted in an open right tibial fracture with severe soft tissue loss over the proximal one-third of the tibia. She had a total of 5 surgeries over 3 years to treat her fracture and overlying infection. A medial gastrocnemius flap was rotated to cover the medial knee and tibia. Her ultimate reconstruction was a knee fusion at age 38, which was stabilized with a cast rather than internal fixation. Her knee fusion surgery was successful. Since her fusion she has had no problems with infection.

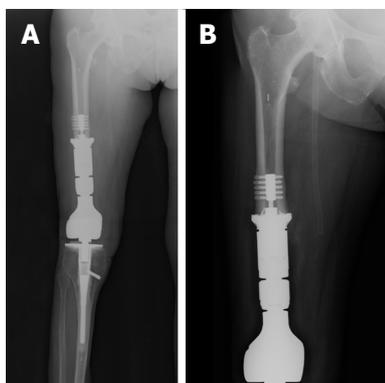
Twenty-four years later, at the age of 62, she presented to our clinic with severe pain in her back and ipsilateral hip. She wanted her knee fusion taken down and converted to a TKA. A careful pre-operative review indicated intact muscular firing of her quadriceps musculature. Clinically, she had an intact patellar tendon into the tibial tubercle. Studies evaluating for residual infection at the knee and tibia were negative. Her pre-operative radiograph of the knee fusion is shown in Figure 1A.

A salvage TKA was performed with segmental resection of her distal femur. She was reconstructed with a custom reduced-size endoprosthesis hinge device based upon the Orthopaedic Salvage System (OSS™) knee design (Zimmer-Biomet, Warsaw, IN, United States). Due to her soft tissue loss over the medial knee and tibia, the prosthetic joint line was placed cephalad. Her post-operative recovery was unremarkable. Her ultimate knee range of motion within the first year was 0-80 degrees. In addition, she had no knee extensor lag. Her reconstruction is shown in Figure 1B.

Six years post-operatively, at her scheduled follow-



**Figure 2** Transverse computed tomography scan images of distal femoral diaphysis centered over lytic lesion. A: Image shows a surrounding soft tissue mass of 2.8 cm. Erosive lytic lesion extends down to the inner cortex. Also note the radiolucent lines between the prosthetic implant and cement mantle, as well as the radiolucent line between the cement mantle and bone; B: Demonstrates septation of the soft tissue mass with peripheral calcification (arrows). This is typically a worrisome sign for a neoplastic process.



**Figure 3** Postoperative radiographs showing the additional bone resection, resection of the soft tissue pseudotumor, and the definitive reconstruction with an extended femoral endoprosthesis. A: Four week post-operative radiograph showing resection of the distal 9 cm of femoral diaphysis and reconstruction with a 9 cm intercalary segment. The intercalary segment is secured to the femoral diaphysis with a femoral compress device (Zimmer Biomet, Warsaw, IN, United States); B: One-year postoperative radiograph showing distal femoral bone remodeling and bone integration into the porous end of the femoral compress device. The patient's thigh pain was completely resolved and her gait returned to a reciprocating smooth gait that appeared symmetrical to the contralateral leg.

up, the patient described mild distal thigh and knee pain while walking. Her knee was cool on examination. Knee range of motion was 0-80 degrees of flexion with no extension lag and her knee felt stable. Radiographs showed concerning findings in the distal diaphysis (Figure 1C). There was a radiolucent line in the distal diaphyseal cement mantle, but more concerning was a periosteal erosion and surrounding soft tissue mass that resembled a possible neoplastic process. A CT scan of the distal femur revealed an eccentric lesion of the distal diaphysis of the femur that appeared to be emanating from the outer cortex of the medial diaphysis. The soft tissue mass was approximately 7 cm in length and 2-3 cm in breadth and was partly surrounded by a calcific border (Figure 2).

Her knee joint aspiration was negative for culture growth, including fungus and acid fast bacillus. The

articular white blood cell count was 259 with 71% neutrophils. Alpha-defensin and Synovasure® (Zimmer-Biomet, Warsaw, IN, United States) tests were both negative. Her serum CRP and ESR levels were normal. Evaluation for metastatic disease was negative.

Our surgical plan was for en bloc removal of the femoral diaphysis, including the femoral stem. We chose not to biopsy the mass in order to avoid neoplastic contamination of the extended endoprosthesis joint space.

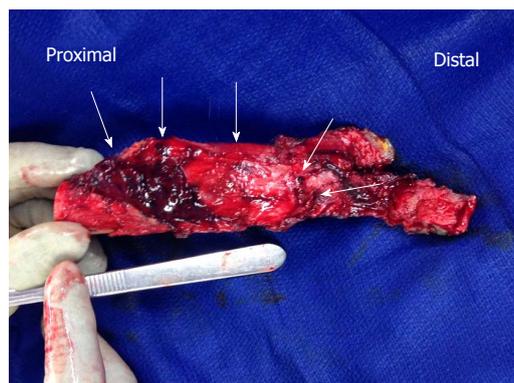
Post-operative radiographs of the revision surgery are shown in Figure 3. Nine centimeters of the femoral diaphysis was resected en bloc with the femoral stem, femoral diaphysis, and tumor mass. The femur was reconstructed with additional intercalary segments using the OSS Knee system. Fixation to the native femur was achieved with a femoral compress device (Zimmer-Biomet, Warsaw, IN, United States). Upon submission of the en bloc specimen to pathology, the tumor was cut open. We saw a multi-cystic, dark grey colored pseudotumor. The base of the pseudotumor emanated from the femoral diaphysis. We did not see any metallosis within the articular joint space (Figure 4).

The microscopic examination (Figure 5) of the resected en bloc section revealed a partially solid and cystic lesion encased in a fibrous pseudo-capsule. There were numerous foreign body histiocytes containing waxy amorphous material. Perivascular lymphocytes and histiocytes were prominent. The specimen was formally diagnosed as a metallic debris pseudotumor. There was no evidence of any neoplastic process.

The patient's post-operative recovery was again uneventful. She had complete wound healing. Her range of motion at one-year follow-up was 0-88 degrees of flexion and there was no extensor lag.

## DISCUSSION

Pseudotumor formation occurs as a result of metallic particulate debris eliciting a cell-mediated immune reaction that attempts to "encapsulate" the debris.

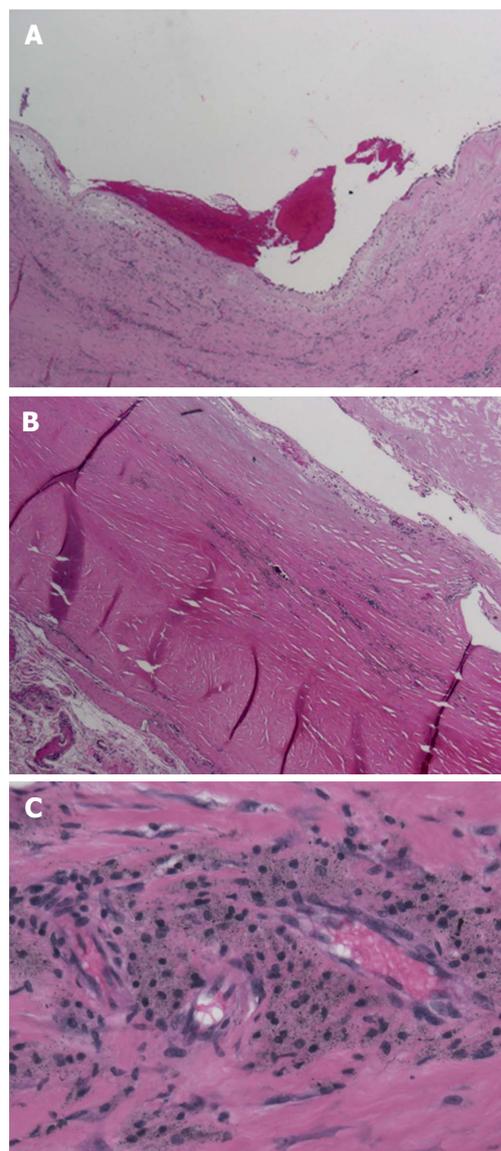


**Figure 4** Resected specimen that contains the distal 9 cm of the femoral diaphysis along with the soft tissue tumor. Specimen is rotated to view the soft tissue mass (arrows). Note the absence of metal debris within the extended joint space.

Unfortunately, the pseudotumor sac does not limit its spread to the articular joint, which is unlike the HM-WPE/PMMA osteolytic reaction. Pseudotumors generally spread along intermuscular planes<sup>[9]</sup>. In THA, pseudotumors are frequently found along the iliopsoas extending into the pelvis, in between the muscular planes of the thigh, and in between the muscular planes of the outer pelvis. Furthermore, pseudotumor masses can also protrude into the subcutaneous tissues when they herniate out from muscular planes.

We have searched the entire Medline database and to the best of our knowledge, have found only 5 case reports describing pseudotumors after a TKA<sup>[10-14]</sup>. We have reviewed all 5 articles carefully. Three of the articles describe an enlarged synovial sac around the total knee due to polyethylene wear debris and are not, in our opinion, "true" pseudotumors from metal wear debris<sup>[11,12,14]</sup>. One case does report a pseudotumor mass into the popliteal fossa. In this case, there was a broken polyethylene bearing and metal to metal contact of the femur onto the tibia creating metal debris. However, localized masses are known to frequently protrude posteriorly, especially with polyethylene debris. We feel this is not a classic metal-induced pseudotumor<sup>[13]</sup>. The fifth case, in our opinion, is most representative of an encapsulated pseudotumor, but the wear debris originated from both polyethylene and metal debris<sup>[10]</sup>.

Our case is unique for several reasons. First, this is the only report of a pseudotumor arising from a loose femoral stem despite a well-functioning TKA implant. Upon sectioning of the pseudotumor to its base, we observed a small black hole emanating from the outer diaphyseal cortex. This hole was actually an anterolateral crack in the distal femoral cortex which communicated into the medullary canal. The debris originated from mechanical abrasion of the femoral stem with adjacent cement and bone. Upon further inspection, we found the distal one-half of the femoral stem to be mechanically debonded from the cement mantle. We also noted broken/cracked cement in the distal one-fourth of the



**Figure 5** Histologic examination of the pseudotumor with specimen taken in the middle of the cystic mass. A: Low power (100 ×) view of mass demonstrating its cystic nature with blood and fibrin products within the centre of cystic structure. The wall of the lesion is very thick, studded with islands of metallic particles; B: Intermediate power (200 ×) view of the wall of pseudotumor mass. In the lower left corner, the cellular reaction is primarily lymphocytic and histiocytic with perivascular lymphocytes. The eosinophilic (red-color) area shows the pseudotumor cyst wall with adherent fibrin debris (top right corner) and microscopic metal particles within the wall; C: High power (400 ×) view of the cellular reaction surrounding pseudotumor mass. This shows the "classic" histologic finding of a reactive pseudotumor due to small metallic particles. The micrograph shows perivascular infiltration of histiocytes, containing particles of metallic debris, along with lymphocytes.

stem region. From microscopic review of the en bloc resection, we deduce that the pseudotumor emanated from within the femoral diaphysis and tracked outward to create an encapsulated mass outside of the femoral diaphysis. With a short, cemented femoral stem, repetitive cantilever bending forces caused the distal stem cement to fatigue, resulting in stem debonding. Subsequently, mechanized stem abrasion created microscopic titanium alloy particles. These particles

then escaped *via* a small diaphyseal crack created by cantilever bend forces. The particles, seeking the path of least resistance, exited through the crack rather than the distal femur. The escaping particles then stimulated the inflammatory response that resulted in the localized pseudotumor. Since the process of titanium debris pumping outward was slow, we assume the encapsulated process was able to contain the exiting debris within the pseudotumor region. The reactive rind responded with an inflammatory response that, in radiographic review, looked like a neoplastic process.

Second, an erosive eccentric periosteal mass in the distal femoral diaphysis in a sexagenarian is rare. The radiographs show a soft tissue mass with peripheral calcification that mimics a periosteal osteosarcoma. The maximum incidence of osteosarcoma occurs in the age group 15-29<sup>[15]</sup>. In our case, although the patient did not fit the typical distributive curve of this tumor, we were still compelled by the radiographic findings to treat this as a neoplastic process. Osteosarcoma in the elderly patient can present as a primary, as well as a secondary, lesion. Secondary lesions occur from sarcomatous transformation in Paget's disease or as a complication of irradiation. Since the patient did not have any of the above mentioned risk factors, our differential diagnosis involved a primary osteosarcoma. Osteosarcoma in the elderly has a poor prognosis if metastatic<sup>[16]</sup>. Our fear was that, with an existing endoprosthetic replacement within an extended joint space, a direct biopsy would have potentially contaminated the entire joint and caused the tumor to spread. We therefore chose not to biopsy the lesion and instead planned for a wide marginal excision. Fortunately, and much to our relief, the tumor was not neoplastic.

Our surgical approach took into consideration several factors. First, assuming the lesion was neoplastic, we wanted a wide marginal excision of the lesion to provide the least amount of local and systemic contamination of tumor cells. Second, this patient was highly satisfied with her endoprosthetic hinge TKA, so we strived to retain her knee function as best as possible. Therefore, our technique of resection was an extended arthrotomy from the knee joint line cephalad to a level just above the stem tip (measured from the end of the native femur). The procedure was performed with a pneumatic tourniquet for precise visualization.

The native femur was transected with a small sagittal saw above the stem tip. From this level and working distally to the knee joint, the intermuscular septum medially and laterally as well as the femur were elevated anteriorly from the posterior compartment along with the tumor mass *via* electrocautery. The hinge knee device was disconnected from the tibia and the entire segment of femur, femoral endoprosthetic construct, and tumor mass (lying upon the medial intermuscular septum) was delivered off the table for pathological examination. We were careful to avoid disrupting the tumor mass, so as not to contaminate

the local joint area. To our surprise, upon cutting into the tumor, a gray pseudotumor mass was observed. This was also confirmed by microscopic frozen section review.

Our decision for a wide marginal excision, in retrospect, was overly aggressive, but we believed this decision to be the safest choice for the patient. Had we instead performed a standard arthrotomy, cut into the tumor, and found a neoplastic mass, we would have contaminated the entire knee region possibly resulting in an eventual high marginal above knee amputation or limb disarticulation. Had we instead performed a radiographic-guided needle biopsy of the lesion, the diagnosis still may have been in doubt as a "negative" tissue biopsy could be considered a false negative result. We thought through the diagnostic process carefully and the option of a wide marginal excision was selected to provide the best definitive choice for diagnosis and treatment.

We find this case to be of further interest because almost all pseudotumors, whether in the hip, knee, or shoulder, usually present with a mass that extends into the soft tissues rather than confining itself to within the joint space. Pseudotumors of the hip tend to extend in between intermuscular planes<sup>[9]</sup>, frequently following along the iliopsoas, gluteus muscles, and thigh muscles. In this case, the pseudotumor stayed within the joint space, which once again pointed in favour of a localised neoplastic lesion. We did not anticipate a pseudotumor presentation in this fashion.

Based on our experience, titanium debris differs from cobalt chrome alloy debris in that the former is dark grey whereas cobalt chrome debris is a light grey. Gross review of the opened pseudotumor showed it to be dark grey in nature. Furthermore, since the cobalt chrome femoral endoprosthesis was articulating with a high molecular weight polyethylene bearing, the chance of cobalt chrome debris formation was low. The knee joint was wearing well and the polyethylene bearing showed no significant wear damage to our gross observation. In our review of OSS endoprosthetic (7 cm) femurs cemented with 90 mm titanium alloy stems ( $n = 93$ ), we have retrospectively found a loosening rate of 9.7%. We feel that a relatively short stem length (90 mm as opposed to 150 mm) paired with the 7 cm endoprosthetic femur is not long enough to resist the continued bending forces placed upon the femur with a hinge mechanism. We now routinely utilize the 150 mm cemented, bowed stem.

In summary, the lesson here is that pseudotumor reactions, unlike osteolytic reactions, form from reactive metallic debris. In the knee, the source of the metallic debris will always be mechanical loosening or catastrophic polyethylene wear-through with abnormal metal-on-metal contact. In the face of a recent joint replacement surgery of the knee, pseudotumor formation is a more likely diagnosis than a neoplastic process when an expanding mass is encountered. Thus,

our experience with this case leads us to believe that an intra-operative biopsy of the lesion at the time of reconstruction, prior to en bloc resection of the femur, would be the recommended course of action.

## ARTICLE HIGHLIGHTS

### Case characteristics

A 68-year-old female, six years after a complex revision total knee arthroplasty (TKA) with an endoprosthesis hinge device, presents with distal thigh pain and an eccentric periosteal mass adjacent to the medial diaphyseal cortex.

### Clinical diagnosis

The radiographic characteristics of the periosteal mass suggested a neoplastic process, but the histologic review of the lesion at the time of wide marginal excision showed the lesion to be a pseudotumor.

### Differential diagnosis

Preoperatively, based on radiographic review and CT scan of the lesion, we strongly suspected the mass to be a neoplasia; we did not suspect this lesion to be a pseudotumor.

### Laboratory diagnosis

As with any abnormal presentation involving a TKA, infection must always be ruled out first. Our laboratory tests included CBC with differential, ESR, and quantitative CRP. We also performed a knee aspiration, sending the fluid for cultures, Alpha-defensin, Synovasure<sup>®</sup> and cell count analysis.

### Imaging diagnosis

For this case, we utilized multiplanar radiographs and a CT scan of the femur and knee.

### Pathological diagnosis

Visual review of the tumor showed the mass to be cystic with a dark grey inner complex and a cavity filled with sero-sanguinous fluid. Histologic examination of the mass showed characteristic cells and structures consistent with a metal debris induced pseudotumor.

### Treatment

The tumor mass was thought to be neoplastic; therefore, we performed an en bloc removal of the distal native femur, femoral endoprosthesis construct, and tumor mass.

### Related reports

In the entire Medline literature, there are only 5 case reports describing a pseudotumor about a TKA; of these 5 reports, only one was, in our opinion, a true metal-induced pseudotumor.

### Term explanation

Pseudotumor: a non-neoplastic, sterile, cystic lesion that develops as a result of an inflammatory reaction to small particulate metal debris.

### Experiences and lessons

In the face of a recent joint replacement surgery of the knee, pseudotumor formation is a more likely diagnosis than a neoplastic process when an expanding mass is encountered.

## REFERENCES

- 1 **Cooper HJ**, Ranawat AS, Potter HG, Foo LF, Koob TW, Ranawat CS. Early reactive synovitis and osteolysis after total hip arthroplasty. *Clin Orthop Relat Res* 2010; **468**: 3278-3285 [PMID: 20419484 DOI: 10.1007/s11999-010-1361-1]
- 2 **Noordin S**, Masri B. Periprosthetic osteolysis: genetics, mechanisms and potential therapeutic interventions. *Can J Surg* 2012; **55**: 408-417 [PMID: 22992398 DOI: 10.1503/cjs.003711]
- 3 **Bitar D**, Parvizi J. Biological response to prosthetic debris. *World J Orthop* 2015; **6**: 172-189 [PMID: 25793158 DOI: 10.5312/wjo.v6.i2.172]
- 4 **Frølich C**, Hansen TB. Complications Related to Metal-on-Metal Articulation in Trapeziometacarpal Joint Total Joint Arthroplasty. *J Funct Biomater* 2015; **6**: 318-327 [PMID: 26020592 DOI: 10.3390/jfb6020318]
- 5 **Sehatazadeh S**, Kaulback K, Levin L. Metal-on-metal hip resurfacing arthroplasty: an analysis of safety and revision rates. *Ont Health Technol Assess Ser* 2012; **12**: 1-63 [PMID: 23074429]
- 6 **Bayley N**, Khan H, Grosso P, Hupel T, Stevens D, Snider M, Schemitsch E, Kuzyk P. What are the predictors and prevalence of pseudotumor and elevated metal ions after large-diameter metal-on-metal THA? *Clin Orthop Relat Res* 2015; **473**: 477-484 [PMID: 25085361 DOI: 10.1007/s11999-014-3824-2]
- 7 **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]
- 8 **Campbell P**, Ebramzadeh E, Nelson S, Takamura K, De Smet K, Amstutz HC. Histological features of pseudotumor-like tissues from metal-on-metal hips. *Clin Orthop Relat Res* 2010; **468**: 2321-2327 [PMID: 20458645 DOI: 10.1007/s11999-010-1372-y]
- 9 **McPherson E**, Dipane M, Sherif S. Massive pseudotumor in a 28mm ceramic-polyethylene revision THA: a case report. *Reconstructive Review* 2014; **4**: 11-17 [DOI: 10.15438/rr.v4i1.53]
- 10 **Benevenia J**, Lee FY, Buechel F, Parsons JR. Pathologic suprapatellar fracture due to osteolytic pseudotumor of knee following cementless total knee replacement. *J Biomed Mater Res* 1998; **43**: 473-477 [PMID: 9855207 DOI: 10.1002/(SICI)1097-4636(199824)43:43.CO;2-9]
- 11 **Kenan S**, Kahn L, Haramati N, Kenan S. A rare case of pseudotumor formation associated with methyl methacrylate hypersensitivity in a patient following cemented total knee arthroplasty. *Skeletal Radiol* 2016; **45**: 1115-1122 [PMID: 27022733 DOI: 10.1007/s00256-016-2372-0]
- 12 **Sivananthan S**, Pirapat R, Goodman SB. A Rare Case of Pseudotumor Formation following Total Knee Arthroplasty. *Malays Orthop J* 2015; **9**: 44-46 [PMID: 28435598 DOI: 10.5704/MOJ.1503.014]
- 13 **Mavrogenis AF**, Nomikos GN, Sakellariou VI, Karaliotas GI, Kontovazenitis P, Papagelopoulos PJ. Wear debris pseudotumor following total knee arthroplasty: a case report. *J Med Case Rep* 2009; **3**: 9304 [PMID: 20062793 DOI: 10.1186/1752-1947-3-9304]
- 14 **Kinney MC**, Kamath AF. Osteolytic pseudotumor after cemented total knee arthroplasty. *Am J Orthop (Belle Mead NJ)* 2013; **42**: 512-514 [PMID: 24340321]
- 15 **Stark A**, Kreicbergs A, Nilsson U, Silfverswärd C. The age of osteosarcoma patients is increasing. An epidemiological study of osteosarcoma in Sweden 1971 to 1984. *J Bone Joint Surg Br* 1990; **72**: 89-93 [PMID: 2298802]
- 16 **Jeon DG**, Lee SY, Cho WH, Song WS, Park JH. Primary osteosarcoma in patients older than 40 years of age. *J Korean Med Sci* 2006; **21**: 715-718 [PMID: 16891818 DOI: 10.3346/jkms.2006.21.4.715]

P- Reviewer: Wu CC S- Editor: Cui LJ L- Editor: A  
E- Editor: Li D





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 June 18; 9(6): 78-91





**MINIREVIEWS**

- 78 Understanding the medial ulnar collateral ligament of the elbow: Review of native ligament anatomy and function

*Labott JR, Aibinder WR, Dines JS, Camp CL*

**ORIGINAL ARTICLE**

**Basic Study**

- 85 Comparison of a simplified skin pointer device compared with a skeletal marker for knee rotation laxity: A cadaveric study using a rotation-meter

*Puah KL, Yew AKS, Chou SM, Lie DTT*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Wing-Hoi Cheung, BSc, PhD, Associate Professor, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong, Hong Kong, China

**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 Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central and Scopus.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Fang-Fang Ji*  
**Proofing Editorial Office Director:** *Jin-Lai Wang*

**NAME OF JOURNAL**  
*World Journal of Orthopedics*

**ISSN**  
 ISSN 2218-5836 (online)

**LAUNCH DATE**  
 November 18, 2010

**FREQUENCY**  
 Monthly

**EDITOR-IN-CHIEF**  
**Bao-Gan Peng, MD, PhD, Professor**, Department of Spinal Surgery, General Hospital of Armed Police Force, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjnet.com/2218-5836/editorialboard.htm>

**EDITORIAL OFFICE**  
 Jin-Lai Wang, Director

*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjnet.com](mailto:editorialoffice@wjnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjnet.com](mailto:bpgoffice@wjnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjnet.com>

**PUBLICATION DATE**  
 June 18, 2018

**COPYRIGHT**  
 © 2018 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.f6publishing.com>

## Understanding the medial ulnar collateral ligament of the elbow: Review of native ligament anatomy and function

Joshua R Labott, William R Aibinder, Joshua S Dines, Christopher L Camp

Joshua R Labott, Mayo Clinic School of Medicine, Mayo Clinic, Rochester, MN 55905, United States

William R Aibinder, Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN 55905, United States

Joshua S Dines, Sports Medicine and Shoulder Service, Hospital of Special Surgery, New York, NY 10021, United States

Christopher L Camp, Department of Orthopedic Surgery and Sports Medicine, Mayo Clinic, Rochester, MN 55905, United States

ORCID number: Joshua R Labott (0000-0001-5020-2434); William R Aibinder (0000-0001-7620-426X); Joshua S Dines (0000-0002-2135-9317); Christopher L Camp (0000-0003-3058-7327).

**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:** Christopher L Camp, MD, Assistant Professor, Department of Orthopedic Surgery and Sports Medicine, Mayo Clinic, 200 First St., Rochester, MN 55905, United States. [camp.christopher@mayo.edu](mailto:camp.christopher@mayo.edu)  
Telephone: +1-507-2842511  
Fax: +1-507-5387802

Received: March 24, 2018

Peer-review started: March 25, 2018

First decision: April 24, 2018

Revised: April 28, 2018

Accepted: May 9, 2018

Article in press: May 10, 2018

Published online: June 18, 2018

### Abstract

The medial ulnar collateral ligament complex of the elbow, which is comprised of the anterior bundle [AB, more formally referred to as the medial ulnar collateral ligament (MUCL)], posterior (PB), and transverse ligament, is commonly injured in overhead throwing athletes. Attenuation or rupture of the ligament results in valgus instability with variable clinical presentations. The AB or MUCL is the strongest component of the ligamentous complex and the primary restraint to valgus stress. It is also composed of two separate bands (anterior and posterior) that provide reciprocal function with the anterior band tight in extension, and the posterior band tight in flexion. In individuals who fail comprehensive non-operative treatment, surgical repair or reconstruction of the MUCL is commonly required to restore elbow function and stability. A comprehensive understanding of the anatomy and biomechanical properties of the MUCL is imperative to optimize reconstructive efforts, and to enhance clinical and radiographic outcomes. Our understanding of the native anatomy and biomechanics of the MUCL has evolved over time. The precise locations of the origin and insertion footprint centers guide surgeons in proper graft placement with relation to bony anatomic landmarks. In recent studies, the ulnar insertion of the MUCL is described as larger than previously thought, with the center of the footprint at varying distances relative to the ulnar ridge, joint line, or sublime tubercle. The purpose of this review is to consolidate and summarize the existing literature regarding the native anatomy, biomechanical, and clinical significance of the entire medial ulnar collateral ligament complex, including the MUCL (AB), PB, and

transverse ligament.

**Key words:** Elbow; Anterior bundle; Medial ulnar collateral ligament; Native anatomy; Biomechanics; Valgus stability

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** The anterior bundle of the medial ulnar collateral ligament complex plays a crucial role in elbow stability, specifically as a valgus and rotational constraint. Based on recent studies and our own cadaveric dissections, the ulnar footprint has a broader insertion that is more tapered and elongated than previously considered. A comprehensive understanding of the anatomy and biomechanical properties of the medial ulnar collateral ligament is imperative to optimize reconstructive efforts, and to enhance clinical and radiographic outcomes.

Labott JR, Aibinder WR, Dines JS, Camp CL. Understanding the medial ulnar collateral ligament of the elbow: Review of native ligament anatomy and function. *World J Orthop* 2018; 9(6): 78-84 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i6/78.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i6.78>

## INTRODUCTION

The medial ulnar collateral ligament [MUCL, also referred to as the ulnar collateral ligament (UCL), medial collateral ligament (MCL), and anterior bundle (AB)] is the primary restraint to valgus instability of the elbow<sup>[1-5]</sup>. The MUCL is one of three ligaments that comprise the “medial ulnar collateral ligament complex” of the elbow with the posterior bundle (PB) and transverse ligament (TL) being the other two (Figure 1). The MUCL, in particular, has been shown to be the primary stabilizer of the elbow during valgus stress, followed by the radial head and dynamic stabilizers of the elbow such as the flexor-pronator muscle mass<sup>[6-10]</sup>. The MUCL is composed of two separate bands (anterior and posterior) that provide reciprocal function with the anterior band tight in extension, and the posterior band tight in flexion.

The MUCL is commonly injured in overhead throwing athletes when a valgus moment is placed on the elbow during the late cocking and early acceleration phases<sup>[11-15]</sup>. Incompetence or rupture of the ligament leads to valgus instability which has varying clinical presentations. Patients may complain of instability, however, most will report pain, reduced accuracy, and decreased velocity. Clinically significant pathology often requires surgical intervention. Ligament reconstruction relies on appropriate graft positioning at both the humeral origin and the ulnar insertion. A thorough understanding of the native anatomy of the MUCL facilitates the surgeon’s ability to effectively restore stability and function.

In 1985, Morrey and An<sup>[10]</sup> published the first quantitative analysis of the medial ulnar collateral ligament

complex. Based on 10 fresh frozen cadavers, they described the dimensions of the AB and PB at various degrees of elbow flexion. Since that time, multiple studies have assessed the anatomy and biomechanics of the AB<sup>[2,3,6,16,17]</sup>. Historically, general consensus held that the AB inserts solely and directly onto the sublime tubercle. However, recent studies have shown that the AB insertion is in fact broader, tapered, and significantly larger in terms of surface area than previously thought.

The purpose of this review is to consolidate and summarize the existing literature regarding the anatomy, biomechanical function, and clinical significance of the native (non-reconstruction) MUCL. It is our hope that this work may serve as a framework for better understanding valgus instability in the elbow and refining surgical techniques in order to optimize post-operative outcomes.

## ANATOMY

As mentioned, the MUCL (AB) is the primary restraint to valgus instability of the elbow<sup>[1-5]</sup>. The PB is a soft tissue stabilizer of the elbow with contributions greatest during flexion<sup>[17]</sup>. It is generally thought that the TL does not provide a significant contribution to elbow stability<sup>[10]</sup>; however, recent study has revealed a direct insertion of the TL onto the AB that may potentially play a role in elbow stability<sup>[18]</sup>. The AB, in particular, has been shown to be the primary stabilizer of the elbow in valgus stress, with the radial head and dynamic stabilizers of the medial elbow also contributing<sup>[6-10]</sup>. It originates on the anteroinferior surface of the medial epicondyle and inserts onto the sublime tubercle of the ulna (Figure 1).

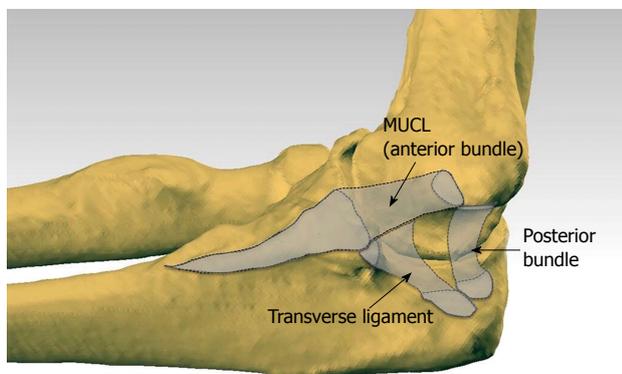
### Origin

**Surface area and footprint center:** The origin of the AB is posterior to the elbow’s axis of rotation, on the anterior, inferior, and lateral aspect of the medial epicondyle<sup>[10]</sup>. The surface area of the humeral origin has been widely variable in the literature (Table 1). Dugas *et al*<sup>[19]</sup> showed that the AB origin was round with a mean surface area of 45.5 mm<sup>2</sup> (range of 25.9-59.4 mm<sup>2</sup>) in 13 fresh frozen cadavers utilizing a three-dimensional (3-D) electromagnetic tracking and digitalizing device. Similar to the findings of Dugas *et al*<sup>[19]</sup>, a recent study by Camp *et al*<sup>[18]</sup> found a mean origin surface area of 32.3 mm<sup>2</sup>. In contrast to these two studies, Frangiamore *et al*<sup>[20]</sup> found this measurement to be notably smaller at 17.0 mm<sup>2</sup> (range of 14.9-19.1 mm<sup>2</sup>) through analysis of 10 fresh frozen cadaver specimens. Potentially due to differences in measurement techniques, these studies demonstrated variable results. Additionally, Frangiamore *et al*<sup>[20]</sup> and Dugas *et al*<sup>[19]</sup> described the center of the ligament origin in different terms, which is of clinical importance when determining the location of humeral tunnel placement during MUCL reconstruction surgery. Dugas *et al*<sup>[19]</sup> described the center of the origin as an area of tissue on a flat surface anterior and inferior to the medial epicondyle. The mean distance they measured was 13.4 mm from the center of the medial ep-

**Table 1 Summary of anatomic studies describing the length, width, and surface area of the anterior bundle**

Ref.	Specimen	AB length (mm)	AB width (mm)	Origin surface area (mm <sup>2</sup> )	Insertion surface area (mm <sup>2</sup> )	AB surface area (mm <sup>2</sup> )
Alcid <i>et al</i> <sup>[2]</sup> 2004	-	27	4.5	-	-	121.5
Beckett <i>et al</i> <sup>[23]</sup> 2000	39	26.7	-	-	-	-
Camp <i>et al</i> <sup>[35]</sup> 2017	10	-	-	32.3	187.6	324.2
Dugas <i>et al</i> <sup>[19]</sup> 2007	13	-	6.8	45.5	127.8	-
Eyendaal <i>et al</i> <sup>[9]</sup> 2002	5	26	5	-	-	-
Farrow <i>et al</i> <sup>[22]</sup> 2014	10	53.9	-	-	-	-
Farrow <i>et al</i> <sup>[21]</sup> 2011	12	51.7	-	-	-	-
Floris <i>et al</i> <sup>[25]</sup> 1998	18	-	5.8	-	-	-
Morrey <i>et al</i> <sup>[10]</sup> 1985	10	27.1	4.7	-	-	-
Regan <i>et al</i> <sup>[17]</sup>	8	21.1	7.6	-	-	-
Safran <i>et al</i> <sup>[5]</sup> 2005	12	-	7.2	-	-	-
Timmerman <i>et al</i> <sup>[26]</sup> 1994	10	-	6	-	-	-
Frangiamore <i>et al</i> <sup>[20]</sup> 2018	10	21.5	-	17	66.4	-

AB: Anterior bundle.



**Figure 1** Medial ulnar collateral ligament complex of the elbow with outlined ligaments generated by co-registering the three dimensional digitized anatomy and computed tomography scan of a cadaveric elbow. Note the tapered and distally elongated insertion of the medial ulnar collateral ligament on the sublime tubercle and ulnar ridge. MUCL: Medial ulnar collateral ligament.

icondyle to the center of the origin, with Camp *et al*<sup>[18]</sup> finding a similar mean distance of 11.7 mm. Rather than describing this as a linear distance with no specific angle, Frangiamore *et al*<sup>[20]</sup> described this measurement in terms of two separate measurements, reporting the center of the origin to be located, on average, 8.5 mm distal (inferior) and 7.8 mm lateral (anterior) to the medial epicondyle. The use of two measurements relative to a single point in the latter study may assist with better reproducibility.

**Insertion**

**Surface area and footprint center:** Historically, the ulnar footprint of the AB has generally been described as inserting solely onto the sublime tubercle, serving as the anatomical landmark for surgical repairs and reconstructions. In one such early report, the mean AB insertional surface area was 66.4 mm<sup>2</sup><sup>[20]</sup>.

Recently, authors have described the AB insertion

as a longer, distally tapered area that follows the ulnar ridge. The surface area of this broader insertion has been reported by Dugas *et al*<sup>[19]</sup> to have a mean surface area of 127.8 mm<sup>2</sup>. In this study, length of the ulnar footprint measured an average of 29.2 mm. Others have found similar lengths when appreciating a tapered insertion with means of 30.2 mm and 29.2 mm<sup>[21,22]</sup>. Further study by Camp *et al*<sup>[18]</sup> identified a tapered insertion with a mean surface area of 187.6 mm<sup>2</sup> and an ulnar footprint length averaging 29.7 mm.

Because the footprint center of a broader tapered insertion may not occur in the location previously assumed (apex of the sublime tubercle), the optimal position of the ulnar tunnel in reconstructive efforts may still need to be elucidated. Clinical relevance of the broader tapered ulnar insertion described in recent studies by Dugas *et al*<sup>[19]</sup> and Camp *et al*<sup>[18]</sup> is in need of further investigation.

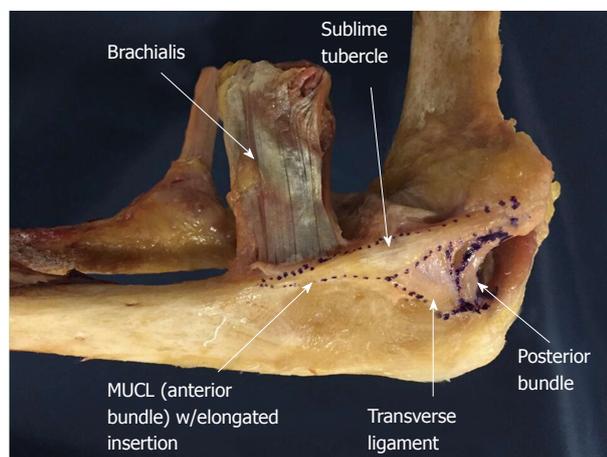
One recent study of 10 cadaveric specimens has shown the mean proximal insertional width to be 9.4 mm which is greater than previously noted<sup>[18]</sup>. This discrepancy in widths leaves room for further investigation to ensure that the native anatomy of the AB is fully documented and understood (Figure 2).

**Overall ligament dimensions**

**Length:** The AB is the longest ligament of the medial elbow, spanning the inferior aspect of the medial epicondyle to the sublime tubercle and extending distally along the ulnar ridge. The average length of AB has been reported between 21.1 mm and 31.4 mm in several older studies<sup>[2,9,10,17,20,23]</sup>. These lengths were measured from the center of the origin to center of sublime tubercle, based on a direct insertion onto the sublime tubercle without a distal extension. In contrast, more recent reports measured from the center of the humeral origin to the most distal point of tapered insertion reported mean lengths of 53.9 mm<sup>[21]</sup> and 51.7 mm<sup>[22]</sup>. The difference in length measured between a non-tapered sublime insertion and a tapered insertion calls for further study

**Table 2** Maximum physiologic valgus demonstrated in various studies with noted elbow position and load applied during testing

Authors	Specimens	Maximum valgus (degrees)	Elbow flexion (degrees)	Load (nm)
Callaway <i>et al</i> <sup>[3]</sup> 1997	28	3.6	30, 60, 90, 120	2
Floris <i>et al</i> <sup>[25]</sup> 1998	18	6	20	0.75
Morrey <i>et al</i> <sup>[4]</sup> 1991	6	5	20	Gravity
Safran <i>et al</i> <sup>[5]</sup> 2005	12	11.1	70	2



**Figure 2** Cadaveric specimen outlining all ligaments of the medial ulnar collateral ligament complex including the medial ulnar collateral ligament/anterior bundle, posterior bundle, and transverse ligament. MUCL: Medial ulnar collateral ligament.

to evaluate native AB anatomy and the clinical relevance of different measurements. In particular, appropriate length of the ligament component has important implications for ligament reconstruction.

It is important to note that the AB is not an isometric soft tissue stabilizer but instead changes in length throughout flexion. Studies have shown the length of the AB changes by 18%, between 2.8 mm and 4.8 mm as the elbow moves from extension to flexion<sup>[6,10,24]</sup>. The dynamic length of the AB is an aspect of native biomechanics that must also be considered during reconstruction procedures.

**Width:** The width of the AB varies, increasing distally to its greatest width at the sublime tubercle before tapering to a point as it inserts distally along the ulnar ridge. Generally, there has been limited variability in the reported widths of the AB, ranging from 4.0 to 7.6 mm<sup>[2,5,10,17,25,26]</sup>.

**Surface area:** The mean surface area of the AB has been reported between 108 mm<sup>2</sup> to 135 mm<sup>2</sup><sup>[2,10]</sup> in studies that did not take the full distal footprint into consideration. Given that Dugas *et al*<sup>[19]</sup> has shown the tapered ulnar footprint alone to have a mean surface area of 127.8 mm<sup>2</sup>, the overall surface area of the ligament will undoubtedly be significantly greater than previously assumed in historical reports. In contrast to these historical reports, and in support of the Dugas *et al*<sup>[19]</sup> findings, a more recent study published by Camp

*et al*<sup>[18]</sup> identified the mean surface area of the entire AB to be 324.2 mm<sup>2</sup> (Figure 3).

## BIOMECHANICS

### Valgus instability

The MUCL provides a vital contribution to the stability of the elbow when a valgus stress is applied. With an intact radial head, a fresh frozen cadaveric model demonstrated that the MUCL contributes 31% and 54% to valgus restraint at 0° and 90° of flexion, respectively<sup>[1]</sup>. In this study, 4 fresh frozen cadavers had a varying valgus load from 0 to 3 nm applied at 0° and 90° of flexion. With the maximum force applied, there was 3° of valgus laxity in full extension and 2° of laxity in flexion. Several studies have performed similar biomechanical testing at various degrees of flexion and various amount of force<sup>[2,3,5,6,10,25,27]</sup>. The amount of valgus laxity varies from 2° to 8° with an intact MUCL (Table 2).

At 30° and 90° of flexion, Callaway *et al*<sup>[3]</sup> showed valgus laxity of 3.6° under a 2nm load compared to an unloaded elbow. Safran *et al*<sup>[5]</sup> analyzed 12 cadaveric specimens with a 2Nm load applied at 30 degrees of elbow flexion, and showed a mean alignment of 10.7° of valgus with a neutral forearm rotation position. This study did not determine the inherent valgus alignment in an unloaded elbow, which affects the ability to compare these studies. Thus, with an intact MUCL and a 2 nm load applied, the amount of valgus laxity is generally greatest at 30° of flexion<sup>[5]</sup>.

Other authors have evaluated the effect of transecting the AB on elbow stability (Table 3). When the AB is disrupted in cadaveric models, the amount of valgus instability increases until the point at which secondary osseous stabilizers such as the radial head impart stability. In the setting of AB deficiency, Callaway *et al*<sup>[3]</sup> demonstrated the greatest instability at 90° of flexion. The study reported a gain of 1.6, 2.8, 3.2, and 3.0 degrees of valgus motion at 30, 60, 90, and 120 degrees of flexion, respectively when compared to the intact state. Additionally, Mullen *et al*<sup>[28]</sup> showed that at 90 degrees of flexion, the transected AB increases valgus instability by 150%. Floris *et al*<sup>[25]</sup> and Sjøbjerg *et al*<sup>[29]</sup> showed the greatest instability occurred at 70 degrees of flexion, with recorded valgus angles of 14.2° and 11.8°. Safran *et al*<sup>[5]</sup> produced a maximal gain of 6.3° of laxity under 2 nm of valgus load with a transected AB at 50° of elbow flexion. Finally, Morrey *et al*<sup>[4]</sup> showed a gain of laxity over baseline ranging from

**Table 3** Maximum valgus reported when the anterior bundle is transected in various studies with noted elbow position and load applied during testing

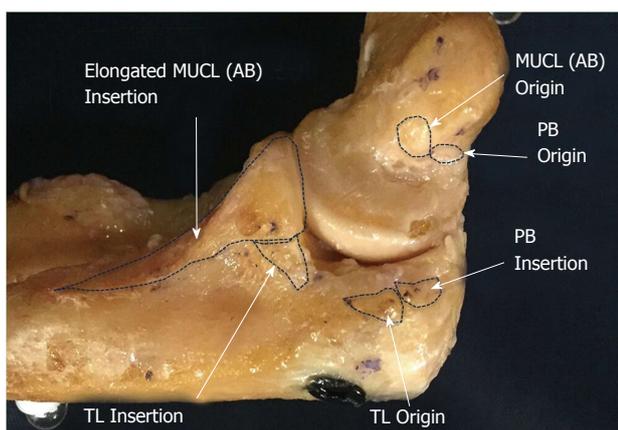
Ref.	Specimens	Maximum valgus gain (degrees)	Maximum absolute valgus	Elbow flexion (degrees)	Load (nm)
Ahmad <i>et al</i> <sup>[6]</sup> 2004	7	7.37	-	30	2
Callaway <i>et al</i> <sup>[3]</sup> 1997	28	3.2	-	90	2
Floris <i>et al</i> <sup>[25]</sup> 1998	18	5.7	-	30	0.75
Morrey <i>et al</i> <sup>[4]</sup> 1991	6	3.9	-	20	gravity
Safran <i>et al</i> <sup>[5]</sup> 2005	12	6.3	-	50	2
Sojbjerg <i>et al</i> <sup>[29]</sup> 1987	12	-	11.8	70	1.5

Some studies reported gain in valgus from physiologic state, while others noted absolute valgus.

**Table 4** Summary of the studies evaluating the effect of the anterior bundle on relative internal rotation of the forearm in the native and pathologic state

Ref.	Specimen	Intact AB internal rotation (degrees)	Cut AB internal rotation (degrees)	Gain of internal rotation with cut AB
Bryce <i>et al</i> <sup>[6]</sup> 2008	-	4	-	-
Floris <i>et al</i> <sup>[25]</sup> 1998	18	6	18.5	12.5
Morrey <i>et al</i> <sup>[4]</sup> 1991	6	2.8	7.8	5

AB: Anterior bundle.



**Figure 3** Cadaveric specimen showing origins and insertions of all ligaments of the medial ulnar collateral ligament complex including: Anterior bundle, posterior bundle and transverse ligament. AB: Anterior bundle; PB: Posterior bundle; TL: Transverse ligament.

3.3° to 4.8° in cadaver specimens at 20 degrees of flexion under gravity. In summary, an intact AB is vital in maintaining valgus stability of the elbow throughout the entire range of flexion.

**Rotational instability**

Internal rotation of the forearm relative to the humerus is constrained by the soft tissues stabilizer of the medial elbow. While there is inherent internal rotation during flexion, the degree of rotation is limited between 2.8°-6° in an uninjured elbow<sup>[4,6,25]</sup>. Transection of the AB permits internal rotation of the forearm to increase to 18.5° at 60° of joint flexion (Table 4)<sup>[25]</sup>. Correct understanding of these biomechanics is important in repair and reconstruction, as a rotatory moment is part of the mechanism of injury.

**Tissue strength**

Despite being the most frequently injured ligament in the overhead throwing athlete, the AB or MUCL has been shown to have the most inherent strength and stiffness<sup>[6,17]</sup>. This fact emphasizes the significant loads placed on the medial side of the elbow during the late cocking and early acceleration phase<sup>[30,31]</sup>. In a cadaveric model with each soft tissue stabilizer evaluated under stress, the AB was the strongest with an average load to failure of 260.9 N<sup>[17]</sup>. During overhead throwing, the elbow experiences 64 nm of mean valgus torque and 290 N of tensile force on the medial side (which is greater than the threshold for failure of 260.9 N)<sup>[30,31]</sup>. Furthermore, a maximal mean valgus load of 90Nm has been reported<sup>[32-34]</sup>. A recent study of 81 professional baseball pitchers (MLB and MiLB) over 82000 throws showed a mean valgus torque of 60 nm with individual participant means ranging from 41 nm to 94 nm<sup>[35]</sup>. Thus, it is clearly evident why the AB fails in this subset of athletes based on the load to failure being below the force imparted on the elbow.

**CONCLUSION**

The AB of the medial ulnar collateral ligament complex plays a crucial role in elbow stability, specifically as a valgus and rotational constraint. The AB originates on the humerus and inserts onto the sublime tubercle of the ulna. Based on recent studies and our own cadaveric dissections, the ulnar footprint has a broader insertion that is more tapered and elongated than previous considered. The data regarding the centers of the ulnar and humeral footprints provides guidance for proper tunnel placement during reconstructive efforts. The width and stiffness of the AB is described and can

be used to guide graft selection during reconstruction.

Lastly, although the ligament is quite strong, the amount of force placed across the elbow in elite overhead throwing athletes is routinely exceeds the ligaments average load to failure. Accordingly, it is not surprising why MUCL injuries are so common amongst baseball players and pitchers.

Understanding native anatomy and biomechanics of the AB/MUCL is clinically important to help understand the pathoanatomy and guide surgical techniques when treating MUCL injuries.

## REFERENCES

- 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]
- Alcid JG, Ahmad CS, Lee TQ. Elbow anatomy and structural biomechanics. *Clin Sports Med* 2004; **23**: 503-517, vii [PMID: 15474218 DOI: 10.1016/j.csm.2004.06.008]
- Callaway GH, Field LD, Deng XH, Torzilli PA, O'Brien SJ, Altchek DW, Warren RF. Biomechanical evaluation of the medial collateral ligament of the elbow. *J Bone Joint Surg Am* 1997; **79**: 1223-1231 [PMID: 9278083 DOI: 10.2106/00004623-199708000-00015]
- 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 DOI: 10.1097/00003086-199104000-00021]
- Safran M, Ahmad CS, Elattrache NS. Ulnar collateral ligament of the elbow. *Arthroscopy* 2005; **21**: 1381-1395 [PMID: 16325092 DOI: 10.1016/j.arthro.2005.07.001]
- Bryce CD, Armstrong AD. Anatomy and biomechanics of the elbow. *Orthop Clin North Am* 2008; **39**: 141-154, v [PMID: 18374805 DOI: 10.1016/j.ocl.2007.12.001]
- Cohen MS, Bruno RJ. The collateral ligaments of the elbow: anatomy and clinical correlation. *Clin Orthop Relat Res* 2001; **383**: 123-130 [PMID: 11210946 DOI: 10.1097/00003086-200102000-00014]
- Ahmad CS, Park MC, Elattrache NS. Elbow medial ulnar collateral ligament insufficiency alters posteromedial olecranon contact. *Am J Sports Med* 2004; **32**: 1607-1612 [PMID: 15494323 DOI: 10.1177/0363546503263149]
- Eyendaal D, Valstar ER, Søjbjerg JO, Rozing PM. Biomechanical evaluation of the elbow using roentgen stereophotogrammetric analysis. *Clin Orthop Relat Res* 2002; **396**: 100-105 [PMID: 11859231 DOI: 10.1097/00003086-200203000-00017]
- Morrey BF, An KN. Functional anatomy of the ligaments of the elbow. *Clin Orthop Relat Res* 1985; **201**: 84-90 [PMID: 4064425 DOI: 10.1097/00003086-198512000-00015]
- Bruce JR, Andrews JR. Ulnar collateral ligament injuries in the throwing athlete. *J Am Acad Orthop Surg* 2014; **22**: 315-325 [PMID: 24788447 DOI: 10.5435/JAAOS-22-05-315]
- Jones KJ, Osbahr DC, Schrupf MA, Dines JS, Altchek DW. Ulnar collateral ligament reconstruction in throwing athletes: a review of current concepts. AAOS exhibit selection. *J Bone Joint Surg Am* 2012; **94**: e49 [PMID: 22517395 DOI: 10.2106/JBJS.K.01034]
- Rohrbough JT, Altchek DW, Hyman J, Williams RJ 3rd, Botts JD. Medial collateral ligament reconstruction of the elbow using the docking technique. *Am J Sports Med* 2002; **30**: 541-548 [PMID: 12130409 DOI: 10.1177/03635465020300041401]
- 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 DOI: 10.2106/00004623-199274010-00009]
- Singh H, Osbahr DC, Wickham MQ, Kirkendall DT, Speer KP. Valgus laxity of the ulnar collateral ligament of the elbow in collegiate athletes. *Am J Sports Med* 2001; **29**: 558-561 [PMID: 11573912 DOI: 10.1177/03635465010290050601]
- O'Driscoll SW, Jalszynski R, Morrey BF, An KN. Origin of the medial ulnar collateral ligament. *J Hand Surg Am* 1992; **17**: 164-168 [PMID: 1538101 DOI: 10.1016/0363-5023(92)90135-c]
- Regan WD, Korinek SL, Morrey BF, An KN. Biomechanical study of ligaments around the elbow joint. *Clin Orthop Relat Res* 1991; **271**: 170-179 [PMID: 1914292 DOI: 10.1097/00003086-199110000-00023]
- Camp CL, Jahandar H, Sinatro AM, Imhauser CW, Altchek DW, Dines JS. Quantitative Anatomic Analysis of the Medial Ulnar Collateral Ligament Complex of the Elbow. *Orthop J Sports Med* 2018; **6**: 2325967118762751 [PMID: 29637082 DOI: 10.1177/2325967118762751]
- 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]
- Frangiamore SJ, Moatshe G, Kruckeberg BM, Civitarese DM, Muckenhirn KJ, Chahla J, Brady AW, Cinque ME, Oleson ML, Provencher MT, Hackett TR, LaPrade RF. Qualitative and Quantitative Analyses of the Dynamic and Static Stabilizers of the Medial Elbow: An Anatomic Study. *Am J Sports Med* 2018; **46**: 687-694 [PMID: 29266961 DOI: 10.1177/0363546517743749]
- Farrow LD, Mahoney AJ, Stefancin JJ, Taljanovic MS, Sheppard JE, Schickendantz MS. Quantitative analysis of the medial ulnar collateral ligament ulnar footprint and its relationship to the ulnar sublime tubercle. *Am J Sports Med* 2011; **39**: 1936-1941 [PMID: 21555509 DOI: 10.1177/0363546511406220]
- Farrow LD, Mahoney AP, Sheppard JE, Schickendantz MS, Taljanovic MS. Sonographic assessment of the medial ulnar collateral ligament distal ulnar attachment. *J Ultrasound Med* 2014; **33**: 1485-1490 [PMID: 25063414 DOI: 10.7863/ultra.33.8.1485]
- Beckett KS, McConnell P, Lagopoulos M, Newman RJ. Variations in the normal anatomy of the collateral ligaments of the human elbow joint. *J Anat* 2000; **197 Pt 3**: 507-511 [PMID: 11117635 DOI: 10.1046/j.1469-7580.2000.19730507.x]
- Armstrong AD, Ferreira LM, Dunning CE, Johnson JA, King GJ. The medial collateral ligament of the elbow is not isometric: an in vitro biomechanical study. *Am J Sports Med* 2004; **32**: 85-90 [PMID: 14754728 DOI: 10.1177/0363546503258886]
- Floris S, Olsen BS, Dalstra M, Søjbjerg JO, Sneppen O. The medial collateral ligament of the elbow joint: anatomy and kinematics. *J Shoulder Elbow Surg* 1998; **7**: 345-351 [PMID: 9752642 DOI: 10.1016/s1058-2746(98)90021-0]
- Timmerman LA, Andrews JR. Histology and arthroscopic anatomy of the ulnar collateral ligament of the elbow. *Am J Sports Med* 1994; **22**: 667-673 [PMID: 7810791 DOI: 10.1177/036354659402200515]
- Rooker JC, Smith JRA, Amirfeyz R. Anatomy, surgical approaches and biomechanics of the elbow. *Orthop Trauma* 2016; **30**: 283-290 [DOI: 10.1016/j.mporth.2016.05.008]
- Mullen DJ, Goradia VK, Parks BG, Matthews LS. A biomechanical study of stability of the elbow to valgus stress before and after reconstruction of the medial collateral ligament. *J Shoulder Elbow Surg* 2002; **11**: 259-264 [PMID: 12070499 DOI: 10.1067/mse.2002.122622]
- 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 DOI: 10.1097/0003086-198705000-00026]
- Werner SL, Fleisig GS, Dillman CJ, Andrews JR. Biomechanics of the elbow during baseball pitching. *J Orthop Sports Phys Ther* 1993; **17**: 274-278 [PMID: 8343786 DOI: 10.2519/jospt.1993.17.6.274]
- 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]
- 32 **Fleisig GS**, Kingsley DS, Loftice JW, Dinnen KP, Ranganathan R, Dun S, Escamilla RF, Andrews JR. Kinetic comparison among the fastball, curveball, change-up, and slider in collegiate baseball pitchers. *Am J Sports Med* 2006; **34**: 423-430 [PMID: 16260466 DOI: 10.1177/0363546505280431]
- 33 **Fleisig GS**, Escamilla RF. Biomechanics of the elbow in the throwing athlete. *Oper Techn Sport Med* 1996; **4**: 62-68 [DOI: 10.1016/S1060-1872(96)80050-5]
- 34 **Loftice J**, Fleisig GS, Zheng N, Andrews JR. Biomechanics of the elbow in sports. *Clin Sports Med* 2004; **23**: 519-530, vii-viii [PMID: 15474219 DOI: 10.1016/j.csm.2004.06.003]
- 35 **Camp CL**, Tubbs TG, Fleisig GS, Dines JS, Dines DM, Altchek DW, Dowling B. The Relationship of Throwing Arm Mechanics and Elbow Varus Torque: Within-Subject Variation for Professional Baseball Pitchers Across 82,000 Throws. *Am J Sports Med* 2017; **45**: 3030-3035 [PMID: 28806094 DOI: 10.1177/0363546517719047]

**P- Reviewer:** Georgiev GPP **S- Editor:** Cui LJ **L- Editor:** A  
**E- Editor:** Tan WW



## Basic Study

**Comparison of a simplified skin pointer device compared with a skeletal marker for knee rotation laxity: A cadaveric study using a rotation-meter**

Ken Lee Puah, Andy Khye Soon Yew, Siaw Meng Chou, Denny Tijauw Tjoen Lie

Ken Lee Puah, Andy Khye Soon Yew, Denny Tijauw Tjoen Lie, Department of Orthopaedic Surgery, Singapore General Hospital, Singapore General Hospital, Singapore 169608, Singapore

Siaw Meng Chou, School of Mechanical and Aerospace Engineering, College of Engineering, Nanyang Technological University, Singapore 639798, Singapore

ORCID number: Ken Lee Puah (0000-0002-8583-456X); Andy Khye Soon Yew (0000-0001-7299-2166); Siaw Meng Chou (0000-0003-3081-0699); Denny Tijauw Tjoen Lie (0000-0002-3638-6625).

**Author contributions:** Puah KL performed the experiment, analysis and wrote the manuscript; Yew AKS designed and performed the experiment and edited the manuscript; Chou SM designed the experiment, obtained funding and edited the manuscript; Lie DTT designed the experiment, obtained funding and edited the manuscript.

**Conflict-of-interest statement:** No potential conflicts of interest relevant to this article were reported.

**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. Ken Lee Puah, FRCS (Ed), Surgeon, Department of Orthopaedic Surgery, Singapore General Hospital, Outram Road, Singapore 169608, Singapore. [puah.ken.lee@singhealth.com.sg](mailto:puah.ken.lee@singhealth.com.sg)  
Telephone: +65-63214603  
Fax: +65-62248100

Received: January 11, 2018

Peer-review started: January 11, 2018

First decision: February 9, 2018

Revised: March 16, 2018

Accepted: May 13, 2018

Article in press: May 13, 2018

Published online: June 18, 2018

**Abstract****AIM**

To compare the measurements of knee rotation laxity by non-invasive skin pointer with a knee rotation jig in cadaveric knees against a skeletally mounted marker.

**METHODS**

Six pairs of cadaveric legs were mounted on a knee rotation jig. One Kirschner wire was driven into the tibial tubercle as a bone marker and a skin pointer was attached. Rotational forces of 3, 6 and 9 nm applied at 0°, 30°, 45°, 60° and 90° of knee flexion were analysed using the Pearson correlation coefficient and paired *t*-test.

**RESULTS**

Total rotation recorded with the skin pointer significantly correlated with the bone marker at 3 nm at 0° (skin pointer  $23.9 \pm 26.0^\circ$  vs bone marker  $16.3 \pm 17.3^\circ$ ,  $r = 0.92$ ;  $P = 0.0$ ), 30° ( $41.7 \pm 15.5^\circ$  vs  $33.1 \pm 14.7^\circ$ ,  $r = 0.63$ ;  $P = 0.037$ ), 45° ( $49.0 \pm 17.0^\circ$  vs  $40.3 \pm 11.2^\circ$ ,  $r = 0.81$ ;  $P = 0.002$ ), 60° ( $45.7 \pm 17.5^\circ$  vs  $34.7 \pm 9.5^\circ$ ,  $r = 0.86$ ;  $P = 0.001$ ) and 90° ( $29.2 \pm 10.9^\circ$  vs  $21.2 \pm 6.8^\circ$ ,  $r = 0.69$ ;  $P = 0.019$ ) of knee flexion and 6 nm at 0° ( $51.1 \pm 37.7^\circ$  vs  $38.6 \pm 30.1^\circ$ ,  $r = 0.90$ ;  $P = 0.0$ ), 30° ( $64.6 \pm 21.6^\circ$  vs  $54.3 \pm 15.1^\circ$ ,  $r = 0.73$ ;  $P = 0.011$ ), 45° ( $67.7 \pm 20.6^\circ$  vs  $55.5 \pm 9.5^\circ$ ,  $r = 0.65$ ;  $P = 0.029$ ), 60° ( $62.9 \pm 22.4^\circ$  vs  $45.8 \pm 13.1^\circ$ ,

$r = 0.65$ ;  $P = 0.031$ ) and  $90^\circ$  ( $43.6 \pm 17.6^\circ$  vs  $31.0 \pm 6.3^\circ$ ,  $r = 0.62$ ;  $P = 0.043$ ) of knee flexion and at 9 nm at  $0^\circ$  ( $69.7 \pm 40.0^\circ$  vs  $55.6 \pm 30.6^\circ$ ,  $r = 0.86$ ;  $P = 0.001$ ) and  $60^\circ$  ( $74.5 \pm 27.6^\circ$  vs  $57.1 \pm 11.5^\circ$ ,  $r = 0.77$ ;  $P = 0.006$ ). No statistically significant correlation with 9 nm at  $30^\circ$  ( $79.2 \pm 25.1^\circ$  vs  $66.9 \pm 15.4^\circ$ ,  $r = 0.59$ ;  $P = 0.055$ ),  $45^\circ$  ( $80.7 \pm 24.7^\circ$  vs  $65.5 \pm 11.2^\circ$ ,  $r = 0.51$ ;  $P = 0.11$ ) and  $90^\circ$  ( $54.7 \pm 21.1^\circ$  vs  $39.4 \pm 8.2^\circ$ ,  $r = 0.55$ ;  $P = 0.079$ ). We recognize that 9 nm of torque may be not tolerated *in vivo* due to pain. Knee rotation was at its maximum at  $45^\circ$  of knee flexion and increased with increasing torque.

### CONCLUSION

The skin pointer and knee rotation jig can be a reliable and simple means of quantifying knee rotational laxity with future clinical application.

**Key words:** Rotatometer; Rottometer; Knee; Laxity; Cruciate; Biomechanics; Measurement

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** We describe a cadaveric study utilising a knee rotation jig paired with a skin pointer for the measurement of knee rotation laxity which has the potential for clinical application.

Puah KL, Yew AKS, Chou SM, Lie DTT. Comparison of a simplified skin pointer device compared with a skeletal marker for knee rotation laxity: A cadaveric study using a rotation-meter. *World J Orthop* 2018; 9(6): 85-91 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i6/85.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i6.85>

### INTRODUCTION

With increased interest in rotational stability with anterior cruciate ligament reconstruction as seen with the anatomical anterior cruciate ligament (ACL) reconstruction and the double-bundle ACL reconstruction, the need for an objective measurement of knee rotation arises in order to compare subjective clinical scores with rotational stability<sup>[1]</sup>. Registry data currently do not show any significant difference in knee outcome scores between single-bundle and double-bundle ACL reconstructions though proponents of the double-bundle technique recommend it as it is considered to be able to restore both rotational stability and anterior-posterior stability<sup>[1,2]</sup>. Stress radiography with the use of Roentgen Stereophotogrammetric Analysis (RSA) has been described previously with accuracy as high as 10-250  $\mu\text{m}$  and 0.03-0.6° for translations and rotations, respectively, though it is an invasive procedure<sup>[3,4]</sup>. With variability of the pivot shift test amongst even trained orthopaedic surgeons, it becomes imperative that a non-invasive objective instrument be available to assess a

patient's knee rotational stability<sup>[5]</sup>. There is a need for a portable, non-invasive yet simple to use device to measure knee rotation laxity in the clinic.

Almquist *et al*<sup>[6-8]</sup> has described a Rottometer which is a modified chair with the foot strapped to a rotating plate with measurements taken off a goniometer at the foot plate. However there was difference in the Rottometer readings compared to RSA at  $90^\circ$  flexion with 6 nm of torque and this has been attributed to be due to the measurements being taken at the foot which would thus include ankle rotation. To negate the effect of ankle rotation, we propose taking measurements off a fixed point more proximal and closer to the knee joint at the tibial tubercle with a non-invasive skin pointer while immobilizing the ankle in a foam boot. We designed a cadaveric study to assess the reliability of taking measurements off a non-invasive skin pointer placed over the tibial tubercle against that of a skeletally-mounted nail using a novel knee rotation jig modified from the Rottometer with a view to extending this to *in-vivo* testing.

To compare a non-invasive method of measuring knee rotation using a skin pointer against a nail fixed to the tibial tuberosity of a cadaveric knee specimen mounted on a knee rotation jig.

### MATERIALS AND METHODS

Six pairs of cadaveric legs were mounted individually on a prototype knee rotation jig modified from the Rottometer described by Almquist *et al*<sup>[7]</sup> with a locking mechanism to set knee flexion at several predetermined flexion angles (Figure 1). These cadaveric legs were stored frozen and were thawed prior to use in this study. The jig, which is collapsible, foldable and portable, was securely clamped to a table using vice clamps. Each specimen was anchored to the jig at the femur with bolts for stability and at the foot and ankle with an Aircast® Foam Walker (Aircast, Summit, NJ, United States) attached to a rotating baseplate (Figure 2). The Aircast® Foam Walker was mounted to the baseplate to negate the effect of ankle rotation by immobilizing the ankle and foot. The jig features two adjustable metal side plates with Velcro straps which will be used for *in-vivo* testing subsequently. One Kirschner wire was driven into the apex of the tibial tubercle as a bone marker for reference and a skin pointer was attached above the tibial tubercle using a Velcro strap.

A torque wrench was attached to the baseplate and each knee was pre-conditioned prior to taking the first measurement against a mounted protractor. Using the torque wrench, a rotational force of 3, 6 and 9 nm was then applied at  $0^\circ$ ,  $30^\circ$ ,  $45^\circ$ ,  $60^\circ$  and  $90^\circ$  of knee flexion. This was repeated 3 times at each torque and knee flexion for both internal and external rotation for each specimen. The respective readings of the bone marker and skin pointer were recorded and analysed using SPSS for Windows using the Pearson correlation coefficient and the paired *t*-test.

**Table 1 Total knee rotation measured at 0°, 30°, 45°, 60° and 90° of knee flexion with 3 nm of torque**

Knee flexion (°)	Total rotation (°)		Pearson's <i>r</i>	<i>r</i> <i>P</i> -value	<i>t</i> -test <i>P</i> -value
	Skin pointer	Nail			
0	23.88 ± 25.99	16.33 ± 17.32	0.92	0.000	0.032
30	41.70 ± 15.49	33.06 ± 14.66	0.63	0.037	0.042
45	48.97 ± 16.97	40.30 ± 11.20	0.81	0.002	0.030
60	45.73 ± 17.45	34.70 ± 9.45	0.86	0.001	0.008
90	29.21 ± 10.89	21.15 ± 6.75	0.69	0.019	0.016



Figure 1 Knee rotation jig prior to mounting of specimen.



Figure 2 Knee rotation jig with specimen mounted with nail through tibial tuberosity and skin pointer in place.

## RESULTS

The readings for total rotation obtained with the skin pointer significantly correlated with that of the bone marker at 3 nm at 0°, 30°, 45°, 60°, and 90° of knee flexion (Table 1 and Figure 3). Similarly the readings for total rotation obtained with the skin pointer significantly correlated with that of the bone marker at 6 nm at 0°, 30°, 45°, 60° and 90° of knee flexion (Table 2 and Figure 4). However, although the readings between the skin pointer and bone marker correlated significantly at 3 nm of torque, there was a significant difference on paired *t*-test between the two readings through all degrees of flexion. With 6 nm of torque, there was a significant difference between the readings at 45°, 60°

and 90° of flexion.

With 9 nm of torque, there was a statistically significant correlation at 0° and 60° but no statistically significant correlation at 30° and 90° of knee flexion though there was a similar trend to 3 and 6 nm of torque (Table 3 and Figure 5). With 9 nm of torque, there was a significant difference between the readings at 45°, 60° and 90° of flexion. We found that at 9 nm torque, the cadaveric specimen would not return to the neutral starting position, suggestive of deformation of the specimen.

The skin pointer exaggerated the amount of rotation compared to the bone marker at all torques and angles of knee flexion with the maximum difference of 15.6° at 45° knee flexion with 9 nm of torque. For both the skin pointer and the bone marker, knee rotation increased with increasing knee flexion with maximum rotation at 45° flexion with subsequent decrease in rotation till 90° of knee flexion was reached (Figures 3-5). With increasing torque at a fixed flexion, knee rotation increased (Figure 6).

## DISCUSSION

Apart from stress radiography with the use of RSA which is an invasive procedure, other instruments have been described to measure knee rotation including Almquist's Rottometer from which our prototype jig is based on, Lars Rotational Laxiometer, Vermont Knee Laxity Device, Tsai *et al*<sup>[9]</sup>'s rotational knee laxity measurement device and Ahrens' torsiometer<sup>[7,10-12]</sup>.

Almquist's Rottometer includes a chair where measurements were taken from the foot which may have contributed to its reported inaccuracy as ankle and foot rotation could still contribute to movement and readings<sup>[6,7]</sup>. The use of an Aircast® Foam Walker boot to immobilize the foot and ankle and the use of a skin pointer close to the knee joint as in our study would help to minimize systematic error from foot and ankle movement. Mouton *et al*<sup>[13,14]</sup> used a prototype rottometer with a similar ski boot and delivered the torque through a rotational handle bar and measured rotation through an inclinometer attached to the bar. Tsai's device utilized a magnetic tracking system with an Aircast® Foam Walker boot with reliable results<sup>[9]</sup>. Ahrens' utilized a torsiometer with Schanz pins to mount the cadaveric limbs skeletally with a potentiometer to measure rotation and demonstrated that cadaveric knees with arthroscopically resected ACLs had greater rotation than cadaveric knees

**Table 2 Total knee rotation measured at 0°, 30°, 45°, 60° and 90° of knee flexion with 6 nm of torque**

Knee flexion (°)	Total rotation (°)		Pearson's <i>r</i>	<i>r</i> P-value	<i>t</i> -test P-value
	Skin pointer	Nail			
0	51.12 ± 37.73	38.61 ± 30.07	0.90	0	0.064
30	64.64 ± 21.61	54.27 ± 15.11	0.73	0.011	0.051
45	67.73 ± 20.60	55.48 ± 9.45	0.65	0.029	0.019
60	62.85 ± 22.43	45.79 ± 13.05	0.65	0.031	0.006
90	43.61 ± 17.56	30.97 ± 6.25	0.62	0.043	0.007

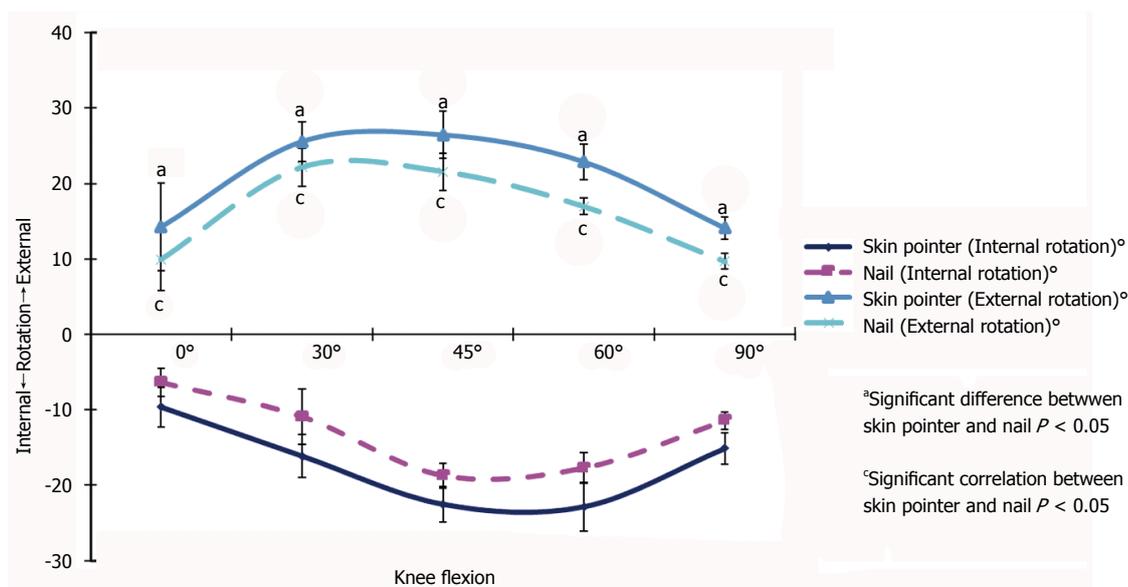


Figure 3 Knee rotation measured at 0°, 30°, 45°, 60° and 90° of knee flexion with 3 nm of torque.

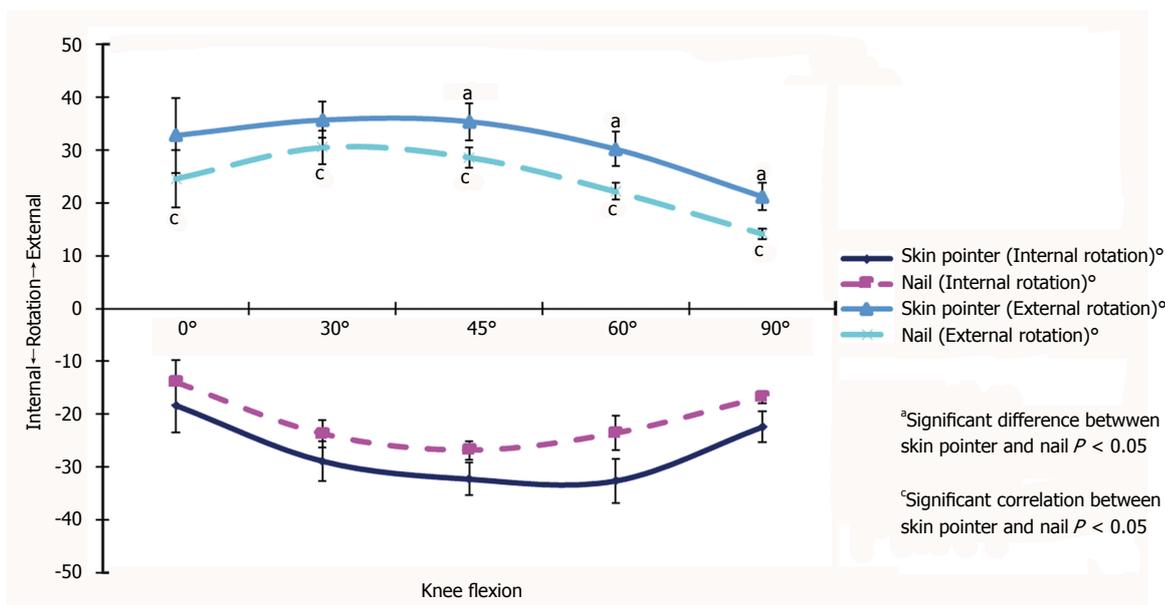


Figure 4 Knee rotation measured at 0°, 30°, 45°, 60° and 90° of knee flexion with 6 nm of torque.

with the ACL intact<sup>[12]</sup>.

Robotic arm technology has also been described to deliver the rotational force to mimic the dial test<sup>[15,16]</sup>. The Rotab<sup>®</sup> device measures medial knee rotation wh-

en delivering an anterior translation force to measure anteromedial knee instability<sup>[17]</sup>. A similar device which measures passive medial knee rotation with anterior translation of the tibia was described by Kurimura *et al*<sup>[18]</sup>.

**Table 3** Total knee rotation measured at 0°, 30°, 45°, 60° and 90° of knee flexion with 9 nm of torque

Knee flexion (°)	Total rotation (°)		Pearson's <i>r</i>	<i>r</i> P-value	<i>t</i> -test P-value
	Skin pointer	Nail			
0	69.67 ± 39.91	55.61 ± 30.61	0.86	0.001	0.046
30	79.18 ± 25.14	66.91 ± 15.42	0.59	0.055	0.072
45	80.67 ± 24.65	65.48 ± 11.23	0.51	0.112	0.040
60	74.52 ± 27.57	57.09 ± 11.50	0.77	0.006	0.017
90	54.70 ± 21.05	39.39 ± 8.22	0.55	0.079	0.018

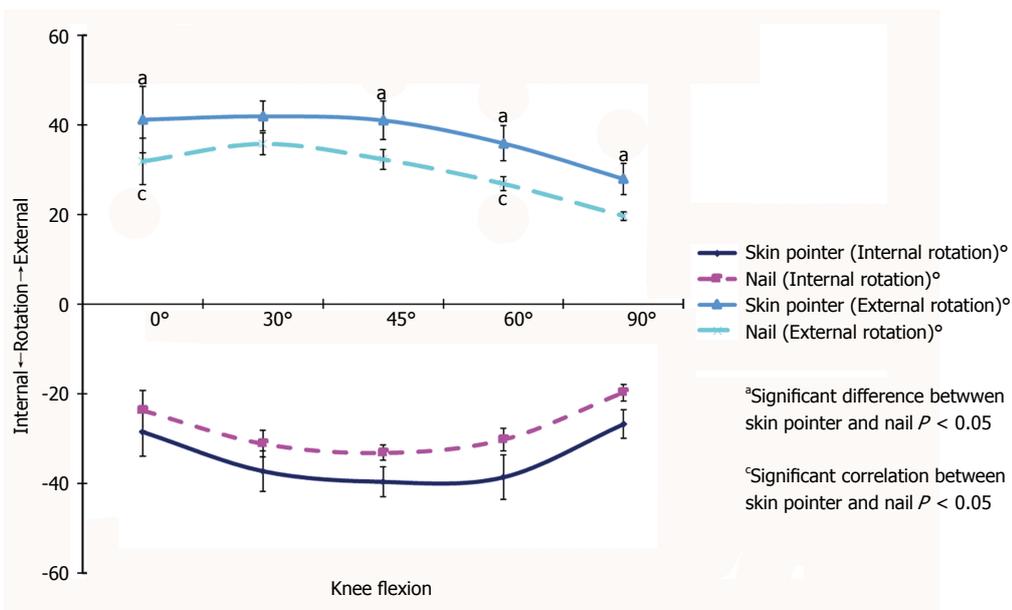


Figure 5 Knee rotation measured at 0°, 30°, 45°, 60° and 90° of knee flexion with 9 nm of torque.

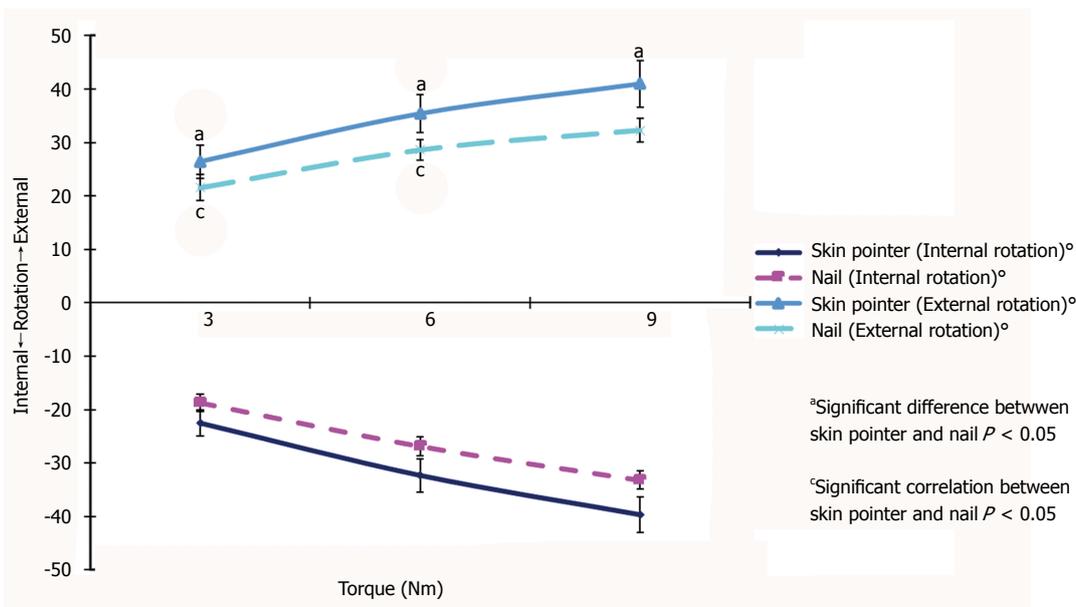


Figure 6 Knee rotation at 45° of flexion with 3, 6, and 9 nm of torque.

Hoshino *et al.*<sup>[19]</sup> described a motion capture method using skin markers to measure the anterior translation of the distal femur in anaesthetised patients undergoing the pivot shift test.

Computer assisted surgery (CAS) devices which use motion-tracking technology and bony reference points can be used too but are invasive and are best used in the operating theatre during surgery<sup>[20,21]</sup>. The benefit

of our setup is that it is simple to set-up, portable and does not rely on bulky electronic equipment allowing it to be used in the clinic and possibly at sports training grounds where a controlled environment with a ready electrical source may not be available.

Our study shows that our simple non-invasive skin pointer used in combination with our knee rotation jig can measure knee rotation similar to that of a skeletally placed marker with our knee rotation jig. We recognize that the skin pointer would exaggerate the amount of rotation compared to the bone marker due to movement of the soft tissue and skin overlying the bone. Hence although the readings between the skin pointer and the bone marker were significantly correlated with a similar trend, with higher torque and greater knee flexion, there were significant differences between the individual measurements. We recognize too that 9 nm of torque may not be well-tolerated in live human subjects due to pain. The effect of soft tissue causing an exaggeration of results has been reported previously<sup>[22]</sup>. Furthermore, 9 nm of torque may have caused deformation of our specimens affecting our results as a limitation of our use of cadavers which we may not observe *in vivo*.

Our jig and measurements assume a global single-axis of rotation of the knee, not taking into account translation of the knee which may occur *in vivo* with live subjects where rigid skeletal mounting to the jig will not be feasible. Hence off-axis movements may not be accurately measured as compared to a system where measurements are taken at both the femur and tibia taking into account movement of the subject in the jig. We recognize that the rotation axis of the tibia changes with knee as reported by Matsumoto and that our simple all-mechanical jig and measurement system may not be able to account for this change in axis<sup>[23]</sup>. Similar to Matsumoto's study, we found that the magnitude of knee rotation increases as the knee is flexed which then decreases as flexion reaches 90°. Knee rotation was observed to be at its maximum at 45° of knee flexion and it increased with increasing torque. Similar to other previously described instruments, our device measures rotation without the effect of weight-bearing<sup>[7,9-11]</sup>.

Our study compared the use of a skin pointer in combination with our knee rotation jig against a skeletally mounted marker which showed significant correlation between the two readings. We recognise the significant difference between the absolute values of the two different measurement methods due to soft tissue movement over the bone and that the soft tissue in a cadaver which has been frozen and thawed will have different properties compared to that of a live subject. Similar experiments with Rotatometers/Rottometers using only live subjects with no skeletally mounted reference for comparison demonstrate high inter- and intra-observer reliability<sup>[24,25]</sup>.

Objective measurement for anterior-posterior laxity using the KT-1000 Arthrometer is well accepted<sup>[26-28]</sup>. Our aim is to eventually develop a portable and user-friendly device analogous to the KT-1000 which can

be used for objective measurement of knee rotation in a non-invasive manner. The investigation of the utility of our rotation jig mated with a robotic arm for kinematic measurements is currently ongoing which may negate the effect of translation of the knee *in vivo*. Our next phase is to collect data on volunteers with uninjured knees followed by patients with knee injuries and patients after surgery to document changes in knee rotational laxity with pathology and treatment.

In conclusion, the skin pointer combined with a knee rotation jig can be a reliable and simple means of quantifying knee rotation in the cadaveric knee with potential application *in vivo* as a non-invasive means of measuring knee rotation in the clinic.

## ARTICLE HIGHLIGHTS

### Research background

With double-bundle and anatomical single-bundle anterior cruciate ligament reconstruction for restoration of rotational knee kinematics, the need for objective clinical measurement of knee rotational laxity arises. Evaluation of knee rotation remains a challenge with intra-observer variability in the pivot shift test.

### Research motivation

We aim to compare a non-invasive skin pointer with a knee rotation jig in cadaveric knees against a skeletally mounted marker.

### Research methods

Six pairs of cadaveric legs were mounted on a knee rotation jig. One Kirschner wire was driven into the tibial tubercle as a bone marker and a skin pointer was attached. Rotational forces of 3, 6 and 9 nm applied at 0°, 30°, 45°, 60° and 90° of knee flexion. Results were analysed using the Pearson correlation coefficient and paired *t*-test.

### Research results

Total rotation recorded with the skin pointer significantly correlated with the bone marker at 3 nm at 0° (skin pointer 23.9 ± 26.0° vs bone marker 16.3 ± 17.3°, *r* = 0.92; *P* = 0.0), 30° (41.7 ± 15.5° vs 33.1 ± 14.7°, *r* = 0.63; *P* = 0.037), 45° (49.0 ± 17.0° vs 40.3 ± 11.2°, *r* = 0.81; *P* = 0.002), 60° (45.7 ± 17.5° vs 34.7 ± 9.5°, *r* = 0.86; *P* = 0.001) and 90° (29.2 ± 10.9° vs 21.2 ± 6.8°, *r* = 0.69; *P* = 0.019) of knee flexion and 6 nm at 0° (51.1 ± 37.7° vs 38.6 ± 30.1°, *r* = 0.90; *P* = 0.0), 30° (64.6 ± 21.6° vs 54.3 ± 15.1°, *r* = 0.73; *P* = 0.011), 45° (67.7 ± 20.6° vs 55.5 ± 9.5°, *r* = 0.65; *P* = 0.029), 60° (62.9 ± 22.4° vs 45.8 ± 13.1°, *r* = 0.65; *P* = 0.031) and 90° (43.6 ± 17.6° vs 31.0 ± 6.3°, *r* = 0.62; *P* = 0.043) of knee flexion and at 9 nm at 0° (69.7 ± 40.0° vs 55.6 ± 30.6°, *r* = 0.86; *P* = 0.001) and 60° (74.5 ± 27.6° vs 57.1 ± 11.5°, *r* = 0.77; *P* = 0.006). No statistically significant correlation with 9 nm at 30° (79.2 ± 25.1° vs 66.9 ± 15.4°, *r* = 0.59; *P* = 0.055), 45° (80.7 ± 24.7° vs 65.5 ± 11.2°, *r* = 0.51; *P* = 0.11) and 90° (54.7 ± 21.1° vs 39.4 ± 8.2°, *r* = 0.55; *P* = 0.079). We recognize that 9 nm of torque may be not tolerated *in vivo* due to pain.

### Research conclusions

We have measured knee rotation on a cadaveric knee utilising a knee rotation jig paired with a skin pointer against that of a skeletally mounted bone marker and have found a significant correlation between the two methods for the same magnitude of torque and knee flexion. We recognise that the use of the skin pointer introduces error due to movement of the soft tissue which increases with increasing torque.

### Research perspectives

Our aim is to eventually develop a portable and user-friendly device which can be used for objective measurement of knee rotation laxity in a non-invasive manner. This may entail the use of accelerometers or robotic arms to measure

kinematics.

## REFERENCES

- 1 Ahldén M, Samuelsson K, Sernert N, Forssblad M, Karlsson J, Kartus J. The Swedish National Anterior Cruciate Ligament Register: a report on baseline variables and outcomes of surgery for almost 18,000 patients. *Am J Sports Med* 2012; **40**: 2230-2235 [PMID: 22962296 DOI: 10.1177/0363546512457348]
- 2 Araki D, Kuroda R, Kubo S, Fujita N, Tei K, Nishimoto K, Hoshino Y, Matsushita T, Matsumoto T, Nagamune K, Kurosaka M. A prospective randomised study of anatomical single-bundle versus double-bundle anterior cruciate ligament reconstruction: quantitative evaluation using an electromagnetic measurement system. *Int Orthop* 2011; **35**: 439-446 [PMID: 20734043 DOI: 10.1007/s00264-010-1110-9]
- 3 Kärrholm J. Roentgen stereophotogrammetry. Review of orthopedic applications. *Acta Orthop Scand* 1989; **60**: 491-503 [PMID: 2683567 DOI: 10.3109/17453678909149328]
- 4 Selvik G. Roentgen stereophotogrammetry. A method for the study of the kinematics of the skeletal system. *Acta Orthop Scand Suppl* 1989; **232**: 1-51 [PMID: 2686344 DOI: 10.3109/17453678909154184]
- 5 Musahl V, Hoshino Y, Ahlden M, Araujo P, Irrgang JJ, Zaffagnini S, Karlsson J, Fu FH. The pivot shift: a global user guide. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 724-731 [PMID: 22210541 DOI: 10.1007/s00167-011-1859-4]
- 6 Almquist PO, Ekdahl C, Isberg PE, Fridén T. Knee rotation in healthy individuals related to age and gender. *J Orthop Res* 2013; **31**: 23-28 [PMID: 22778072 DOI: 10.1002/jor.22184]
- 7 Almquist PO, Arnbjörnsson A, Zätterström R, Ryd L, Ekdahl C, Fridén T. Evaluation of an external device measuring knee joint rotation: an in vivo study with simultaneous Roentgen stereometric analysis. *J Orthop Res* 2002; **20**: 427-432 [PMID: 12038614 DOI: 10.1016/S0736-0266(01)00148-6]
- 8 Almquist PO, Ekdahl C, Isberg PE, Fridén T. Measurements of knee rotation-reliability of an external device in vivo. *BMC Musculoskelet Disord* 2011; **12**: 291 [PMID: 22208736 DOI: 10.1186/1471-2474-12-291]
- 9 Tsai AG, Musahl V, Steckel H, Bell KM, Zantop T, Irrgang JJ, Fu FH. Rotational knee laxity: reliability of a simple measurement device in vivo. *BMC Musculoskelet Disord* 2008; **9**: 35 [PMID: 18366671 DOI: 10.1186/1471-2474-9-35]
- 10 Bleday RM, Fanelli GC, Giannotti BF, Edson CJ, Barrett TA. Instrumented measurement of the posterolateral corner. *Arthroscopy* 1998; **14**: 489-494 [PMID: 9681541 DOI: 10.1016/S0749-8063(98)70077-5]
- 11 Uh BS, Beynon BD, Churchill DL, Haugh LD, Risberg MA, Fleming BC. A new device to measure knee laxity during weightbearing and non-weightbearing conditions. *J Orthop Res* 2001; **19**: 1185-1191 [PMID: 11781022 DOI: 10.1016/S0736-0266(01)00055-9]
- 12 Ahrens P, Kirchhoff C, Fischer F, Heinrich P, Eisenhart-Rothe R, Hinterwimmer S, Kirchhoff S, Imhoff AB, Lorenz SG. A novel tool for objective assessment of femorotibial rotation: a cadaver study. *Int Orthop* 2011; **35**: 1611-1620 [PMID: 21181404 DOI: 10.1007/s00264-010-1159-5]
- 13 Mouton C, Theisen D, Seil R. Objective measurements of static anterior and rotational knee laxity. *Curr Rev Musculoskelet Med* 2016; **9**: 139-147 [PMID: 26970758 DOI: 10.1007/s12178-016-9332-0]
- 14 Mouton C, Seil R, Agostinis H, Maas S, Theisen D. Influence of individual characteristics on static rotational knee laxity using the Rotameter. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 645-651 [PMID: 22246548 DOI: 10.1007/s00167-011-1877-2]
- 15 Branch T, Stinton S, Sternberg M, Hutton W, Lavoie F, Guier C, Neyret P. Robotic axial lower leg testing: repeatability and reproducibility. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2892-2899 [PMID: 26359177 DOI: 10.1007/s00167-015-3768-4]
- 16 Stinton SK, Siebold R, Freedberg H, Jacobs C, Branch TP. The use of a robotic tibial rotation device and an electromagnetic tracking system to accurately reproduce the clinical dial test. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 815-822 [PMID: 26891963 DOI: 10.1007/s00167-016-4042-0]
- 17 Senioris A, Rousseau T, L'Hermette M, Gouzy S, Duparc F, Dujardin F. Validity of rotational laxity coupled with anterior translation of the knee: A cadaveric study comparing radiostereometry and the Rotab<sup>®</sup>. *Knee* 2017; **24**: 289-294 [PMID: 28139332 DOI: 10.1016/j.knee.2017.01.009]
- 18 Kurimura M, Matsumoto H, Fujikawa K, Toyama Y. Factors for the presence of anteromedial rotatory instability of the knee. *J Orthop Sci* 2004; **9**: 380-385 [PMID: 15278776 DOI: 10.1007/s00776-004-0797-0]
- 19 Hoshino Y, Araujo P, Irrgang JJ, Fu FH, Musahl V. An image analysis method to quantify the lateral pivot shift test. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 703-707 [PMID: 22203048 DOI: 10.1007/s00167-011-1845-x]
- 20 Colombet P, Robinson J, Christel P, Franceschi JP, Djian P. Using navigation to measure rotation kinematics during ACL reconstruction. *Clin Orthop Relat Res* 2007; **454**: 59-65 [PMID: 17119463 DOI: 10.1097/BLO.0b013e31802baf56]
- 21 Musahl V, Voos JE, O'Loughlin PF, Choi D, Stueber V, Kendoff D, Pearle AD. Comparing stability of different single- and double-bundle anterior cruciate ligament reconstruction techniques: a cadaveric study using navigation. *Arthroscopy* 2010; **26**: S41-S48 [PMID: 20692120 DOI: 10.1016/j.arthro.2010.01.028]
- 22 Alam M, Bull AM, Thomas Rd, Amis AA. Measurement of rotational laxity of the knee: in vitro comparison of accuracy between the tibia, overlying skin, and foot. *Am J Sports Med* 2011; **39**: 2575-2581 [PMID: 21997728 DOI: 10.1177/0363546511424872]
- 23 Matsumoto H, Seedhom BB, Suda Y, Otani T, Fujikawa K. Axis location of tibial rotation and its change with flexion angle. *Clin Orthop Relat Res* 2000; **371**: 178-182 [PMID: 10693565]
- 24 Lorbach O, Wilmes P, Theisen D, Brockmeyer M, Maas S, Kohn D, Seil R. Reliability testing of a new device to measure tibial rotation. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 920-926 [PMID: 19305971 DOI: 10.1007/s00167-009-0772-6]
- 25 Chung JH, Ryu KJ, Lee DH, Yoon KH, Park YW, Kim HJ, Kim JH. An analysis of normative data on the knee rotatory profile and the usefulness of the Rotatometer, a new instrument for measuring tibiofemoral rotation: the reliability of the knee Rotatometer. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2727-2733 [PMID: 24817107 DOI: 10.1007/s00167-014-3039-9]
- 26 Robnett NJ, Riddle DL, Kues JM. Intertester reliability of measurements obtained with the KT-1000 on patients with reconstructed anterior cruciate ligaments. *J Orthop Sports Phys Ther* 1995; **21**: 113-119 [PMID: 7711760 DOI: 10.2519/jospt.1995.21.2.113]
- 27 Sernert N, Kartus J, Köhler K, Ejerhed L, Karlsson J. Evaluation of the reproducibility of the KT-1000 arthrometer. *Scand J Med Sci Sports* 2001; **11**: 120-125 [PMID: 11252461 DOI: 10.1034/j.1600-0838.2001.011002120.x]
- 28 Pugh L, Mascarenhas R, Arneja S, Chin PY, Leith JM. Current concepts in instrumented knee-laxity testing. *Am J Sports Med* 2009; **37**: 199-210 [PMID: 18940931 DOI: 10.1177/0363546508323746]

P- Reviewer: Angoules A S- Editor: Cui LJ L- Editor: A  
E- Editor: Tan WW





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 July 18; 9(7): 92-104





**SYSTEMATIC REVIEWS**

- 92 Systematic review of dynamization vs exchange nailing for delayed/non-union femoral fractures  
*Vaughn JE, Shah RV, Samman T, Stirton J, Liu J, Ebraheim NA*

**CASE REPORT**

- 100 Anterior transolecranon dislocation of the elbow in a child: A case report and review of literature  
*Bouaziz W, Guidara AR, Trabelsi A, Bardaa T, Hammami M, Ellouz Z, Keskes H*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Efstathios Drampalos, MD, MSc, PhD, Senior Postdoctoral Fellow, Surgeon, Department of Orthopaedics, Manchester NHS Foundation Trust, Manchester M13 9WL, 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, 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 Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central and Scopus.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Fang-Fang Ji*  
**Proofing Editorial Office Director:** *Jin-Lai Wang*

**NAME OF JOURNAL**  
*World Journal of Orthopedics*

**ISSN**  
 ISSN 2218-5836 (online)

**LAUNCH DATE**  
 November 18, 2010

**FREQUENCY**  
 Monthly

**EDITOR-IN-CHIEF**  
**Bao-Gan Peng, MD, PhD, Professor**, Department of Spinal Surgery, General Hospital of Armed Police Force, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjnet.com/2218-5836/editorialboard.htm>

**EDITORIAL OFFICE**  
 Jin-Lai Wang, Director

*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjnet.com](mailto:editorialoffice@wjnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjnet.com](mailto:bpgoffice@wjnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjnet.com>

**PUBLICATION DATE**  
 July 18, 2018

**COPYRIGHT**  
 © 2018 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.f6publishing.com>

## Systematic review of dynamization *vs* exchange nailing for delayed/non-union femoral fractures

Jacob E Vaughn, Ronit V Shah, Tarek Samman, Jacob Stirton, Jiayong Liu, Nabil A Ebraheim

Jacob E Vaughn, Ronit V Shah, Tarek Samman, College of Medicine and Life Sciences, University of Toledo, Toledo, OH 43614, United States

Jacob Stirton, Jiayong Liu, Nabil A Ebraheim, Department of Orthopedic Surgery, University of Toledo Medical Center, Toledo, OH 43614, United States

ORCID number: Jacob E Vaughn (0000-0001-9711-7309); Ronit V Shah (0000-0003-2944-4193); Tarek Samman (0000-0002-6189-7224); Jacob Stirton (0000-0003-4669-4696); Jiayong Liu (0000-0002-5895-8276); Nabil A Ebraheim (0000-0002-0950-3689).

Author contributions: Vaughn JE, Shah RV and Samman T performed the research and analyzed the data and wrote the paper; Stirton J, Liu J and Ebraheim NA provided structure for the article as well as edited and revised the paper.

Conflict-of-interest statement: The authors report 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: Unsolicited manuscript

Correspondence to: Jiayong Liu, MD, Assistant Professor, Department of Orthopedic Surgery, University of Toledo Medical Center, 3065 Arlington Avenue, Toledo, OH 43614, United States. [jiayong.liu@utoledo.edu](mailto:jiayong.liu@utoledo.edu)  
Telephone: +1-800-5865336  
Fax: +1-419-3835362

Received: February 3, 2018  
Peer-review started: February 6, 2018  
First decision: March 2, 2018  
Revised: April 24, 2018

Accepted: May 30, 2018

Article in press: May 30, 2018

Published online: July 18, 2018

### Abstract

#### AIM

To analyze the literature on efficacy of dynamization *vs* exchange nailing in treatment of delayed and non-union femur fractures.

#### METHODS

Ultimately, 31 peer-reviewed articles with 644 exchanged nailing patients and 131 dynamization patients were identified and analyzed. The following key words were inputted in different combinations in order to search the field of publications in its entirety: "non-union", "delayed union", "ununioned", "femur fracture", "femoral fracture", "exchange nailing", "dynamization", "secondary nailing", "dynamic", "static", and "nail revision". The initial search yielded over 150 results, and was refined based on the inclusion criteria: Only studies reporting on humans, non-unions and delayed unions, and the usage of exchange nailing and/or dynamization as a secondary treatment after failed IM nailing. The resulting 66 articles were obtained through online journal access. The results were filtered further based on the exclusion criteria: No articles that failed to report overall union rates, differentiate between success rates of their reported techniques, or articles that analyzed less than 5 patients.

#### RESULTS

Exchange nailing lead to fracture union in 84.785% of patients compared to the 66.412% of dynamization with statistically comparable durations until union ( $5.193 \pm 2.310$  mo and  $4.769 \pm 1.986$  mo respectively). Dynamically locking exchange nails resulted in an average union time of  $5.208 \pm 2.475$  mo compared to  $5.149 \pm 2.366$  mo ( $P = 0.8682$ ) in statically locked

exchange nails. The overall union rate of the two procedures, statically and dynamically locked exchange nailing yielded union rates of 84.259% and 82.381% respectively. Therefore, there was no significant difference between the different locking methods of exchange nailing for union rate or time to union at a significance value of  $P < 0.05$ . The analysis showed exchange nailing to be the more successful choice in the treatment of femoral non-unions in respect to its higher success rate (491/567 EN, 24/57 dynam,  $P < 0.0001$ ). However, there was no significant difference between the success rates of the two procedures for delayed union fractures (25/27 EN, 45/55 dynam,  $P = 0.3299$ ). Nevertheless, dynamization was more efficient in the treatment of delayed unions (at rates comparable to exchange nailing) than in the treatment of non-unions.

### CONCLUSION

In conclusion, after examination of factors, dynamization is recommended treatment of delayed femur fractures, while exchange nailing is the treatment of choice for non-unions.

**Key words:** Non-union; Delayed union; Dynamization; Femoral fracture; Exchange nailing

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Information from previously published articles investigating patients treated for delayed union and non-union femur fractures by either dynamization or exchange nailing was combined and analyzed to better understand which technique was more efficient at achieving osseous union. When treating femoral non-unions, exchange nailing was shown to achieve osseous union in a higher percentage of patients than dynamization with comparable recovery times. However, dynamization appears to be equally as effective as exchange nailing in the treatment of delayed unions.

Vaughn JE, Shah RV, Samman T, Stirton J, Liu J, Ebraheim NA. Systematic review of dynamization vs exchange nailing for delayed/non-union femoral fractures. *World J Orthop* 2018; 9(7): 92-99 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i7/92.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i7.92>

### INTRODUCTION

Delayed union and non-union are two designations for the slowed or absent progression of callus formation and osseous healing in a fracture from 3-6 mo, and greater than 6 mo, respectively. Although IM nailing is an effective treatment method for femoral fractures with union rates reported between 90%-100%<sup>[1]</sup>, non-union rates have increased due to the higher probability of survival in complex injuries and improved limb salvage

techniques<sup>[2]</sup>. As a result, secondary surgical techniques have become increasingly important in achieving osseous union in femur fractures.

Two of the more common secondary surgical techniques used in the treatment of delayed union and non-union after IM nail failure are dynamization and exchange nailing. Dynamization involves the removal of proximal or distal locking screws in a statically locked IM nail allowing weight bearing to stimulate osseous growth at the fracture site. Previously, surgeons used this technique before delayed union occurred in an attempt to avoid complications and improve union rates. However, studies have failed to find any advantage to this choice<sup>[3]</sup>, resulting in it mainly being used as a secondary treatment.

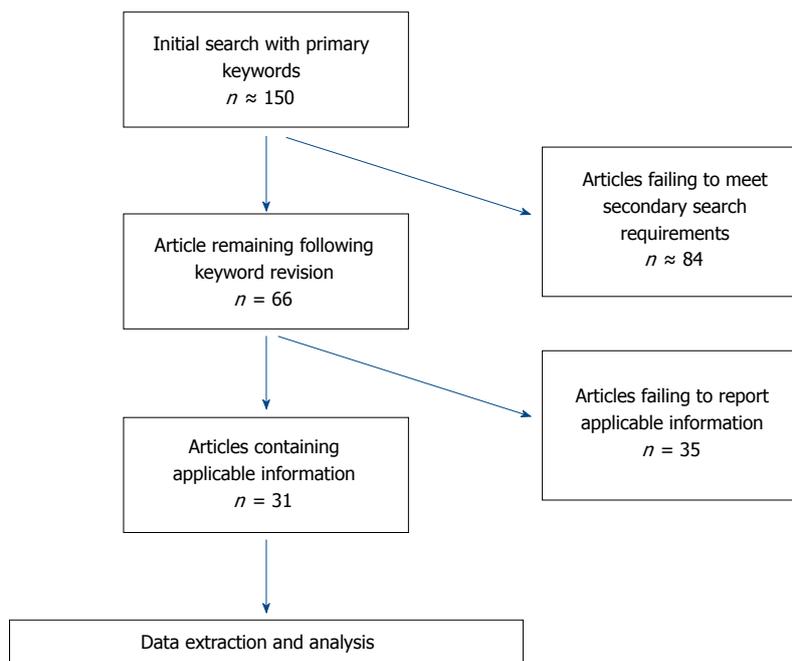
An alternate treatment strategy, exchange nailing, consists of the removal of the current IM nail, debridement of the medullary cavity, followed by insertion of a larger IM nail. This procedure utilizes reaming and increased fracture stability to stimulate osseous growth. Different variations of this procedure have been reported, with varying rates of success attributed to factors such as the use of bone grafting, size of medullary reaming, and different nail locking methods<sup>[4,5]</sup>.

Unfortunately, the overall reported rates of successful unions achieved using these techniques range from 33.3%-90% in dynamization<sup>[6-12]</sup> and 28.6%-100% in exchange nailing<sup>[8,9,13-36]</sup>. Additional factors including infection, locations of injury, and major surgical complications have been reported at varying rates across literature resulting in a lack of consensus in the field<sup>[5]</sup>.

The results of multiple studies were examined in an attempt to consolidate the published information across the field and clarify which procedure to use. Consolidation of these results into a larger subject pool across the existing literature increases the strength of its conclusions compared to individual reports. Additionally, the locking method of exchange nails, either static or dynamic, has been identified as a possible factor affecting union rates<sup>[5]</sup>. Dynamic locking attempts to combine these procedures in order to improve healing rates, as compared to static exchange nailing, but results have been varied. Finally, dynamization has been suggested to result in different rates of success between the treatments of delayed unions in comparison to non-unions<sup>[1]</sup>. This may allow procedures to be utilized more effectively, based on the different progressions of patients' injuries. Currently there is lack updated systematic review and meta-analysis on this topic in the literature. This systematic review and meta-analysis were designed to analyze the current literature on these two procedures in their treatment of delayed and non-union femur fractures to determine their overall efficacy and factors related to their success.

### MATERIALS AND METHODS

MEDLINE and OVID search databases were used to identify relevant, peer-reviewed articles published within



**Figure 1** Flow diagram for studies included in analysis. The following boxes starting from the top depicts the progression from initial studies found pertaining to the desired procedures followed by the removal of different studies based on our exclusion criteria.

scientific and medical research journals. The following key words were inputted in different combinations in order to search the field of publications in its entirety: "non-union", "delayed union", "ununioned", "femur fracture", "femoral fracture", "exchange nailing", "dynamization", "secondary nailing", "dynamic", "static", and "nail revision". The initial search yielded over 150 results, and was refined based on the inclusion criteria: Only studies reporting on humans, non-unions and delayed unions, and the usage of exchange nailing and/or dynamization as a secondary treatment after failed IM nailing. The resulting 66 articles were obtained through online journal access. The results were filtered further based on the exclusion criteria: No articles that failed to report overall union rates, differentiate between success rates of their reported techniques, or articles that analyzed less than 5 patients. In all, 31 articles (including retrospective studies and randomized controlled studies), published between 05/1973 and 12/2015, were included in the study (Figure 1).

Isolation and pooling of dependent variables and summary measures from the 31 papers were completed using set guidelines. Patients treated in each study were required to have previously undergone treatment with an IM nail that was still in place at the time of the secondary surgery being studied. Therefore, implantation of a dynamically locked IM nail following external fixation/plating was considered neither exchange nailing nor dynamization. Dynamization of IM nails were required to be in response to failed progression towards union (delayed/non-union). Patients receiving dynamization as part of their original treatment plan were excluded from the analysis. When analyzing patient

demographics, patient information tables included in the studies were the primary source used. Bilateral fractures were recorded as separate fractures with independent characteristics. Additionally, revision surgeries and progression to union were recorded but repeated surgeries were not considered in overall union rates (three exchange nailing procedures to achieve union were considered as a failure of the secondary treatment under investigation to achieve union). Verified infections were recorded and included only when discrete from other patient information, so as to prevent skewing of the overall results. Finally, patients lost to follow-up were excluded from the analysis unless osseous union was confirmed prior to them leaving the study.

### Statistical analysis

In order to analyze the information, all of the demographic information for patients from each surgical procedure was combined and used to compare each demographic category against the overall union rate of its respective surgical procedure as well as against the same category of the opposite surgical procedure. Statistical significance was determined using graphpad™ to run Fischer exact or  $\chi^2$  tests (based on category sizes) with *P*-values reported next to statistically significant information. Time to union was analyzed using a two-tail *T*-test. Significance for all analyses was determined to be *P* < 0.05.

## RESULTS

Exchange nailing showed to be the significantly more effective treatment procedure with an overall union rate

**Table 1 Overall outcomes of surgeries studied**

Surgical procedure	Surgical subtype	No. of articles reporting on secondary procedure (patient number)	Average union %	Average reported time to union
Dynamization	All	7 (131)	66.412 <sup>b</sup>	4.769 ± 1.986 mo (26 pts) <sup>a</sup>
Exchange nailing	All	26 (644)	84.785 <sup>b</sup>	5.193 ± 2.310 mo (372 pts) <sup>a</sup>
Exchange nailing	Static locking	15 (235 pts)	84.259	5.149 ± 2.366 mo (103 pts)
Exchange nailing	Dynamic locking	13 (211 pts)	82.381	5.208 ± 2.475 mo (84 pts)

<sup>b</sup> $P < 0.0001$ , significant; <sup>a</sup> $P = 0.3622$ , not significant.

of 84.785% compared to 66.412% in dynamization ( $P < 0.0001$ ). There was no significant difference in the average time to osseous union following either surgical procedure (4.769 ± 1.986 mo dynamization, 5.193 ± 2.310 mo exchange nailing,  $P = 0.3622$ ). Therefore, the overall difference found while comparing the two procedures was their successful union rates (Table 1).

Dynamically locking exchange nails resulted in an average union time of 5.208 ± 2.475 mo compared to 5.149 ± 2.366 ( $P = 0.8682$ ) in statically locked exchange nails. The overall union rate of the two procedures, statically and dynamically locked exchange nailing yielded union rates of 84.259% and 82.381% respectively. Therefore, there was no significant difference between the different locking methods of exchange nailing for union rate or time to union at a significance value of  $P < 0.05$  (Table 1).

Union rates of specific demographics were compared across procedures and compared against each procedure's overall union rates. Several demographics in exchange nailing yielded significantly different overall rates of union compared to exchange nailing as a whole. Of these demographics, tobacco use (54/74,  $P = 0.0023$ ), infra and supra-isthmal fracture location (5/9,  $P = 0.0265$ , 10/16,  $P = 0.0045$ ) and infection (19/30,  $P = 0.0019$ ) were shown to have a significant negative impact on the outcome of exchange nailing (Tables 2-5). The isthmal classification system yielded significantly lower union rates compared to the overall rates of exchange nailing while proximal, middle, and distal thirds categories did not yield a difference. Therefore, in comparison, the isthmal classification system appears to be more useful for predicting surgical outcomes based on fracture location. However, a larger patient pool would be preferable to confirm these results.

Of the dynamization factors, union rates of delayed union (45/55,  $P = 0.0228$ ) and non-union fractures (24/57,  $P < 0.0063$ ) were significantly better and worse, respectively, in comparison to dynamization's overall union rate (84/131) (Table 4). Dynamization of delayed unions proved to be a more successful procedure than dynamization of non-unions in femurs. When comparing demographics across surgical procedures, there was a lack of a statistical difference between female patients (72/86 EN and 17/26 dynam,  $P = 0.0544$ ), hypertrophic fractures (72/83 EN and 9/11 dynam,  $P = 0.6563$ ), and delayed union (25/27 EN and 45/55 dynam,  $P = 0.3199$ ) (Table 2 and 4)

The analysis showed exchange nailing to be the more successful choice in the treatment of femoral non-unions in respect to its higher success rate (491/567 EN, 24/57 dynam,  $P < 0.0001$ ). However, there was no significant difference between the success rates of the two procedures for delayed union fractures (25/27 EN, 45/55 dynam,  $P = 0.3299$ ). Without a clear preference in overall success rates for one procedure over the other, additional surgical factors were examined. Dynamization, in comparison to exchange nailing, is a significantly less invasive procedure, has a lower financial cost, and comparable complication rates<sup>[1]</sup> (Table 4). With these factors in mind, in addition to the comparable success rates, the overall results suggest dynamization as the treatment of choice in patients with delayed union femur fractures.

On the other hand, exchange nailing showed a significantly higher success rate in non-unions when compared to dynamization (491/567 EN, 24/57 dynam,  $P < 0.001$ ). In order to avoid the need for further surgical interventions, exchange nailing should be the first consideration in the treatment of non-union femur fractures. Furthermore, there was no significant difference in the success rates or time to union between static and dynamic locking modes of exchange nailing (Table 1). When performing exchange nailing, clinicians should look to alternate factors specific to each patient when deciding which locking method to use in their treatment plans.

## DISCUSSION

While exchange nailing and dynamization have been used as revision techniques for decades, the overall efficacy of each procedure is currently disputed<sup>[6-36]</sup>. Multiple factors and varying rates of success were published in the field with little consistency between papers. The current study examines the literature, utilizing a large subject pool of all published information in the field regarding these procedures.

Several previous authors raised concern for the use of a distal vs mid vs proximal fracture classification when considering treatments in favor of the infra, supra, sub, and isthmal classification<sup>[16]</sup>. The current analysis lent favor to their speculation in favor of the isthmal classification system (Table 3). Additionally, some authors even went on to propose different algorithms for the proper treatment of non-unions based of fracture

**Table 2 Overall demographics of patients involved in studies**

	Exchange nailing		Dynamization		EN <i>vs</i> dynam
	Union/total reported	Significant <i>vs</i> total union rate	Union/total reported	Significant <i>vs</i> total union rate	P-values
No. of patients	556/644	-	84/131	-	<i>P</i> < 0.0001
Ages					
Mean	38.002	-	32.234	-	-
Gender					
Male	244/284	NS	37/66	NS	<i>P</i> < 0.0001
Female	72/86	NS	17/26	NS	NS
Tobacco use					
Yes	54/74	<i>P</i> = 0.0023	2/3	NS	NS
No	49/62	NS	0/3	<i>P</i> = 0.0500	<i>P</i> = 0.0128
NSAIDs use					
Yes	4/8	<i>P</i> = 0.0166	0/0	-	-
No	38/52	<i>P</i> = 0.0093	2/6	NS	<i>P</i> = 0.0463
Diabetic					
Yes	0/0	-	0/0	-	-
No	10/19	<i>P</i> = 0.0006	0/0	-	-
IDDM (type 1)	0/0	-	0/0	-	-

NS: Not significant; NSAID: Nonsteroidal antiinflammatory drug; IDDM: Insulin-dependent diabetes mellitus.

**Table 3 Fracture information of patients involved throughout studies**

	Exchange nailing		Dynamization		EN <i>vs</i> dynam
	Union/total reported	Significant <i>vs</i> total union rate	Union/total reported	Significant <i>vs</i> total union rate	P-values
No. of patients	556/644	-	84/131	-	<i>P</i> < 0.0001
Mechanism of injury					
Crush	2/2	NS	0/0	-	-
Gun shot wound	2/2	NS	0/0	-	-
Motorcycle Accident	27/35	NS	0/0	-	-
Pedestrian/bike <i>vs</i> motor vehicle	2/6	<i>P</i> = 0.0045	0/0	-	-
Motor vehicle accident	146/163	NS	14/24	NS	<i>P</i> = 0.0004
Fall	1/5	<i>P</i> = 0.0017	0/0	-	-
Sporting accident	1/1	NS	0/0	-	-
Industrial accident	2/3	NS	0/0	-	-
Non-traumatic	0/0	-	0/0	-	-
Bombing injury	0/0	-	0/0	-	-
Location of injury					
Proximal shaft	26/30	NS	2/3	NS	NS
Mid-shaft/isthmal	139/154	NS	32/51	NS	<i>P</i> < 0.0001
Distal shaft	38/43	NS	1/3	NS	NS
Supra-isthmal	10/16	<i>P</i> = 0.0172	1/1	NS	NS
Sub-trochanteric	4/4	NS	2/3	NS	NS
Infra-isthmal	5/9	<i>P</i> = 0.0265	0/0	-	-
Fracture pattern					
Oblique	21/21	NS	0/0	NS	-
Segmental	0/0	-	2/5	NS	-
Transverse	14/14	NS	0/0	NS	-
Comminuted	19/21	NS	17/30	NS	<i>P</i> = 0.0219
Open <i>vs</i> closed					
Closed	133/162	NS	14/24	NS	<i>P</i> < 0.0001
Opened	25/32	NS	0/0	-	-
I	1/2	NS	0/0	-	-
II	2/4	NS	0/0	-	-
III A	1/2	NS	0/0	-	-
III B/C	1/1	NS	0/0	-	-
Winqvist-Hansen classification					
Stable	41/64	<i>P</i> < 0.0001	20/29	NS	NS
O	7/13	<i>P</i> = 0.0054	0/0	-	-
I	18/23	NS	12/17	NS	NS
II	16/27	<i>P</i> = 0.0007	6/9	NS	NS
Unstable	14/23	<i>P</i> = 0.0028	22/36	NS	NS

III	11/17	$P = 0.0234$	6/9	NS	NS
IV	3/6	$P = 0.0387$	2/2	NS	NS
V	0/0	-	2/2	NS	-
Presence of fracture graph					
Present	0/0	-	29/44	NS	-
No gap	0/0	-	1/1	NS	-

NS: Not significant.

**Table 4 Nonunion/delayed union information including secondary surgery information**

	Exchange nailing		Dynamization		EN vs dynam
	Union/total reported	Significant vs total union rate	Union/total reported	Significant vs total union rate	P-values
No. of patients	556/644	-	84/131	-	$P < 0.0001$
Reamed vs unreamed					
Reamed	516/598	NS	NA	-	-
Unreamed	19/22	NS	NA	-	-
Static vs dynamic					
Dynamic	97/115	NS	NA	-	-
Static	173/210	NS	NA	-	-
No locking (/Kuntschner)	35/36	NS	NA	-	-
Delayed union	25/27	NS	45/55	$P = 0.0228$	$P = 0.3199$
Nonunion (+type)	491/567	NS	24/57	$P = 0.0063$	$P < 0.0001$
Elephant	6/7	NS	0/0	-	-
Horse	12/18	$P = 0.0310$	0/0	-	-
Oligotrophic	22/22	NS	16/22	NS	$P = 0.0211$
Hypotrophic	9/13	NS	0/0	-	-
Atrophic	80/99	NS	5/12	NS	$P = 0.0064$
Hypertrophic	72/83	NS	9/11	NS	NS
Bone grafting used					
Yes	98/106	NS	2/2	NS	NS
No	165/190	NS	32/53	NS	$P < 0.0001$
Infected	19/30	$P = 0.0019$	0/0	-	-
Patients lost to follow-up	28	-	4	-	-
Major complications following surgery	45	-	13	-	NS
Patients achieving union after additional surgery vs surgeries attempted	82/92	-	34/34	-	-

NA: Not available; NS: Not significant.

characteristics, including fracture stability<sup>[36]</sup>. Following the analysis, the differences found between the individual isthmal classifications lend favor to its use over other systems.

In addition to fracture location, authors have raised questions over other factors that may affect procedural outcomes. While over-reaming is considered standard in most exchange nailing procedures, the suggested amount varies. Some articles report significant increase in union rates with different reaming sizes, while others found no difference. There was difficulty in comparing these claims across the literature due to the variation in reporting. Of the authors reporting reaming sizes, different ranges in millimeters (*i.e.*, 1 mm, 2 mm, 3 mm vs 0-1 mm, 2-4 mm) were typically used disallowing consolidation of the information.

Authors additionally raised concern over the success rates of exchange nailing based on the anteropgrade or retrograde revision technique<sup>[17]</sup>, as well as the open or closed techniques<sup>[29]</sup>. Wu *et al*<sup>[29]</sup> found the closed revision technique of exchange nailing lead to faster union times while requiring less operating time

to complete the procedure. However, they found the overall union rates of the procedures to be identical at 100%. In the other study, Wu *et al*<sup>[17]</sup> investigated the use of retrograde dynamic nailing after anteropgrade locked nailing had failed. In all 13 patients, retrograde revision techniques lead to osseous union of the femur fracture. Information in additional articles addressing these procedural techniques was not found leaving their comparisons for future research to address.

While a large amount of patient information regarding these secondary treatments was gathered, the analysis was limited by the variation in reporting and characteristic descriptions across all papers. Some papers lacked specific patient information in regard to procedure successes and failures, while others reported characteristics in ways that hindered consolidation of the data. As such, the total patient population was restricted. In order to provide a more representative review of entire field of research, increased patient numbers and more consistent reporting styles are needed.

Future analysis of these procedures should be performed once more data has been published. While the

**Table 5 Union rates of each peer-reviewed article by procedure type**

PMID	Procedure(s) analyzed	Union rate (%)
21726859	Dynamization	33.333
9462352	Dynamization	41.667
8370009	Dynamization	45.455
9291371	Dynamization	58.33
22841533	Dynamization	71.795
12142827	Dynamization	78.947
10088839	Dynamization	90
20101132	Exchange nailing	28.571
10926240	Exchange nailing	55.56
12719163	Exchange nailing	57.895
24978947	Exchange nailing	69.444
6488644	Exchange nailing	75
26489394	Exchange nailing	75.676
22327999	Exchange nailing	78.049
10791668	Exchange nailing	78.26
1738973	Exchange nailing	81.25
25300373	Exchange nailing	81.966
19897987	Exchange nailing	85.714
22338431	Exchange nailing	90.698
18579143	Exchange nailing	90.909
12142827	Exchange nailing	90.909
12479620	Exchange nailing	91.667
18090018	Exchange nailing	91.892
10476292	Exchange nailing	96
4707299	Exchange nailing	100
10088839	Exchange nailing	100
20820792	Exchange nailing	100
Kim JR <sup>1</sup>	Exchange nailing	100
9253919	Exchange nailing	100
10513972	Exchange nailing	100
1126078	Exchange nailing	100
7965294	Exchange nailing	100
22009873	Exchange nailing	100

<sup>1</sup>No accessible PMID<sup>[36]</sup>.

analysis yielded some significant results, other patient characteristics need to be investigated more thoroughly to gain a comprehensive insight into the common factors influencing procedure outcomes. Additionally, a comparison of external fixation/plating and internal fixation procedures in femoral non-unions could lead to a more comprehensive understanding of the situations that require each secondary treatment technique.

While exchange nailing showed higher union rates with comparable healing times to dynamization overall and in non-unions, the two procedures showed no significant difference in their results for the treatment of delayed unions. Upon examination of additional factors, specifically cost and invasiveness, dynamization should be considered the first treatment of delayed femur fractures. Conversely, in order to avoid further complications, including the need for additional surgery, exchange nailing is the treatment of choice for non-unions.

## ARTICLE HIGHLIGHTS

### Research background

Dynamization involves the removal of proximal or distal locking screws in a

statically locked IM nail which allowing weight bearing to stimulate osseous growth at the fracture site.

### Research motivation

Although rare, delayed union and non-union of fractures are major complications in the treatment of femoral fractures with intramedullary (IM) nailing. Surgeons use dynamization and exchange nailing to treat these complications and achieve osseous union.

### Research objectives

The purpose of this study is to analyze the literature on these procedures in their treatment of delayed and non-union femur fractures to determine their efficacy and factors related to their success.

### Research methods

Exchange nailing consists of the removal of the current IM nail, debridement of the medullary cavity, followed by insertion of a larger IM nail. Currently there is lack updated systematic review and meta-analysis on efficacy of dynamization vs exchange nailing in treatment of delayed and non-union femur fractures.

### Research results

Ultimately, 31 peer-reviewed articles with 644 exchanged nailing patients and 131 dynamization patients were identified and analyzed. It was found that when treating femoral non-unions, exchange nailing was shown to achieve osseous union in a higher percentage of patients than dynamization with comparable recovery times. However, dynamization appears to be equally as effective as exchange nailing in the treatment of delayed unions.

### Research conclusions

Exchange nailing is the procedure of choice between the two in the treatment of femoral non-unions due to its significantly higher success rate.

### Research perspectives

Clinical randomized controlled studies on this topic will help further elucidate this conclusion.

## ACKNOWLEDGEMENTS

We thank the University of Toledo College of Medicine and Life Sciences' Medical Student Summer Research Program for allowing collaboration between students and faculty, making this research project possible.

## REFERENCES

- 1 **Vaughn J**, Gotha H, Cohen E, Fantry AJ, Feller RJ, Van Meter J, Hayda R, Born CT. Nail Dynamization for Delayed Union and Nonunion in Femur and Tibia Fractures. *Orthopedics* 2016; **39**: e1117-e1123 [PMID: 27575039 DOI: 10.3928/01477447-20160819-01]
- 2 **Lynch JR**, Taitsman LA, Barei DP, Nork SE. Femoral nonunion: risk factors and treatment options. *J Am Acad Orthop Surg* 2008; **16**: 88-97 [PMID: 18252839 DOI: 10.5435/00124635-200802000-00006]
- 3 **Tigani D**, Fravisini M, Stagni C, Pascarella R, Boriani S. Interlocking nail for femoral shaft fractures: is dynamization always necessary? *Int Orthop* 2005; **29**: 101-104 [PMID: 15714303 DOI: 10.1007/s00264-004-0627-1]
- 4 **Gelalis ID**, Politis AN, Arnaoutoglou CM, Korompilias AV, Pakos EE, Vekris MD, Karageorgos A, Xenakis TA. Diagnostic and treatment modalities in nonunions of the femoral shaft: a review. *Injury* 2012; **43**: 980-988 [PMID: 21741650 DOI: 10.1016/j.injury.2011.06.030]
- 5 **Brinker MR**, O'Connor DP. Exchange nailing of ununited fr-

- actures. *J Bone Joint Surg Am* 2007; **89**: 177-188 [PMID: 17200326 DOI: 10.2106/00004623-200701000-00025]
- 6 **Huang KC**, Tong KM, Lin YM, Loh el-W, Hsu CE. Evaluation of methods and timing in nail dynamisation for treating delayed healing femoral shaft fractures. *Injury* 2012; **43**: 1747-1752 [PMID: 22841533 DOI: 10.1016/j.injury.2012.06.024]
  - 7 **Papakostidis C**, Psyllakis I, Vardakas D, Grestas A, Giannoudis PV. Femoral-shaft fractures and nonunions treated with intramedullary nails: the role of dynamisation. *Injury* 2011; **42**: 1353-1361 [PMID: 21726859 DOI: 10.1016/j.injury.2011.06.024]
  - 8 **Pihlajamäki HK**, Salminen ST, Böstman OM. The treatment of nonunions following intramedullary nailing of femoral shaft fractures. *J Orthop Trauma* 2002; **16**: 394-402 [PMID: 12142827 DOI: 10.1097/00005131-200207000-00005]
  - 9 **Wolinsky PR**, McCarty E, Shyr Y, Johnson K. Reamed intramedullary nailing of the femur: 551 cases. *J Trauma* 1999; **46**: 392-399 [PMID: 10088839 DOI: 10.1097/00005373-199903000-00007]
  - 10 **Wu CC**, Chen WJ. Healing of 56 segmental femoral shaft fractures after locked nailing. Poor results of dynamization. *Acta Orthop Scand* 1997; **68**: 537-540 [PMID: 9462352 DOI: 10.3109/17453679708999022]
  - 11 **Wu CC**. The effect of dynamization on slowing the healing of femur shaft fractures after interlocking nailing. *J Trauma* 1997; **43**: 263-267 [PMID: 9291371 DOI: 10.1097/00005373-199708000-00010]
  - 12 **Wu CC**, Shih CH. Effect of dynamization of a static interlocking nail on fracture healing. *Can J Surg* 1993; **36**: 302-306 [PMID: 8370009]
  - 13 **Tsang ST**, Mills LA, Baren J, Frantzas J, Keating JF, Simpson AH. Exchange nailing for femoral diaphyseal fracture non-unions: Risk factors for failure. *Injury* 2015; **46**: 2404-2409 [PMID: 26489394 DOI: 10.1016/j.injury.2015.09.027]
  - 14 **Hierholzer C**, Glowalla C, Herrler M, von Rüden C, Hungerer S, Bühren V, Friederichs J. Reamed intramedullary exchange nailing: treatment of choice of aseptic femoral shaft nonunion. *J Orthop Surg Res* 2014; **9**: 88 [PMID: 25300373 DOI: 10.1186/s13018-014-0088-1]
  - 15 **Swanson EA**, Garrard EC, Bernstein DT, O Connor DP, Brinker MR. Results of a systematic approach to exchange nailing for the treatment of aseptic femoral nonunions. *J Orthop Trauma* 2015; **29**: 21-27 [PMID: 24978947 DOI: 10.1097/BOT.0000000000000166]
  - 16 **Yang KH**, Kim JR, Park J. Nonisthmal femoral shaft nonunion as a risk factor for exchange nailing failure. *J Trauma Acute Care Surg* 2012; **72**: E60-E64 [PMID: 22327999 DOI: 10.1097/TA.0b013e318239caca]
  - 17 **Wu CC**. Retrograde dynamic locked nailing for aseptic nonunion of femoral supracondyle after antegrade locked nailing. *Arch Orthop Trauma Surg* 2011; **131**: 513-517 [PMID: 20820792 DOI: 10.1007/s00402-010-1183-3]
  - 18 **Naeem-ur-Razaq M**, Qasim M, Sultan S. Exchange nailing for non-union of femoral shaft fractures. *J Ayub Med Coll Abbottabad* 2010; **22**: 106-109 [PMID: 22338431]
  - 19 **Park J**, Kim SG, Yoon HK, Yang KH. The treatment of nonisthmal femoral shaft nonunions with im nail exchange versus augmentation plating. *J Orthop Trauma* 2010; **24**: 89-94 [PMID: 20101132 DOI: 10.1097/BOT.0b013e3181b8dafd]
  - 20 **Shroeder JE**, Mosheiff R, Khoury A, Liebergall M, Weil YA. The outcome of closed, intramedullary exchange nailing with reamed insertion in the treatment of femoral shaft nonunions. *J Orthop Trauma* 2009; **23**: 653-657 [PMID: 19897987 DOI: 10.1097/BOT.0b013e3181a2a337]
  - 21 **Gao KD**, Huang JH, Li F, Wang QG, Li HQ, Tao J, Wang JD, Wu XM, Wu XF, Zhou ZH, Wang F, Lu HM. Treatment of aseptic diaphyseal nonunion of the lower extremities with exchange intramedullary nailing and blocking screws without open bone graft. *Orthop Surg* 2009; **1**: 264-268 [PMID: 22009873 DOI: 10.1111/j.1757-7861.2009.00041.x]
  - 22 **Oh JK**, Bae JH, Oh CW, Biswal S, Hur CR. Treatment of femoral and tibial diaphyseal nonunions using reamed intramedullary nailing without bone graft. *Injury* 2008; **39**: 952-959 [PMID: 18579143 DOI: 10.1016/j.injury.2008.02.024]
  - 23 **Wu CC**. Exchange nailing for aseptic nonunion of femoral shaft: a retrospective cohort study for effect of reaming size. *J Trauma* 2007; **63**: 859-865 [PMID: 18090018 DOI: 10.1097/01.ta.0000233663.24838.76]
  - 24 **Banaszkiewicz PA**, Sabboubeh A, McLeod I, Maffulli N. Femoral exchange nailing for aseptic non-union: not the end to all problems. *Injury* 2003; **34**: 349-356 [PMID: 12719163 DOI: 10.1016/S0020-1383(02)00191-2]
  - 25 **Yu CW**, Wu CC, Chen WJ. Aseptic nonunion of a femoral shaft treated using exchange nailing. *Chang Gung Med J* 2002; **25**: 591-598 [PMID: 12479620]
  - 26 **Wu CC**, Shih CH. Treatment of 84 cases of femoral nonunion. *Acta Orthop Scand* 1992; **63**: 57-60 [PMID: 1738973 DOI: 10.3109/17453679209154851]
  - 27 **Weresh MJ**, Hakanson R, Stover MD, Sims SH, Kellam JF, Bosse MJ. Failure of exchange reamed intramedullary nails for ununited femoral shaft fractures. *J Orthop Trauma* 2000; **14**: 335-338 [PMID: 10926240 DOI: 10.1097/00005131-200006000-00005]
  - 28 **Hak DJ**, Lee SS, Goulet JA. Success of exchange reamed intramedullary nailing for femoral shaft nonunion or delayed union. *J Orthop Trauma* 2000; **14**: 178-182 [PMID: 10791668 DOI: 10.1097/00005131-200009000-00015]
  - 29 **Wu CC**, Shih CH, Chen WJ, Tai CL. Treatment of ununited femoral shaft fractures associated with locked nail breakage: comparison between closed and open revision techniques. *J Orthop Trauma* 1999; **13**: 494-500 [PMID: 10513972 DOI: 10.1097/00005131-199909000-00006]
  - 30 **Oh I**, Nahigian SH, Rascher JJ, Farrall JP. Closed intramedullary nailing for ununited femoral shaft fractures. *Clin Orthop Relat Res* 1975; **106**: 206-215 [PMID: 1126078 DOI: 10.1097/00003086-197501000-00032]
  - 31 **Wu CC**, Chen WJ. Treatment of femoral shaft aseptic nonunions: comparison between closed and open bone-grafting techniques. *J Trauma* 1997; **43**: 112-116 [PMID: 9253919 DOI: 10.1097/00005373-199707000-00026]
  - 32 **Christensen NO**. Küntscher intramedullary reaming and nail fixation for non-union of fracture of the femur and the tibia. *J Bone Joint Surg Br* 1973; **55**: 312-318 [PMID: 4707299 DOI: 10.1302/0301-620X.55B2.312]
  - 33 **Harper MC**. Ununited fractures of the femur stabilized with the fluted rod. *Clin Orthop Relat Res* 1984; **190**: 273-278 [PMID: 6488644 DOI: 10.1097/00003086-198411000-00048]
  - 34 **Iannacone WM**, Bennett FS, DeLong WG Jr, Born CT, Dalsey RM. Initial experience with the treatment of supracondylar femoral fractures using the supracondylar intramedullary nail: a preliminary report. *J Orthop Trauma* 1994; **8**: 322-327 [PMID: 7965294 DOI: 10.1097/00005131-199408000-00008]
  - 35 **Furlong AJ**, Giannoudis PV, DeBoer P, Matthews SJ, MacDonald DA, Smith RM. Exchange nailing for femoral shaft aseptic non-union. *Injury* 1999; **30**: 245-249 [PMID: 10476292 DOI: 10.1016/S0020-1383(99)00073-X]
  - 36 **Kim JR**, Chung WC, Shin SJ, Seo KB. The management of aseptic nonunion of femoral shaft fractures after interlocking intramedullary nailing. *Eur J Orthop Surg Tr Name* 2011; **21**: 171-177 [DOI: 10.1007/s00590-010-0679-4]

**P- Reviewer:** Drampalos E, Emara KM **S- Editor:** Ji FF  
**L- Editor:** A **E- Editor:** Tan WW



## Anterior transolecranon dislocation of the elbow in a child: A case report and review of literature

Wajdi Bouaziz, Ahmed Racem Guidara, Ahmed Trabelsi, Tarek Bardaa, Mourad Hammami, Zoubaier Ellouz, Hassib Keskes

Wajdi Bouaziz, Ahmed Racem Guidara, Ahmed Trabelsi, Tarek Bardaa, Zoubaier Ellouz, Hassib Keskes, Department of Orthopaedic Surgery and Traumatology, Habib Bourguiba University Hospital, Sfax 3000, Tunisia

Mourad Hammami, Department of Orthopaedic Surgery and Traumatology, Tataouine Regional Hospital, Sfax 3263, Tunisia

ORCID number: Wajdi Bouaziz (0000-0002-0839-8127); Ahmed Racem Guidara (0000-0002-1406-9872); Ahmed Trabelsi (0000-0001-9587-2319); Tarek Bardaa (0000-0002-8075-6849); Mourad Hammami (0000-0001-7210-9361); Zoubaier Ellouz (0000-0003-3211-9850); Hassib Keskes (0000-0003-2231-760X).

**Author contributions:** All the authors contributed in outlining the manuscript, gathering the data, and writing the manuscript.

**Informed consent statement:** The patient's mother provided written informed consent authorizing the use and disclosure of her son's protected health information.

**Conflict-of-interest statement:** None of the authors have any financial or other conflicts of interest that may bias the current study.

**CARE Checklist (2013) statement:** The authors have read the CARE Checklist (2013), and the manuscript was prepared and revised according to the CARE Checklist (2013).

**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:** Ahmed Racem Guidara, MD, Doctor, Surgeon, Department of Orthopaedic Surgery and Traumatology,

Habib Bourguiba University Hospital, El Ain Street, Sfax 3000, Tunisia. [rassimou@live.fr](mailto:rassimou@live.fr)  
Telephone: +216-22-650267

Received: May 4, 2018

Peer-review started: May 5, 2018

First decision: June 6, 2018

Revised: June 15, 2018

Accepted: June 28, 2018

Article in press: June 28, 2018

Published online: July 18, 2018

### Abstract

Anterior transolecranon dislocation of the elbow is rarely observed in children, reported in only a small series. The present case involves an anterior transolecranon dislocation of the left elbow joint in a 7-year-old child, which was surgically treated. Two attempts of closed reduction failed because the radial head had buttonholed via the joint capsule. After its release, open reduction was easily performed; osteosynthesis of the olecranon was not performed. Remarkably, good result was obtained, despite a mild flexion deformity at the last follow-up. This case report aims to highlight this treatment method, which may be considered for such an uncommon injury.

**Key words:** Elbow; Children; Anterior dislocation; Open reduction; Olecranon osteosynthesis

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Anterior transolecranon dislocation is rarely observed in children and rarely reported in the literature. This case shows that the management of this injury can be difficult, requiring surgery with or without osteosynthesis of the olecranon.

Bouaziz W, Guidara AR, Trabelsi A, Bardaa T, Hammami M, Ellouz Z, Keskes H. Anterior transolecranon dislocation of the elbow in a child: A case report and review of literature. *World J Orthop* 2018; 9(7): 100-104 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i7/100.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i7.100>

## INTRODUCTION

Although anterior transolecranon dislocation of the elbow is not uncommon in adults, it is rarely seen in children<sup>[1]</sup>. Limited published recommendations for the management of these lesions in children are available. Closed reduction is possible in most elbow dislocations. We report a rare case of irreducible anterior transolecranon fracture dislocation of the left elbow joint in a 7-year-old child who was surgically treated.

## CASE REPORT

A 7-year-old boy was admitted to the emergency department of the Habib Bourguiba University Hospital, Tunisia, for direct left elbow trauma sustained in a fall 2 h earlier while playing with his friends on the street. The patient presented with severe pain, swelling, and deformity of the elbow, with functional disability of the left upper limb. The neurovascular status of the limb was intact, range of motion was restricted by pain, and the fingers were mobile and sensitive. In addition, the radial pulse was palpable and equal to that of the contralateral side. X-rays of the elbow revealed anterior and lateral transolecranon dislocation (Figure 1). The child was transferred to the operating room and placed in the decubitus position, with his arm on a hand table. Closed reduction was attempted twice under general anesthesia and using an X-ray image intensifier. Maneuver was conducted as recommended in a previous report by Winslow<sup>[2]</sup>; however, both attempts were unsuccessful. Therefore, the patient was surgically treated.

A lateral approach to expose the elbow joint found that the olecranon and radial head were anteriorly dislocated, and the annular ligament was torn. The closed reduction attempts failed because the radial head was buttonholed through the torn anterior capsule of the elbow joint. Subsequently, the radial head was released, and the joint was reduced under direct vision (Figure 2). Reduction was perfect, as verified by an X-ray image intensifier. Because the joint was found to be stable following reduction, internal fixation of the olecranon fracture was not performed. Using a splint, the reduced joint was externally immobilized for four weeks (Figure 3). Recovery was uncomplicated. Eventually, the patient was discharged after wound inspection on the third postoperative day. The splint was removed a month later, with the initiation of healing of the olecranon revealed on X-ray by incomplete densification of the fracture (Figure 4). Although the patient had complete flexion of

the elbow joint, extension was incomplete (Figure 5). He was referred for rehabilitation and assisted active range of motion exercises. After three months, the patient recovered good range of motion. He showed only 10° of sequellar extension lag, complete range of pronation, and supination movements, and was able to perform all daily activities. His quickDASH score was 4.54. Plain radiographs indicated healing of the olecranon fracture (Figure 6).

## DISCUSSION

By far, posterior elbow dislocations are the most common dislocations among children, and these are an effect of indirect forces transmitted to the elbow following a fall on the outstretched hand<sup>[3,4]</sup>. Till date, a few number of anterior transolecranon dislocations of the elbow has been reported<sup>[5]</sup>.

Anterior dislocations of the elbow among children were often associated with fractures around the elbow, and some cases included neurovascular injury<sup>[6,7]</sup>. Closed reduction has commonly been performed, except in cases involving soft-tissue interposition or buttonholing of the radial head through the capsule that have prevented it<sup>[8,9]</sup>. Closed reduction was attempted in this case, but it failed because of buttonholing of the radial head through the capsule of the joint, which was discovered during surgery, along with a torn annular ligament. Similar cases of close reduction failure because of buttonholing of the anterior capsule have been reported in Japan by Takase *et al*<sup>[8]</sup> and in the United States by Aversano *et al*<sup>[10]</sup>. The anatomic pathology of anterior transolecranon fracture dislocation described by Tiemdjo *et al*<sup>[11]</sup> and as shown in Table 1, includes 4 types, each with a proposed treatment. This classification has prognostic and therapeutic values.

No clear conclusions regarding the surgical approach and technique to reduce and stabilize the dislocated elbow joint can be drawn from the available published reports. We selected the lateral approach for better visualization of the articular surface of the joint and chiefly for direct control of the radial head. Reduction of the dislocated joint was easy to perform following the release of the buttonholed radial head. In most reports, surgical reduction was followed by osteosynthesis of the olecranon. We selected simple immobilization of the elbow until consolidation because stable reduction of the olecranon was achieved. Contrary to what was recommended Tiemdjo *et al*<sup>[11]</sup>, we did not perform osteosynthesis to limit damages of the growth plate and avoid clutter by the material, which may probably perturb the range of motion later. In addition, no other further intervention was required to remove the osteosynthesis material. Postoperative stability was maintained by a splint with a 75°-80° flexed elbow to obtain less tension of the olecranon. The result was considered good, despite the sequellar mild flexion deformity. An enhanced reduction is associated with better result. Osteosynthe-

**Table 1 Tiemdjo classification and proposed therapeutic indications of anterior trans-olecranon fractures-dislocations in children**

Classification	Description	Treatment
Type 1	Epiphyseal splinting or proximal fracture of the olecranon	Reduction + Tension-band Wiring
Type 2	If the periosteum is intact Transverse fracture	Reduction + Plaster Reduction + Tension-band Wiring
Type 3	Oblique fracture	Reduction + Screwed plate
Type 4	Olecranon fracture + associated injury (radius, humerus)	Reduction + Osteosynthesis of the olecranon fracture and the associated injury



Figure 1 Preoperative radiographs showing anterior trans olecranon dislocation of the elbow.

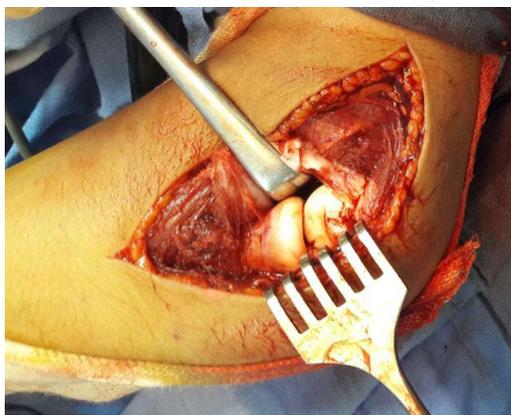


Figure 2 Open radial head release and reduction of the radio humeral joint using a lateral approach.

sis of the olecranon could improve results only if a perfect reduction was achieved. The reduction in this patient was good and stable. Therefore, immobilization did not allow immediate rehabilitation. This explains the mild flexion deformity at the last follow-up. Accordingly, accelerated functional treatment and rehabilitation following surgery are recommended, as long periods of immobilization are not beneficial<sup>[12]</sup>. In this patient, splint removal after only four weeks following the surgery allowed relatively early mobilization.

In conclusion, this uncommon case of anterior trans-olecranon dislocation could not be successfully manag-

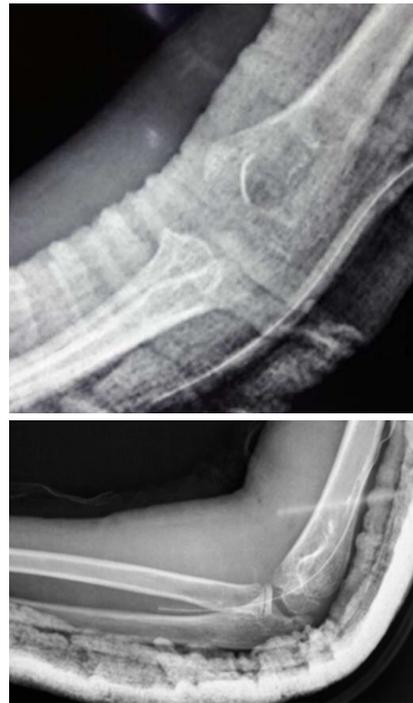


Figure 3 Immediate post-operative X-rays showing good reduction of the elbow joint.



Figure 4 Four week post-operative X-rays showing the initiation of healing of the olecranon.

ed using simple closed reduction. Open reduction without osteosynthesis of the olecranon had an excellent result at the last follow-up. This indicates that perfect reduction must be the main goal of any approach and th-



Figure 5 Incomplete extension of the elbow after 4 wk.

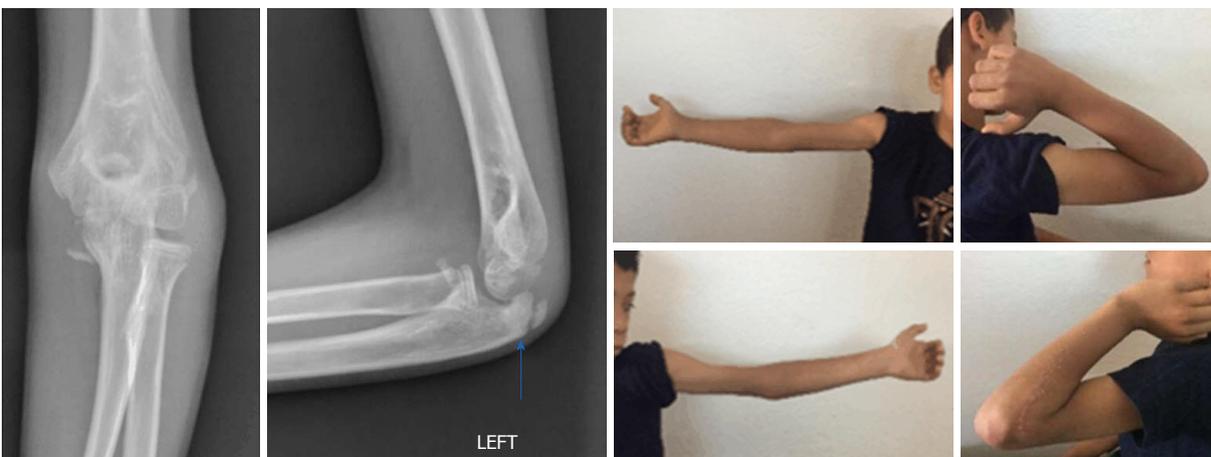


Figure 6 Healing of the olecranon and good motion after rehabilitation.

at osteosynthesis is not the only way to recover anterior function of the elbow.

## ARTICLE HIGHLIGHTS

### Case characteristics

Anterior transolecranon dislocation of the elbow is rarely observed in children and is reported in only a small series of cases. This case report aimed to highlight that osteosynthesis is not essential in such an uncommon injury.

### Clinical diagnosis

Anterior transolecranon dislocation.

### Differential diagnosis

Simple elbow dislocation.

### Imaging diagnosis

Plain radiographs revealed anterior dislocated elbow with olecranon fracture.

### Treatment

Open reduction without osteosynthesis.

### Related reports

Only few cases of anterior transolecranon dislocation in children have been reported in the literature. We think that our case may be the first one reported in the African continent.

### Experiences and lessons

This case will contribute to improvements in our understanding of the management of anterior transolecranon dislocation in children. The main lesson learned was that osteosynthesis is not essential for the management of such fractures.

## ACKNOWLEDGEMENTS

We thank the boy's parents for allowing us to share his details and thank Dr. Wajdi Bouaziz for advice and for performing the surgery.

## REFERENCES

- 1 **Guillon TG**, Albers RG, Ring D. Anterior olecranon fracture-dislocations of the elbow in children. A report of four cases. *J Bone Joint Surg Am* 2009; **91**: 1487-1490 [PMID: 19487529 DOI: 10.2106/JBJS.H.00855]
- 2 **Winslow R**. A case of complete anterior dislocation of both bones of the forearm at the elbow. *Surg Gynecol Obstet* 1913; **16**: 570-571
- 3 **Altuntas AO**, Balakumar J, Howells RJ, Graham HK. Posterior divergent dislocation of the elbow in children and adolescents: a report of three cases and review of the literature. *J Pediatr Orthop* 2005; **25**: 317-321 [PMID: 15832146 DOI: 10.1097/01.bpo.0000153877.20561.8a]
- 4 **Kaziz H**, Naouar N, Osman W, Ayeche M. Outcomes of Paediatric

- Elbow Dislocations. *Malays Orthop J* 2016; **10**: 44-49 [PMID: 28435546 DOI: 10.5704/MOJ.1603.008]
- 5 **Ring D**, Jupiter JB, Sanders RW, Mast J, Simpson NS. Transolecranon fracture-dislocation of the elbow. *J Orthop Trauma* 1997; **11**: 545-550 [PMID: 9415859 DOI: 10.1097/00005131-199711000-00001]
  - 6 **Lasanianos N**, Garnavos C. An unusual case of elbow dislocation. *Orthopedics* 2008; **31**: 806 [PMID: 19292413 DOI: 10.3928/01477447-20080801-10]
  - 7 **Fadili M**, Wichou M, Haddoun AR, Harfaoui A, Dkhissi M, Zryouil B. [Anterior luxation of the elbow. A case report]. *Tunis Med* 2001; **79**: 251-252 [PMID: 11515487]
  - 8 **Takase K**, Mizuochi J. Irreducible dislocation of the radial head with undisplaced olecranon fracture in a child: a case report. *J Pediatr Orthop B* 2011; **20**: 345-348 [PMID: 21460738 DOI: 10.1097/BPB.0b013e32834534cb]
  - 9 **Takami H**, Takahashi S, Ando M. Irreducible isolated dislocation of the radial head. *Clin Orthop Relat Res* 1997; **345**: 168-170 [PMID: 9418635 DOI: 10.1097/00003086-199712000-00023]
  - 10 **Aversano F**, Kepler CK, Blanco JS, Green DW. Rare cause of block to reduction after radial head dislocation in children. *J Orthop Trauma* 2011; **25**: e38-e41 [PMID: 21399463 DOI: 10.1097/BOT.0b013e3181dc245d]
  - 11 **Tiemdjo H**, Kinkpe C, Coulibaly NF, Sane A, Ndiaye A, Seye SI. [Anterior transolecranon fracture-dislocations of the elbow in children: A case report and review of the literature]. *Arch Pediatr* 2015; **22**: 737-740 [PMID: 26047739 DOI: 10.1016/j.arcped.2015.03.022]
  - 12 **Riel KA**, Bernett P. [Simple elbow dislocation. Comparison of long-term results after immobilization and functional treatment]. *Unfallchirurg* 1993; **96**: 529-533 [PMID: 8235672]

**P- Reviewer:** Canavese F, Massoud EIE **S- Editor:** Ji FF

**L- Editor:** A **E- Editor:** Tan WW





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 August 18; 9(8): 105-111





**ORIGINAL ARTICLE**

**Retrospective Cohort Study**

105 Effect of opioid dependence or abuse on opioid utilization after shoulder arthroplasty

*Berglund DD, Rosas S, Kurowicki J, Mijic D, Levy JC*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Elsayed Ibraheem Elsayed Mas-soud, MD, MSc, Assistant Professor, Professor, Department of Orthopaedic, Sohag Teaching Hospital, General Organization for Teaching Hospitals and Institutes, Sohag 0026280, Egypt

**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* (*WJO*) is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), China National Knowledge Infrastructure (CNKI), and Superstar Journals Database.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Fang-Fang Ji*  
**Proofing Editorial Office Director:** *Jin-Lai Wang*

**NAME OF JOURNAL**  
*World Journal of Orthopedics*

**ISSN**  
 ISSN 2218-5836 (online)

**LAUNCH DATE**  
 November 18, 2010

**FREQUENCY**  
 Monthly

**EDITOR-IN-CHIEF**  
**Bao-Gan Peng, MD, PhD, Professor**, Department of Spinal Surgery, General Hospital of Armed Police Force, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com/2218-5836/editorialboard.htm>

**EDITORIAL OFFICE**  
 Jin-Lai Wang, Director

*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 August 18, 2018

**COPYRIGHT**  
 © 2018 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.f6publishing.com>

## Retrospective Cohort Study

**Effect of opioid dependence or abuse on opioid utilization after shoulder arthroplasty**

Derek D Berglund, Samuel Rosas, Jennifer Kurowicki, Dragomir Mijic, Jonathan C Levy

Derek D Berglund, Samuel Rosas, Jennifer Kurowicki, Dragomir Mijic, Jonathan C Levy, Department of Orthopedic Surgery, Holy Cross Orthopedic Institute, Fort Lauderdale, FL 33334, United States

Samuel Rosas, Department of Orthopedic Surgery, Wake Forest School of Medicine, Winston-Salem, NC 27157-1070, United States

Jennifer Kurowicki, Department of Orthopaedic Surgery, Seton Hall University School of Health and Medical Sciences, South Orange, NJ 07079, United States

ORCID number: Derek D Berglund (0000-0003-0360-4347); Samuel Rosas (0000-0002-7330-3753); Jennifer Kurowicki (0000-0002-1966-2157); Dragomir Mijic (0000-0003-3715-3513); Jonathan C Levy (0000-0002-1699-0841).

**Author contributions:** Berglund DD, Rosas S, Kurowicki J, Mijic D and Levy JC contributed significantly towards project design, analysis, and manuscript writing/editing.

**Institutional review board statement:** This study has been determined exempt from Institutional Review Board (IRB) review by the Holy Cross Hospital Research Office.

**Informed consent statement:** As this study utilizes publicly available data from a nationwide database, informed consent was not obtained from individual subjects included in the study. Study data contained no patient identifiers and cannot be linked to an individual patient.

**Conflict-of-interest statement:** No potential conflicts of interest relevant to this article were reported.

**STROBE statement:** The authors have read the STROBE Statement-checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-checklist of items.

**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. Jonathan C Levy, MD, Staff Physician, Surgeon, Chief of Orthopedics, Department of Orthopedic Surgery, Holy Cross Orthopedic Institute, 5597 North Dixie Highway, Fort Lauderdale, FL 33334, United States. [jonlevy123@yahoo.com](mailto:jonlevy123@yahoo.com)  
**Telephone:** +1-954-4894579  
**Fax:** +1-954-2298698

**Received:** March 5, 2018  
**Peer-review started:** March 6, 2018  
**First decision:** March 23, 2018  
**Revised:** May 17, 2018  
**Accepted:** May 23, 2018  
**Article in press:** May 23, 2018  
**Published online:** August 18, 2018

**Abstract****AIM**

To examine whether opioid dependence or abuse has an effect on opioid utilization after anatomic or reverse total shoulder arthroplasty (TSA).

**METHODS**

All anatomic TSA (ICD-9 81.80) and reverse shoulder arthroplasty (RSA) (ICD-9 81.88) procedures from 2007 to 2015 were queried from within the Humana claims database utilizing the PearlDiver supercomputer (Colorado Springs, CO). Study groups were formed based on the presence or absence of a previous history of opioid dependence (ICD-9 304.00 and 304.03) or abuse (ICD-9 305.50 and 305.53). Opioid utilization among the groups was tracked monthly up to 1 year post-operatively utilizing National Drug Codes. A sec-

ondary analysis was performed to determine risk factors for pre-operative opioid dependence or abuse.

### RESULTS

Two percent of TSA (157 out of 7838) and 3% of RSA (206 out of 6920) patients had a history of opioid dependence or abuse. For both TSA and RSA, opioid utilization was significantly higher in opioid dependent patients at all post-operative intervals ( $P < 0.01$ ) although the incidence of opioid use among groups was similar within the first post-operative month. After TSA, opioid dependent patients were over twice as likely to fill opioid prescriptions during the post-operative months 1-12. Following RSA, opioid dependent patients were over 3 times as likely to utilize opioids from months 3-12. Age less than 65 years, history of mood disorder, and history of chronic pain were significant risk factors for pre-operative opioid dependence/abuse in patients who underwent TSA or RSA.

### CONCLUSION

Following shoulder arthroplasty, opioid use between opioid-dependent and non-dependent patients is similar within the first post-operative month but is greater among opioid-dependent patients from months 2-12.

**Key words:** Opioid; Narcotic; Abuse; Dependence; Anatomic total shoulder arthroplasty; Reverse shoulder arthroplasty; Chronic pain; Mood disorder

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** A retrospective analysis of the Humana claims determined that patients with pre-operative opioid dependence or abuse had higher post-operative opioid utilization after anatomic total shoulder arthroplasty and reverse shoulder arthroplasty. Younger age, mood disorders, and chronic pain diagnoses were significant risk factors for pre-operative opioid dependence or abuse.

Berglund DD, Rosas S, Kurowicki J, Mijic D, Levy JC. Effect of opioid dependence or abuse on opioid utilization after shoulder arthroplasty. *World J Orthop* 2018; 9(8): 105-111 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i8/105.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i8.105>

## INTRODUCTION

Opioid analgesics have proven to be effective in treating severe pain. However, increasing utilization along with highly addictive properties of opioid medications has led to significant societal consequences. The utilization of opioids for analgesia in the United States increased substantially from the late 1990's to the early 2010's<sup>[1,2]</sup>. In the United States opioid consumption is significantly higher than any other country<sup>[3,4]</sup> and this has in turn led to an increase in opioid abuse and dependence among

patients. Opioid utilization has a profound impact on the practice of orthopaedics as orthopaedic surgeons are the 3<sup>rd</sup> highest prescribers of opioid medications among physicians<sup>[5]</sup>. Opioid dependence or abuse among patients undergoing elective orthopedic surgery has increased by 152% from 2002 to 2011 and has been associated with increased inpatient morbidity and mortality<sup>[6]</sup>.

Increasing rates of opioid dependence or abuse has a significant negative impact on patients undergoing shoulder arthroplasty as pre-operative opioid use has been associated with worse patient-reported outcomes post-operatively<sup>[7,8]</sup>. Previous national database studies have shown that patients using opioids prior to knee arthroplasty or rotator cuff repair are more likely to continue using opioids for prolonged post-operative periods<sup>[9,10]</sup>. However, no study to date has analyzed the impact of diagnosed opioid dependence or abuse on opioid utilization after shoulder arthroplasty. The purpose of the current study is to examine whether diagnosed pre-operative opioid dependence or abuse has an effect on opioid utilization following total shoulder arthroplasty (TSA) or reverse shoulder arthroplasty (RSA). Our hypothesis was that patients with pre-operative opioid abuse or dependence would have greater opioid utilization. Secondly, we sought to evaluate potential risk factors for pre-operative opioid dependence or abuse within this patient population.

## MATERIALS AND METHODS

The PearlDiver supercomputer (PearlDiver Inc, Colorado Springs, CO) was utilized to query the Humana Inc administrative claims database. This database contains claims data from 2007 through 2015 for over 20 million patients that are insured privately/commercially or through Medicare/Medicare Advantage. The data retrieved from the database is retrospective, publicly available, and is compliant with the Health Insurance Portability and Accountability Act (HIPAA). This study was therefore deemed exempt from institutional review board review.

Patients who underwent anatomic TSA and RSA were identified using International Classification of Disease Ninth Edition (ICD-9) codes 81.80 and 81.88, respectively. Separate analyses were performed for each arthroplasty type. Patients were divided into study groups based on whether there was a history of diagnosed opioid dependence or abuse prior to surgery. This was delineated using ICD-9 codes for opioid dependence (304.00 and 304.03) and opioid abuse (305.50 and 305.53). Patients who received a brachial plexus nerve block on the day of surgery were identified using the Current Procedural Terminology (CPT) code 64415 and the proportion of patients receiving nerve blocks were compared between groups.

Generic drug codes for commonly prescribed opioid medications (Table 1) were used to determine the number of patients within each study group that filled

**Table 1** Generic drug codes for opioid medications tracked in the current study

Opioid medication	Generic drug codes
Oxycodone	101126, 101215, 106757, 108546, 111094, 107000, 109518, 100548, 100504, 110286, 109192, 106437
Hydrocodone	106414, 112157, 101854, 100055, 110070, 105295, 112625, 102382, 101434, 109398, 110812, 100358, 101802, 108359, 106104, 106326, 106622, 107601, 103995, 111636, 106030, 106747, 101805, 110605, 108113, 112007
Morphine sulfate	104592, 106367, 108034, 104962, 100074, 103380, 108114, 110174, 112832
Codeine	101623, 100873, 107990, 103275, 104787, 104710, 107214, 112297, 104491, 112574, 112774, 108218, 101073, 107402, 103943, 107406, 104952, 108825, 102621, 110215, 101274, 109769, 105010, 105460, 111188, 107202, 112555, 104895, 108556, 102273, 107506, 110492, 110760, 112140, 107410, 103069, 109078, 101383, 109320, 104915, 112523, 100351, 111016, 108443, 106918, 105070, 104040, 109446, 111749, 108445, 108480, 112775, 105654, 110799, 109752, 100679, 109086, 108889, 110743, 106810, 102890, 110671
Fentanyl	100599, 104678, 101119, 103260, 100142
Hydromorphone	101111, 100978
Meperidine	101505, 101784, 112026
Methadone hydrochloride	100319
Oxymorphone hydrochloride	101242

**Table 2** Patients receiving a brachial plexus block on the day of surgery *n* (%)

	With pre-op opioid dependence/abuse	Without pre-op opioid dependence/abuse	<i>P</i> -value
TSA	92 (58.60)	4105 (53.44)	0.199
RSA	108 (52.43)	3461 (51.55)	0.803

TSA: Total shoulder arthroplasty; RSA: Reverse shoulder arthroplasty.

at least one opioid prescription within specific post-operative time periods. These codes are mapped to eleven-digit National Drug Codes (NDC) on patient charging records. The percent of patients filling opioid prescriptions was compared between patients with and without a history of opioid dependence or abuse for both TSA and RSA. This was performed on a month-by-month basis up to one year post-operatively.

A secondary analysis was performed to determine risk factors for pre-operative opioid dependence or abuse among patients undergoing TSA or RSA. The relative risk of opioid dependence/abuse was determined for gender, age, the presence of chronic pain (ICD-9 codes 338.29, 338.4, 338.21, 338.28, and 338.22) and mood disorder (ICD-9 codes 296.00 and 296.99) diagnoses. Charlson Comorbidity Index was also compared for patients with opioid dependence/abuse vs those without.

### Statistical analysis

Statistical analysis was conducted with descriptive

and comparative evaluations based on data type (continuous vs categorical). Incidences were used to calculate relative risk ratios and 95% CIs through univariate regressions. Age (younger or older than 65), pre-operative opioid abuse (present or not) and the presence of chronic pain (defined as present or not) were dichotomized into 2 groups for comparison. Statistical analysis was conducted with SPSS (version 20, IBM corporation, Armonk, NY, United States).

## RESULTS

### Anatomic TSA

Our query returned 7838 patients (3417 male and 4421 female) that underwent TSA between 2007 and 2015. Of that, 157 patients (2.0%) had diagnoses of opioid dependence or abuse prior to surgery and were placed in the opioid dependence/abuse group while the remainder of patients, 7681 (98.0%) without diagnoses of opioid dependence or abuse were placed in the non-opioid dependent group. The proportion of patients receiving a brachial plexus nerve block was not significantly different between patients with and without opioid dependence or abuse ( $P = 0.199$ , Table 2).

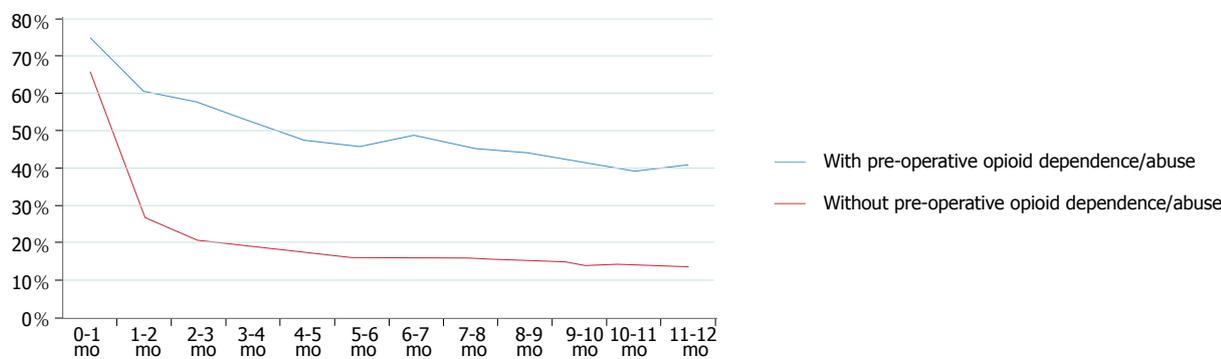
Within the first post-operative month, 75.16% of patients with opioid dependence/abuse and 66.01% of patients without opioid dependence/abuse filled at least one opioid prescription. The incidence of opioid use in the opioid-dependent group decreased to 60.51% from 1-2 mo and subsequently continued to decrease until 6 mo post-operatively where it plateaued. Opioid use ranged from 39.49%-48.41% from 6-12 mo in the opioid-dependent group. For patients without a history of opioid dependence or abuse, opioid use decreased to 26.92% after the first month and then slowly decreased from post-operative months 2-12 (range 13.74%-20.82%). Opioid use among patients with a history of dependence/abuse was significantly greater than in the non-opioid dependent patients at all postoperative time intervals ( $P < 0.01$ ). Within the first post-operative month, patients with a history of opioid dependence/abuse were only slightly more likely to use opioids (RR = 1.14, 95%CI: 1.04-1.25). However, from months 1-12 they were over twice as likely to fill opioid prescriptions (RR ranged 2.25-3.00, 95%CI: 1.97-3.61) (Table 3 and Figure 1).

Analysis of risk factors showed that patients less than 65 years old (RR = 2.12, 95%CI: 1.46-3.08,  $P = 0.0001$ ), patients with previous diagnosis of a mood disorder (RR = 6.70, CI: 4.92-9.11,  $P < 0.0001$ ), and patients with diagnosis of chronic pain (RR = 10.31, 95%CI: 7.51-14.17,  $P < 0.0001$ ) were more likely to have abused opioids or be opioid dependent prior to TSA surgery. Gender did not have an impact on the risk for opioid dependence/abuse prior to surgery (RR = 1.06 for female gender, 95%CI: 0.78-1.46,  $P = 0.69$ ). The mean CCI was significantly higher ( $4 \pm 3.71$  vs  $2 \pm 2.73$ ,  $P < 0.001$ ) in patients with a history of opioid

**Table 3** Relative risk of opioid utilization at post-operative intervals for patients with *vs* without a history of opioid dependence/abuse

Post-operative interval	TSA			RSA		
	RR	95%CI	P value	RR	95%CI	P value
0-1 mo	1.14	1.04-1.25	0.005	1.36	1.27-1.45	< 0.001
1-2 mo	2.25	1.97-2.56	< 0.0001	2.28	2.06-2.53	< 0.001
2-3 mo	2.78	2.42-3.20	< 0.0001	2.69	2.40-3.02	< 0.001
3-4 mo	2.80	2.39-3.27	< 0.0001	3.20	2.85-3.60	< 0.001
4-5 mo	2.78	2.34-3.30	< 0.0001	3.23	2.82-3.69	< 0.001
5-6 mo	2.84	2.38-3.40	< 0.0001	3.09	2.67-3.57	< 0.001
6-7 mo	3.00	2.54-3.56	< 0.0001	3.26	2.82-3.75	< 0.001
7-8 mo	2.87	2.40-3.43	< 0.0001	3.34	2.87-3.88	< 0.001
8-9 mo	2.88	2.39-3.46	< 0.0001	3.30	2.83-3.85	< 0.001
9-10 mo	2.90	2.39-3.52	< 0.0001	3.47	2.95-4.08	< 0.001
10-11 mo	2.81	2.30-3.44	< 0.0001	3.50	2.98-4.10	< 0.001
11-12 mo	2.97	2.44-3.61	< 0.0001	3.36	2.83-3.98	< 0.001

TSA: Total shoulder arthroplasty; RSA: Reverse shoulder arthroplasty.



**Figure 1** Percent of patients filling at least one opioid prescription within each post-operative interval following reverse shoulder arthroplasty. Within the first post-operative month, patients with a history of opioid dependence/abuse were slightly more likely to fill opioid prescriptions (RR = 1.36, 95%CI: 1.27-1.45, *P* < 0.001). However, they were over 3 times as likely to use opioids during post-operative months 3-12 (RR ranged 3.09-3.50, 95%CI: 2.67-4.10, *P* < 0.001).

dependence/abuse (Table 4).

**RSA**

Among the 6920 patients that underwent RSA within the study period, 206 (3.0%) had a previous diagnosis of opioid dependence/abuse and 6714 (97.0%) did not. The proportion of patients receiving a brachial plexus block did not differ significantly between groups (*P* = 0.803, Table 2).

Eighty-one point five five percent of patients in the opioid-dependent group filled opioid prescriptions within the first post-operative month. This percentage fell to 66.50% after the first month and gradually decreased to 42.72% from 1 to 12 mo post-operatively (range 42.72%-66.50%). Of the patients in the non-opioid dependent group, 60.05% filled prescriptions within the first post-operative month. This percentage quickly fell to less than 30% after the first month and then slowly decreased from 4 to 12 mo (range 12.72%-17.16%). Opioid use was significantly higher for patients with previously diagnosed dependence/abuse at all post-operative intervals (*P* < 0.001). Within the first post-operative month, opioid dependent patients were slightly more likely to fill opioid prescriptions (RR = 1.36, 95%CI: 1.27-1.45). However, they were over 3 times as likely to use opioids during post-operative months

3-12 (RR ranged 3.09-3.50, 95%CI: 2.67-4.10) (Table 3 and Figure 2).

Age less than 65 years (RR = 1.60, 95%CI: 1.06-2.41, *P* = 0.0240), prior diagnosis of mood disorder (RR = 5.27, 95%CI: 4.04-6.87, *P* < 0.0001), and chronic pain diagnosis (RR = 10.10, 95%CI: 7.53-13.57, *P* < 0.0001) were significant risk factors for opioid dependence or abuse prior to RSA. Female patients were slightly more likely to have pre-operative opioid dependence/abuse (RR = 1.30, 95%CI: 0.96-1.75) but this result was not statistically significant (*P* = 0.0848). The mean CCI was significantly higher for the opioid dependent group (5 ± 3.85 vs 3 ± 3.20, *P* = 0.001) (Table 4).

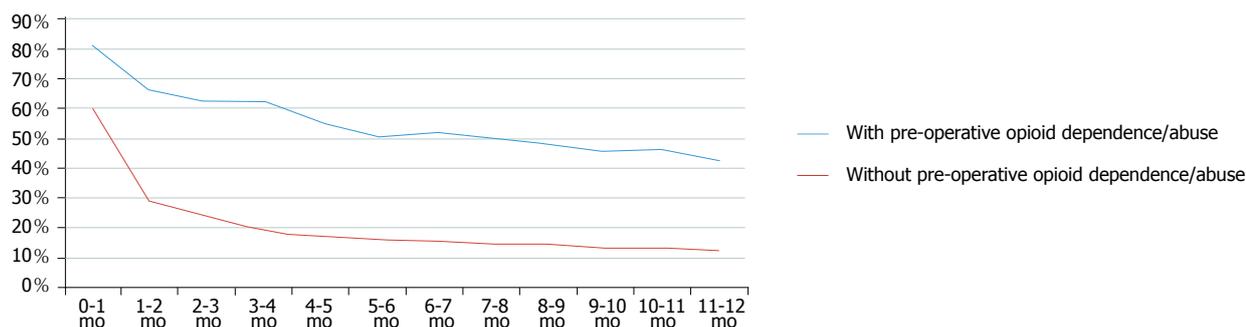
**DISCUSSION**

The results of the current study show that, following TSA and RSA, both opioid dependent and non-opioid dependent patients had similar opioid use within the first post-operative month. However, opioid use was much more prevalent among patients previously diagnosed with opioid dependence beyond the initial post-operative period. Younger age, mood disorders, and chronic pain diagnoses were significant risk factors for pre-operatively diagnosed opioid dependence or abuse.

**Table 4 Analysis of risk factors for pre-operative opioid dependence/abuse**

Variable	TSA			RSA		
	RR	95%CI	P value	RR	95%CI	P value
Female	1.07	0.78-1.46	0.691	1.3	0.96-1.75	0.085
Age < 65	2.12	1.46-3.08	0.000	1.6	1.06-2.41	0.024
Mood disorder	6.70	4.92-9.11	< 0.0001	5.27	4.04-6.87	< 0.0001
Chronic pain	10.31	7.51-14.17	< 0.0001	10.10	7.53-13.57	< 0.0001

TSA: Total shoulder arthroplasty; RSA: Reverse shoulder arthroplasty.



**Figure 2 Percent of patients filling at least one opioid prescription within each post-operative interval following reverse shoulder arthroplasty.** Within the first post-operative month, patients with a history of opioid dependence/abuse were slightly more likely to fill opioid prescriptions (RR = 1.36, 95%CI: 1.27-1.45,  $P < 0.001$ ). However, they were over 3 times as likely to use opioids during post-operative months 3-12 (RR ranged 3.09-3.50, 95%CI: 2.67-4.10,  $P < 0.001$ ).

Several previous studies utilizing national databases have analyzed the impact of pre-operative opioid use on post-operative use after orthopaedic surgery. Bedard *et al.*<sup>[9]</sup> found that pre-operative opioid use was a strong predictor of post-operative use following total knee arthroplasty. The incidences of opioid use at post-operative months 2-12 for “opioid users” in their study were similar to those for opioid-dependent patients in the current study. However, “non-opioid users” in their study had lower overall incidences of opioid use compared to the non-opioid dependent patients in the current study. This discrepancy may be related to differences in the specific opioid medications included in each analysis. “All common oral and transdermal opioids” were included in Bedard’s analysis with the exception of tramadol. However, the authors did not disclose detailed information on the specific medications included. It is therefore possible that post-operative opioid use was under-reported in the “non-opioid users”. Westermann *et al.*<sup>[10]</sup> utilized the Humana dataset to analyze opioid use following arthroscopic rotator cuff repair (RCR). They found that patients using opioids within 3 mo prior to surgery were more likely to fill opioid prescriptions post-operatively. Following the first post-operative month, the monthly incidences of opioid use for both opioid and non-opioid users was lower than opioid-dependent and non-opioid dependent patients in the current study, respectively. Similar to Bedard *et al.*<sup>[9]</sup>, the specific opioid medications tracked in Westermann’s analysis may have contributed to this difference as the drugs analyzed in their study were not specified.

The American Academy of Orthopaedic Surgeons

(AAOS) currently has no clinical practice guidelines recommending for or against the use of opioids following shoulder arthroplasty. Yet, opioid utilization is common following these procedures and the negative effects of pre-operative use on post-operative outcomes are clear<sup>[7,8]</sup>. In a recent Information Statement, the AAOS has advocated for the development of standardized opioid prescription protocols that include limits on prescription number and duration<sup>[11]</sup>. We support this statement and recommend that orthopaedic surgeons collaborate with primary care physicians and pain specialists as a part of a multidisciplinary team in the development these protocols. Based on the findings of our study, it would be prudent for physicians to closely monitor opioid utilization for patients with a history of opioid dependence or abuse. The current study clearly demonstrates that patients with a history of opioid dependence or abuse are at increased risk for prolonged postoperative opioid use. Furthermore, use of a risk-assessment tool for behaviors associated with prolonged opioid use<sup>[12]</sup> could be utilized to help identify risk factors for opioid dependence such as mood disorders and chronic pain diagnoses. As demonstrated in the current study, patients with risk factors such as mood disorder or chronic pain diagnosis are more prone to opioid dependence/abuse and, subsequently, to greater post-operative opioid use.

A key strength of the current study rests in the analysis of patients with any previous history of diagnosed opioid dependence or abuse, whereas the studies by Bedard<sup>[9]</sup> and Westermann<sup>[10]</sup> focused on patients who filled an opioid prescription within 3 mo prior to surgery.

It is quite possible that patients assessed in other studies did not have diagnosis of opioid dependence or abuse, and received opioids for temporary pain management prior to surgery. This likely explains the discrepancy between the percentages of opioid users in their studies (31% for THA, 43% for RCR) and the percentages of opioid dependent patients in our study (2% for TSA, 3% for RSA). It is our opinion that investigating patients with a history of diagnosed opioid dependence/abuse is a more meaningful analysis. While it is still possible that patients with previously diagnosed opioid dependence/abuse may not have been taking opioids immediately before surgery, having a history of diagnosed opioid dependence/abuse is a patient characteristic that can have lasting negative implications on postoperative outcomes even after cessation of opioid use<sup>[13]</sup>. During preoperative assessment, orthopedic surgeons should be encouraged to investigate any history of opioid dependence/abuse, however remote. As shown in the current study, these patients are at a higher risk for prolonged post-operative opioid use.

Certain limitations exist for the current study. First of all, the accuracy of data within large national databases such as the Humana claims dataset is dependent on proper coding. Errors in documentation have the potential to skew results. Secondly, previous studies have shown that brachial plexus nerve blocks prior to shoulder surgery decrease postoperative opioid utilization<sup>[14,15]</sup>, thus acting as a potential confounding variable. However, the proportion of patients receiving brachial plexus nerve blocks in this study was equivalent between study groups (Table 2) and thus did not likely affect the results. Third, the incidence of diagnosed opioid dependence/abuse is quite low. However, the use of a large national database is beneficial in providing the power required to show significant differences in smaller patient populations. Finally, wide standard deviations existed for CCI. For both TSA and RSA, the CCI standard deviation in patients without opioid dependence/abuse was greater than the mean. The difference in CCI between patients with and without opioid dependence/abuse history was significant but the wide distribution of CCI scores must be taken into account when determining patients' risk for opioid dependence/abuse.

In patients undergoing TSA and RSA, opioid use was similar within the first post-operative month for patients with and without a history of diagnosed opioid dependence/abuse. However, opioid use was much more prevalent among diagnosed opioid dependent patients from months 2-12. Younger age, mood disorders, and chronic pain diagnoses were significant risk factors for pre-operative opioid dependence or abuse. We recommend that orthopaedic surgeons carefully examine patients' opioid use history, as this may have a significant impact on prolonged post-operative opioid use after shoulder arthroplasty and the overall postoperative outcomes.

## ARTICLE HIGHLIGHTS

### Research background

While opioid medications have proven an effective method of analgesia after orthopaedic surgery, increased utilization of these medications in the United States has led to an opioid epidemic with higher levels of opioid dependence and abuse. Opioid dependence and abuse have been linked to worse outcomes after shoulder arthroplasty. Previous studies have shown that patients using opioids prior to total knee arthroplasty or rotator cuff repair have a greater risk of prolonged postoperative use. However, no study to our knowledge has analyzed the effect of diagnosed dependence or abuse on postoperative opioid utilization after shoulder arthroplasty.

### Research motivation

With opioid dependence and abuse rapidly increasing in the United States, it is imperative to determine their effects on postoperative opioid use. The current study addresses this question within the setting of shoulder arthroplasty, as orthopedic surgeons have been shown to be one of the largest prescribers of opioid medications. The knowledge gained from this study may impact providers' decisions to proceed with elective surgery, as opioid dependent patients are more likely to continue opioid use postoperatively and therefore perpetuate their dependence on opioid medications. The study will likely encourage future research pertaining to postoperative opioid monitoring in opioid dependent patients as well as the use of risk assessment tools for opioid dependence or abuse.

### Research objectives

The purpose of this study was to analyze the impact of diagnosed opioid dependence or abuse on postoperative opioid utilization after anatomic and reverse total shoulder arthroplasty (TSA). Furthermore, the authors sought to identify risk factors for preoperative opioid dependence or abuse. The study results highlight the importance of future research on the topic of identifying these risk factors, preventing the development of operative opioid dependence or abuse prior to orthopaedic surgery, and subsequently limiting postoperative opioid utilization.

### Research methods

Patients who underwent anatomic (RSA) or reverse TSA were identified from within the Humana claims database and were stratified into groups based on whether they had a history of opioid dependence or abuse. Postoperative opioid utilization was tracked on a month-by-month basis up to one year after surgery and was compared between the groups. A secondary analysis was performed to determine risk factors for preoperative opioid dependence or abuse.

### Research results

Patients with a history of opioid dependence or abuse had significantly higher opioid utilization at all postoperative intervals after both TSA and RSA ( $P < 0.01$ ), although the difference was not as prominent within the first postoperative month. Furthermore, age less than 65 years, history of mood disorder, and history of chronic pain were found to be significant risk factors for pre-operative opioid dependence or abuse. These results emphasize the importance of identifying patients preoperatively with a history of opioid dependence/abuse, or risk factors for developing opioid dependence/abuse, so that prolonged postoperative opioid use may be prevented. Further research is needed to determine specifically how these risk factors lead to opioid dependence and for establishing consistent postoperative opioid prescription protocols for shoulder arthroplasty.

### Research conclusions

New findings of the current study include that patients with a history of opioid dependence or abuse prior to shoulder arthroplasty are at least twice as likely to remain on opioids after TSA or RSA. Patients with risk factors such as mood disorders or chronic pain diagnoses were found to be more prone to opioid dependence/abuse and the authors theorize that this subsequently leads to

greater post-operative opioid use. The study provided a summarization of the current knowledge by offering similar findings to previous studies showing that opioid use prior to orthopaedic procedures leads to increased postoperative use. It offered original insights into the current knowledge by focusing on patients with diagnosed opioid dependence or abuse and establishing risk factors for these diagnoses. It proposed a new hypothesis that patients with pre-operative opioid abuse or dependence would have greater opioid utilization after TSA. The authors utilized methodology that identified preoperative opioid dependence or abuse, along with its risk factors, through the use of ICD-9 codes and tracked postoperative utilization through National Drug Codes. The authors found the new phenomena of significantly greater postoperative opioid utilization in opioid dependent patients after shoulder arthroplasty, though opioid use was similar within the first postoperative month. The study experiments confirmed the hypothesis that patients with previously diagnosed opioid dependence or abuse would have greater postoperative opioid utilization and that other factors such as mood disorders and chronic pain diagnoses are associated with opioid dependence/abuse. These findings imply that opioid utilization in opioid dependent patients, or those with risk factors for opioid dependence/abuse, must be monitored closely after shoulder arthroplasty in order to prevent prolonged use. Steps should be taken to implement postoperative opioid protocols for shoulder arthroplasty.

### Research perspectives

Patients with a history of opioid dependence or abuse are at a higher risk of increased postoperative opioid utilization after shoulder arthroplasty. Future research should be directed at the implementation of postoperative opioid protocols and the use of risk assessment calculators for opioid dependence.

## REFERENCES

- 1 **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]
- 2 **Gilson AM**, Ryan KM, Joranson DE, Dahl JL. A reassessment of trends in the medical use and abuse of opioid analgesics and implications for diversion control: 1997-2002. *J Pain Symptom Manage* 2004; **28**: 176-188 [PMID: 15276196 DOI: 10.1016/j.jpainnsymman.2004.01.003]
- 3 **Fischer B**, Keates A, Bühringer G, Reimer J, Rehm J. Non-medical use of prescription opioids and prescription opioid-related harms: why so markedly higher in North America compared to the rest of the world? *Addiction* 2014; **109**: 177-181 [PMID: 23692335 DOI: 10.1111/add.12224]
- 4 **Lindenhovius AL**, Helmerhorst GT, Schnellen AC, Vrahas M, Ring D, Kloen P. Differences in prescription of narcotic pain medication after operative treatment of hip and ankle fractures in the United States and The Netherlands. *J Trauma* 2009; **67**: 160-164 [PMID: 19590328 DOI: 10.1097/TA.0b013e31818c12ee]
- 5 **Volkow ND**, McLellan TA, Cotto JH, Karithanom M, Weiss SR. Characteristics of opioid prescriptions in 2009. *JAMA* 2011; **305**: 1299-1301 [PMID: 21467282 DOI: 10.1001/jama.2011.401]
- 6 **Menendez ME**, Ring D, Bateman BT. Preoperative Opioid Misuse is Associated With Increased Morbidity and Mortality After Elective Orthopaedic Surgery. *Clin Orthop Relat Res* 2015; **473**: 2402-2412 [PMID: 25694266 DOI: 10.1007/s11999-015-4173-5]
- 7 **Morris BJ**, Laughlin MS, Elkousy HA, Gartsman GM, Edwards TB. Preoperative opioid use and outcomes after reverse shoulder arthroplasty. *J Shoulder Elbow Surg* 2015; **24**: 11-16 [PMID: 25037063 DOI: 10.1016/j.jse.2014.05.002]
- 8 **Morris BJ**, Sciascia AD, Jacobs CA, Edwards TB. Preoperative opioid use associated with worse outcomes after anatomic shoulder arthroplasty. *J Shoulder Elbow Surg* 2016; **25**: 619-623 [PMID: 26652698 DOI: 10.1016/j.jse.2015.09.017]
- 9 **Bedard NA**, Pugely AJ, Westermann RW, Duchman KR, Glass NA, Callaghan JJ. Opioid Use After Total Knee Arthroplasty: Trends and Risk Factors for Prolonged Use. *J Arthroplasty* 2017; **32**: 2390-2394 [PMID: 28413136 DOI: 10.1016/j.arth.2017.03.014]
- 10 **Westermann RW**, Anthony CA, Bedard N, Glass N, Bollier M, Hettrich CM, Wolf BR. Opioid Consumption After Rotator Cuff Repair. *Arthroscopy* 2017; **33**: 1467-1472 [PMID: 28571723 DOI: 10.1016/j.arthro.2017.03.016]
- 11 **American Academy of Orthopaedic Surgeons**. Opioid Use, Misuse, and Abuse in Orthopaedic Practice. 2015: Information Statement 1045
- 12 **Webster LR**, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. *Pain Med* 2005; **6**: 432-442 [PMID: 16336480 DOI: 10.1111/j.1526-4637.2005.00072.x]
- 13 **Ren ZY**, Shi J, Epstein DH, Wang J, Lu L. Abnormal pain response in pain-sensitive opiate addicts after prolonged abstinence predicts increased drug craving. *Psychopharmacology (Berl)* 2009; **204**: 423-429 [PMID: 19172249 DOI: 10.1007/s00213-009-1472-0]
- 14 **Abdallah FW**, Halpern SH, Aoyama K, Brull R. Will the Real Benefits of Single-Shot Interscalene Block Please Stand Up? A Systematic Review and Meta-Analysis. *Anesth Analg* 2015; **120**: 1114-1129 [PMID: 25822923 DOI: 10.1213/ANE.0000000000000688]
- 15 **Chen HP**, Shen SJ, Tsai HI, Kao SC, Yu HP. Effects of Interscalene Nerve Block for Postoperative Pain Management in Patients after Shoulder Surgery. *Biomed Res Int* 2015; **2015**: 902745 [PMID: 26688821 DOI: 10.1155/2015/902745]

P- Reviewer: Kurosawa S S- Editor: Ji FF L- Editor: A  
E- Editor: Tan WW





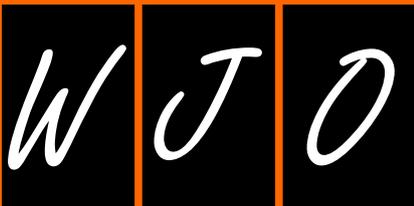
Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 September 18; 9(9): 112-184





### MINIREVIEWS

- 112 Robotic exoskeletons: The current pros and cons  
*Gorgey AS*

### ORIGINAL ARTICLE

#### Basic Study

- 120 Vascular endothelial growth factor for the treatment of femoral head osteonecrosis: An experimental study in canines  
*Dailiana ZH, Stefanou N, Khaldi L, Dimakopoulos G, Bowers JR, Fink C, Urbaniak JR*

- 130 Assessment of palmar subcutaneous tissue vascularization in patients with Dupuytren's contracture  
*Shchudlo N, Varsegova T, Stupina T, Dolganova T, Shchudlo M, Shihaleva N, Kostin V*

#### Prospective Study

- 138 Single rod instrumentation in patients with scoliosis and co-morbidities: Indications and outcomes  
*Tsirikos AI, Loughenbury PR*
- 149 Outcomes of mobile bearing unicompartmental knee arthroplasty in medial osteoarthritis knee with and without preoperative genu recurvatum  
*Pongcharoen B, Boontanapibul K*

#### Randomized Clinical Trial

- 156 Acute effects of partial-body vibration in sitting position  
*Faes Y, Banz N, Buscher N, Blasimann A, Radlinger L, Eichelberger P, Elfering A*
- 165 Corticosteroid injection alone vs additional physiotherapy treatment in early stage frozen shoulders  
*Kraal T, Sierevelt I, van Deurzen D, van den Bekerom MPJ, Beimers L*

### EVIDENCE-BASED MEDICINE

- 173 Is there consensus regarding surgical treatment of bone sarcomas?  
*Baad-Hansen T, Freund SS, Bech BH, Keller J*

### CASE REPORT

- 180 Spontaneous and simultaneous complete bilateral rupture of the quadriceps tendon in a patient receiving hemodialysis: A case report and literature review  
*Zribi W, Zribi M, Guidara AR, Ben Jemaa M, Abid A, Krid N, Naceur A, Keskes H*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Lars Victor von Engelhardt, MD, PhD, Assistant Professor, Chief Doctor, Reader (Associate Professor), Surgeon, Department of Orthopedics, Trauma Surgery and Sports Medicine, University of Witten/Herdecke and Katholisches Karl-Leisner Klinikum Kleve, Kleve 47533, Germany

**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 abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), China National Knowledge Infrastructure (CNKI), and Superstar Journals Database.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Fang-Fang Ji*  
**Proofing Editorial Office Director:** *Jin-Lei Wang*

**NAME OF JOURNAL**  
*World Journal of Orthopedics*

**ISSN**  
 ISSN 2218-5836 (online)

**LAUNCH DATE**  
 November 18, 2010

**FREQUENCY**  
 Monthly

**EDITOR-IN-CHIEF**  
**Bao-Gan Peng, MD, PhD, Professor**, Department of Spinal Surgery, General Hospital of Armed Police Force, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com/2218-5836/editorialboard.htm>

**EDITORIAL OFFICE**  
 Jin-Lei Wang, Director

*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f0publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f0publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 September 18, 2018

**COPYRIGHT**  
 © 2018 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.f0publishing.com>

## Robotic exoskeletons: The current pros and cons

Ashraf S Gorgey

Ashraf S Gorgey, Spinal Cord Injury and Disorders Center, Hunter Holmes McGuire VAMC, Richmond, VA 23249, United States

Ashraf S Gorgey, Department of Physical Medicine and Rehabilitation, Virginia Commonwealth University, Richmond, VA 23249, United States

ORCID number: Ashraf S Gorgey (0000-0002-9157-6034).

Author contributions: Gorgey AS solely contributed to this paper.

Conflict-of-interest statement: The author has nothing to declare related to the current 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/>

Manuscript source: Invited manuscript

Correspondence to: Ashraf S Gorgey, PhD, Academic Research, Associate Professor, Physiotherapist, Research Scientist, Spinal Cord Injury and Disorders Center, Hunter Holmes McGuire VAMC, 1201 Broad Rock Boulevard, Richmond, VA 23249, United States. [ashraf.gorgey@va.gov](mailto:ashraf.gorgey@va.gov)  
Telephone: +1-804-6755000  
Fax: +1-804-6755223

Received: April 3, 2018

Peer-review started: April 3, 2018

First decision: June 5, 2018

Revised: July 2, 2018

Accepted: July 10, 2018

Article in press: July 10, 2018

Published online: September 18, 2018

### Abstract

Robotic exoskeletons have emerged as rehabilitation tool that may ameliorate several of the existing health-related consequences after spinal cord injury (SCI). However, evidence to support its clinical application is still lacking considering their prohibitive cost. The current mini-review is written to highlight the main limitations and potential benefits of using exoskeletons in the rehabilitation of persons with SCI. We have recognized two main areas relevant to the design of exoskeletons and to their applications on major health consequences after SCI. The design prospective refers to safety concerns, fitting time and speed of exoskeletons. The health prospective refers to factors similar to body weight, physical activity, pressure injuries and bone health. Clinical trials are currently underway to address some of these limitations and to maximize the benefits in rehabilitation settings. Future directions highlight the need to use exoskeletons in conjunction with other existing and emerging technologies similar to functional electrical stimulation and brain-computer interface to address major limitations. Exoskeletons have the potential to revolutionize rehabilitation following SCI; however, it is still premature to make solid recommendations about their clinical use after SCI.

**Key words:** Spinal cord injury; Exoskeleton; Robotics; Rehabilitation; Locomotion

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Robotic exoskeletons have emerged as rehabilitation tool for persons with spinal cord injury (SCI). Clinical evidence related to applications of exoskeletons is still lacking considering their prohibitive cost. Clinical trials are currently underway to address some of these limitations and to maximize their benefits in different rehabilitation settings. Exoskeletons have the potential

to revolutionize rehabilitation following SCI; however, it is still premature to make solid recommendations about their clinical use after SCI. The current mini-review highlights the basic applications and limitations as well as future directions regarding applications and exoskeletons.

Gorgey AS. Robotic exoskeletons: The current pros and cons. *World J Orthop* 2018; 9(9): 112-119 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/112.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.112>

## INTRODUCTION

Robotic exoskeletons or powered exoskeletons are considered wearable robotic units controlled by computer boards to power a system of motors, pneumatics, levers, or hydraulics to restore locomotion<sup>[1,2]</sup>. The topic of exoskeletons is timely given the number of devices currently being studied as well as purchased by facilities for rehabilitation purposes in medical centers or for home use<sup>[1-7]</sup>. Exoskeletons have emerged as an advantageous rehabilitation tool for disabled individuals with spinal cord injury (SCI)<sup>[1]</sup>. Rehabilitation specialists, clinicians, researchers, and patients welcome their use for over ground ambulation<sup>[2-7]</sup>. Compared to previously existing locomotor training paradigms, exoskeletons may offer a great deal of independence in medical centers and communities including shopping malls, local parks and movie theaters as well as improving the level of physical activity<sup>[1-3]</sup>. There is a pressing need for this population to improve their levels of physical activity. This feature may encourage continuous usage of exoskeletons in conjunction with wheelchairs.

## CURRENT APPLICATIONS OF EXOSKELETONS

Different brands of powered exoskeletons are now commercially available for SCI rehabilitation with different levels of injury<sup>[1-7]</sup>. However, there is still a limited accessibility to exoskeletons in clinical settings, partly because of their prohibitive cost and the high level of training required before supervising individuals with SCI. Despite these limitations, limited research and anecdotal evidence support the use of exoskeleton to improve quality of life and health related medical conditions after SCI<sup>[1-3]</sup>. Previous excellent reviews have summarized and highlighted the potential benefits of using exoskeleton for rehabilitation of persons with SCI<sup>[2-4]</sup>. It is crucial before expanding the applications of exoskeletons that we carefully analyze the available research and clinical evidence regarding this technology. Considering the limited data and/or small sample size of the current published studies, it is premature to draw solid conclusions about the efficacy of exoskeletons in

maximizing rehabilitation outcomes or ameliorating several of the health-related consequences following SCI. However, clinical trials are underway to confirm these benefits and to understand the underlying mechanisms that lead to such improvement. Clinical trials site (clinicaltrials.gov) indicated that out of 870 studies for SCIs, there are 28 studies (approximately 3%) addressing different applications of exoskeletons in this population. These statistics may highlight our limited knowledge and the need for additional clinical trials to address the major limitations of exoskeletons. The current use of robotic exoskeletons remains investigational and premature to decide whether exoskeletons are clinically effective in the rehabilitation of persons with SCI. The primary focus of the current review is to allow critical analysis of the available research evidence and to encourage interdisciplinary approach to advance the use of technology in clinical settings. The rehabilitation community should not be discouraged from the use of exoskeletons, but rather to proceed with caution regarding their clinical applications. Moreover, the mini-review will provide the reader with the current pros and cons regarding exoskeletons and will summarize in a non-exhaustive manner the theoretic or potential benefits after recognizing the primary limitations of exoskeletons. It is not the intention of the current review to list types or characteristics of different exoskeletons that were recently published in details<sup>[1]</sup>. The published work provided details on the average cost per unit and clear illustrations of different exoskeleton units available in rehabilitation settings<sup>[1]</sup>.

## BENEFITS AND LIMITATIONS FROM THE DESIGN PROSPECTIVE

### *Safety and efficacy of exoskeletons*

From the clinical health-prospective, several reports have demonstrated that exoskeleton training is safe and likely to be used in different settings to encourage over ground ambulation<sup>[1-7]</sup>. A recent study that involved nine European rehabilitation centers demonstrated the safety, feasibility and training characteristics in persons with SCI following 8 wk of training<sup>[6]</sup>. Out of 52 participants, three dropped out following ankle swelling and four presented with grade II pressure injury but managed to continue the study<sup>[6]</sup>. Personal communication indicated that fracture may occur at the distal tibia or calcaneus bone during exoskeleton walking. Potential health benefits have been highlighted for the use of exoskeletons in rehabilitation settings, and studies have examined the effects of exoskeletons on different health-related outcomes<sup>[1-9]</sup>. These studies provided preliminary evidence on the efficacy of exoskeletons on cardiovascular health, energy expenditure, body composition, gait parameters, level of physical activity and quality of life<sup>[2-9]</sup>. Robotic exoskeletons may prove

an attractive rehabilitation tool not only to restore locomotion but also to improve the level of physical activity years after injury<sup>[6,7]</sup>. Robotic exoskeletons may decrease seated time, increase standing and walking time as well as social engagements with family and friends<sup>[6,7]</sup>. Decreased sitting time is likely to ameliorate several of the health-related consequences that negatively impact this population<sup>[10-15]</sup>.

### **Fitting time across different brands**

Most of the current brands require special measurements to custom fit participants before donning/doffing. This may require special adjustments for persons with SCI in case there is leg length discrepancy, pelvic obliquity, severe muscle wasting or even highly sensitive skin; which may require up to 2-3 sessions to accomplish this task (e.g., Rewalk and Ekso)<sup>[1-9]</sup>. Different brands have different donning/doffing strategies which may range from 10 to 30 min to safely fit subjects before walking (e.g., Indego). After completion of the initial measurements of the participants, exoskeleton fitting may require at least 1 h to safely complete the required checklist steps before standing up and walking. This is usually preceded with detailed physical examination to safely screen participants for eligibility. The detailed physical examination will make a safe clinical decision prior to including or excluding any participants in the program. After fitting sessions, the time needed to adjust devices to custom fit each participant may also interfere with future training sessions. This has the potential to limit the allotted training time set for each subject as covered by his/her medical insurance. Other available brands have a shorter fitting time and may be as simple as measuring the length from greater trochanter to the knee joint followed by measuring the length from the knee joint to the heel of the patient<sup>[8]</sup>. Moreover, most of the available brands require transfer to the mat or transfer to piano-type chair to accomplish the fitting purpose which may increase the risk of falling. Many SCI participants with limited hand functions or push-down performance may not be candidates for this technology because of difficulty in achieving safe transfer<sup>[1,5-7]</sup>. Therefore, future brands need to consider shorter fitting time and allow fitting in wheelchairs without the need to transfer from one place to another. Indego exoskeleton was successful in designing their product into parts that can be easily assembled together while the participants were still in their wheelchairs. This is likely to cut the fitting time and provide safe accessibility to the community. Another aspect is that some brands (e.g., Rewalk) may require higher intellectual capabilities to perform and learn weight shifting and stepping in order to walk or navigate thresholds or carpets. This motor learning capability may vary from one patient to another and may require 3-5 d of continuous training to grasp this procedure. As the technology advances, different manufactures will develop their products to be simply fitted to the participants in a short time and provide variable options for persons with

wide motor learning capabilities.

### **Speed and community ambulation**

Exoskeletons offer a range of varying speed and most are characterized by a modest speed that is slightly greater than 0.2 m/sec, which may impede their general use in the community<sup>[2,3,5]</sup>. Others have demonstrated that speed may exceed 0.7 m/sec especially in persons with incomplete SCI<sup>[5]</sup>. The slow speed may preserve balance and prevent frequent falling; however, ambulation speed may increase following continuous training. In a case report, we demonstrated the ability of a person with C5 complete SCI to increase his walking speed to 0.4 m/sec<sup>[7]</sup>. Gaining confidence and securing balance are motor learning strategies that influence walking speed. Most of these brands were primarily tested indoors on tiled surfaces and walking on uneven terrains may impose additional challenges to persons with SCI. Currently, there are two brands that have received Food and Drug Administration approval for personal use<sup>[5,8]</sup>. Compared to wheelchairs, these brands are still not adequate to provide ambulation on muddy, pebbles, rainy and/or snowy terrains. This may impede their applications in other states or countries having roads or weather conditions not suitable for locomotion with exoskeletons. Development of lighter materials for exoskeletons may facilitate increasing the speed for community ambulation. Current existing brands weigh 50-66 lbs, which may be a hurdle for some individuals with SCI to carry or lift for transportation compared to ultralight wheelchairs<sup>[3-9]</sup>. Other brands have different components and can be broken down and carried separately<sup>[8]</sup>. Future designs should focus on choosing highly durable materials that provide less weight and allow faster speed without compromising balance after SCI. Moreover, it is highly recommended to design water-proof brands that can facilitate walking in different weather conditions or on uneven terrains.

---

## **BENEFITS AND LIMITATIONS FROM HEALTH PROSPECTIVE**

---

### **Exoskeletons and levels of SCI**

Persons with tetraplegia represent 55% of the SCI population<sup>[16]</sup>. The current technology (Ekso) is FDA approved to be used for those with C7 and below SCI, primarily because of safety concerns. The level of injury cut-off was set because reasonable hand functions are required to hold the assistive device (walker or crutches) and to initiate weight shifting during stepping and walking. Lack of appropriate hand grip may eliminate a considerable number of this population from benefitting from this technology. This means that a large segment with C1-C5 level of injury may be ineligible to benefit from this technology. Another brand (REX) has emerged to address this issue and

allows running the machine with a joystick or controller without relying on the participants' hand functions<sup>[17,18]</sup>; however, this brand is still not FDA approved and its speed is very limited, less than 0.1 m/sec, to initiate any recognized cardiometabolic benefits compared to a regular standing frame. However, the brand can offer other benefits similar to ambulatory exercise and upper body exercise in upright position<sup>[18]</sup>. This technology may be beneficial to those with C4-C8 level of SCI or even higher level of injury similar to cases diagnosed with locked-in syndrome. Compared to other approved brands, the REX exoskeleton does not require a two or four point assisted device. In other approved brands, it is crucial to have reasonable hand functions to initiate walking using a controller, to control the assistive device, to help shifting body weight and to provide balance in the standing position. Proactive means of using platforms walker or other devices (e.g., hand splints) are warranted to overcome this problem and to provide safe accessibility in large segment of SCI population despite their level of injury.

#### **Exoskeletons and body weight / body composition**

Two-thirds of persons with SCI are either overweight or obese<sup>[15]</sup>. Exoskeletons may facilitate waging the war on obesity syndrome after SCI by helping to decrease sitting time, increase level of physical activity and improve parameters of body composition after SCI. However, the existing technology is only limited to those with body weight less than 100 kg (220 lbs). This may exclude a considerable number of individuals from benefitting from this technology. The weight cut-off may motivate SCI participants to engage in effective dietary plans and participate in SCI wellness and exercise programs to maintain a healthy body weight. Anecdotal evidence supports this notion, several persons with SCI started a rigorous diet program to lose weight after initially being disqualified from enrolling because of exceeding the body weight cut-off limit recommended by the manufacture. Further studies are warranted to investigate whether exoskeleton training may independently help persons with SCI to lose weight especially decreasing percentage of whole body and regional fat mass.

Another important consideration is whether exoskeleton training is likely to improve parameters of body composition as indicated by decreased fat mass and increased fat-free mass. Decreased fat mass is likely to improve parameters of cardio-metabolic health after SCI<sup>[11]</sup>. A recent report demonstrated that improvement in cardio-metabolic health is tightly associated with positive body composition characteristics compared to parameters of physical activity<sup>[19]</sup>. There is still limited evidence to support the positive effects of exoskeleton ambulation on parameters of body composition. A recent case report demonstrated that 15 wk of exoskeleton training resulted in decreased body mass by 6 kg including 2 kg loss in fat mass and 4 kg loss in fat-free

mass in a person with T4 complete SCI<sup>[7]</sup>.

#### **Exoskeletons and physical activity**

Physical inactivity is a key feature following SCI, which is likely to lead to a sedentary lifestyle and increased sitting time<sup>[12,20-22]</sup>. Prolonged sitting time has been shown to be an independent risk factor for cardiovascular disease, cancer as well as a factor for increasing all-cause mortality<sup>[10]</sup>. A very important point that needs to be considered is low metabolic cost during exoskeleton training. Cardio-respiratory fitness is used as a key feature to determine overall health and inverse relationships were noted between VO<sub>2</sub> max and cardiovascular disorders, insulin resistance and type 2 diabetes mellitus<sup>[23]</sup>. Recently released ISCOS guidelines recommended that persons with SCI engage in at least 20 min of moderate to vigorous intensity aerobic exercise three times per week to improve cardio-respiratory fitness<sup>[20]</sup>. This supports the notion adopted by other organizations and research groups on the significance of increasing the level of physical activity to decrease chronic disease risk factors after SCI<sup>[10,21,22]</sup>. It is unclear whether exoskeleton locomotion may induce this moderate intensity training, but it can definitely decrease sitting time and improve parameters of physical activity as demonstrated by increasing number of steps, duration and distance of walking<sup>[6,7]</sup>.

According to the World Health Organization, physical activity is defined as the bodily movement resulting from muscle actions that increases energy expenditure. Exoskeletons provide bodily passive movement of the lower extremity without muscle contraction. This is likely to be accompanied with low oxygen uptake and energy expenditure during exoskeleton ambulation<sup>[7]</sup>. Therefore, incorporating functional electrical stimulation (FES) in conjunction with exoskeleton training may be an effective strategy to offset this problem by initiating muscle contraction and increasing energy expenditure<sup>[24,25]</sup>. Currently, hybrid exoskeleton brands may offer this feature; however, studies are currently underway to prove the effectiveness of this combination in persons with SCI. The combination of FES and robotic control is a challenging issue, due to the non-linear behavior of muscle under stimulation and the lack of developments in the field of hybrid control<sup>[24,25]</sup>. The hybrid system may overcome electromechanical timing delays and muscle fatigue as well as balance muscular and robotic actuation during walking.

#### **Exoskeletons and range of motion**

Joint contractures at the hips, knees and ankle joints are another problem that is likely to disqualify participation from exoskeleton training program<sup>[26]</sup>. Persons with SCI need to attain hip extension range of motion within 10-15 degrees and knee extension with less than 10 degrees flexion in supine or standing position with ankle joints in neutral position<sup>[1-9]</sup>. Participants who fail to attain this range of motion may be encouraged to

participate in a stretching program to improve muscle flexibility around these joints. This may include the use of standing frame or application of a dyna-splint around the knee joint to provide soft tissue stretching for long duration<sup>[26]</sup>. An extensive stretching program may take up to 6 mo to gain 6-10-degree improvement in the range of motion. Because of disuse after high level SCI, persons may also suffer from joint contractures or tenodesis grasp, which may likely limit their ability to use assistive devices and failure to evoke weight shifting during exoskeleton ambulation. Therapists may need to be proactive and use a platform walker or help cuffing the hand to the assistive device to overcome these problems. It is worth noting that maintaining functional range of motion during locomotion is essential for neuro-recovery following SCI. Compared to other forms of walking similar to knee-ankle foot orthosis (KAFO) or hip-knee-ankle-foot orthosis (HKAFO), exoskeleton ambulation may facilitate natural recovery over encouraging compensatory techniques of using trunk muscles following SCI. However, further studies are still warranted to support this assertion.

### **Exoskeletons and bone health**

Sixty percent of individuals with SCI suffer from osteopenia or osteoporosis; a progressive disease that leads to bone loss, especially in the distal femur and proximal tibia<sup>[27]</sup>. Bone remodeling and demineralization is a continuous process and it is a function of both osteoblastic and osteoclastic activities. The pattern of bone loss in persons with SCI differs from other clinical population and it is commonly referred to as neurogenic osteoporosis<sup>[14]</sup>. Bone loss occurs sublesionally at a rapid rate and approaching 1% of bone mineral density per week<sup>[27-29]</sup>. Most of bone loss occurs within the first 12 to 24 mo after SCI and reaches steady state within 3-8 years post-injury<sup>[27-29]</sup>. Furthermore, persons with SCI are likely to experience lower extremity fracture that may require close to several months to one year to re-initiate weight bearing using a standing frame or any other assistive devices. The high susceptibility of fracture in these regions may lead to other health consequences following immobilization similar to joint contractures and pressure injuries. Imaging techniques are now available to provide clinicians with insights regarding bone health after SCI. These techniques include X-rays, dual energy X-ray absorptiometry (DXA), quantitative computed tomography (CT), magnetic resonance imaging (MRI)<sup>[27]</sup>. The first two techniques provide two-dimensional assessment of bone health and the latter ones provide 3-dimensional volumetric assessment of bone architecture. A recent review has clearly demonstrated the differences among imaging approaches in highlighting the risk of fractures after SCI<sup>[27]</sup>. Longitudinal monitoring of bone health in persons with SCI has become a crucial element for any rehabilitation program. This may ensure safe standing and weight bearing prior to locomotion programs including

exoskeleton.

Recommendations based on early evidence suggest that a BMD below 0.6 g/cm<sup>2</sup> of the knee joint (*i.e.*, distal femur and proximal tibia) or T-scores less than 3.5 standard deviations at the hip joints or femoral neck can be used as cut-offs to exclude individuals from participating in standing activities. This is likely to exclude a considerable number of participants from engaging in exoskeleton training programs. Moreover, these cut-offs do not guarantee certainty that fracture at any of these sites may not occur<sup>[27-29]</sup>. Bone biomarkers have been previously used in rehabilitation programs to highlight these activities<sup>[30]</sup>. These biomarkers are not widely introduced and underutilized in clinical settings. Therefore, it is highly recommended that all persons with SCI undergo DXA scans for knees and hips as well as X-ray at the ankle joints prior to exoskeleton training. It is essential to conduct X-ray exam at the ankle joints to assess participants' risk of fracture at the distal tibia or calcaneus bone during standing or walking training with exoskeleton. Moreover, evidence-based guidelines need to be established on what clinical biomarkers should be utilized to decrease the risk of bone fracture. It is still unclear, based on available evidence, whether incorporating pharmacological intervention with or without neuromuscular electrical stimulation can alleviate the problem of osteoporosis after SCI.

### **Exoskeleton and pressure injuries**

It is well documented that 70%-75% of persons with SCI experience pressure injuries during their lifetime with dramatic changes in their skin structures that are likely to break down with a minimal amount of shear<sup>[31,32]</sup>. This should make us cautious about choosing the appropriate candidate, utilizing their past medical history to identify those likely to benefit from exoskeleton use without exposure to such shear stress. Powered exoskeletons are likely to have straps to help maintaining static and dynamic posture during standing and walking<sup>[17]</sup>. With diminished sensation and impaired peripheral circulation, these straps are likely to cause excessive shear to the surrounding soft tissues and may lead to pressure injuries<sup>[17]</sup>. To circumvent this problem, researchers developed pressure sensors to monitor pressure exerted by physical human-machine interfaces and provide feedback about levels of skin/body pressure in fastening straps<sup>[17]</sup>. These pressure sensors are likely to protect against ischemia and necrosis by maintaining pressure in range of 30-35 mmHg to allow for adequate circulation or below 50 mmHg to maintain tissue oxygenation<sup>[17]</sup>. Pressure heat maps were recently measured in one person with SCI performing exoskeleton locomotion. The authors highly suggested that thigh straps may induce pressures ranging from 80-120 mmHg while performing upright locomotion. Anecdotal unpublished evidence supports that extensive strapping may result in cyst formation at the pressure site<sup>[17]</sup>. Therefore, clinicians working with exoskeletons

need to check different pressure skin zones especially when working with complete SCI.

---

## FUTURE DIRECTIONS IN EXOSKELETON AMBULATION

---

### *Current challenges facing community use*

The transition from hospital setting to rehabilitation use or community ambulation requires the need of a well-trained caregiver<sup>[1,5]</sup>. It is likely to be challenging for persons with SCI to identify a dedicated caregiver, who is willing to dedicate the time and effort to support their partner during exoskeleton ambulation. Work related commitment, divorce, liability in case of falling or injury have been identified as precluding factors to having a committed caregiver. Moreover, it is the total responsibility of a certified exoskeleton trainer to provide hands-on training for the caregiver and ensure that the patient is safe before getting released in the community. There is increased prevalence of SCI with aging; as a result of falling or cervical myelopathy that may prevent baby-boomers with SCI to benefit from this technology. Their next of kin is likely to be older or unable to provide the time to be qualified as a trained caregiver. Designing systems that do not require or decrease reliance on a caregiver may be an advantageous future goal in the rehabilitation of persons with SCI.

### *The cost and standard wheelchair*

Finally, the current cost of this equipment is prohibitive and may interfere with accessibility in the developed countries as well as less developed parts of the world. The cost may drop with increased numbers of emerging brands and studies demonstrating their efficacy. However, policy makers and governments need to determine whether the technology deserves wide spread application such that medical insurance can offer an exoskeleton unit per patient similar to a wheelchair. As of now, it remains unclear whether this emerging technology offers benefits beyond the existing standard of care, such as a regular wheelchair or a standing frame. Current research is underway to answer these questions. It should be noted that someone who has been in a wheelchair for 20-30 years may not be willing to make daily lifestyle changes to adopt the new technology. Current technology may offer accessibility in the community, but it is still limited in its ability to navigate special terrains, climb stairs, or move in water. It has yet to be determined whether persons with SCI are willing to compromise his/her comfort zone of using his daily wheelchair over experiencing the luxury of ambulating in a costly robotic suit. From the recreational point of view, recreation programs may need to encourage community trips using exoskeletons to help increasing public awareness and facilitate their use in conjunction with wheelchairs. It is highly recommended to encourage exoskeleton sports during the annual wheelchair games similar to

power wheelchair soccer or other activities. This is likely to provide competitions among the available brands and increase their popularity in recreational settings.

Future directions may need to consider a number of research questions including the effects of exoskeleton training on acute compared to chronic injury and whether early use is likely to attenuate or slow the changes that occur in body composition after SCI. A recent study demonstrated that those with an acute injury (< 1 year) showed improvement in parameters of gait function by 36% compared to only 3% for those with chronic injury<sup>[6]</sup>. Moreover, it is still unclear whether exoskeleton training can be used as a task specific training to reinforce neural plasticity and recovery of gait especially in persons with incomplete SCI. Implementing the exoskeleton technology with electrical stimulation, epidural stimulation and brain-computer interphase (BCI) may be available features in future brands<sup>[33]</sup>. This may provide the end-user with a control over the robotic limbs *via* the use of electrical stimulation, BCI or both<sup>[30,31,33,34]</sup>. The technology of the exoskeleton is likely to evolve as more partnerships developed to produce future generations that are likely to be lighter and faster. Moreover, robotic exoskeletons may need to be considered within developmental stages to help children with SCI and other clinical population<sup>[35,36]</sup>. This is highly important to provide early weight bearing and avoid postural abnormalities or deformities. The National Institutes of Health just released an attempt to help kids with cerebral palsy to walk on their feet and prevent crouched gait<sup>[35,36]</sup>. As cheaper brands of exoskeletons become available, participants may continue to use them in conjunction with wheelchairs because of their recognized benefits on spasticity, physical activity, bowel movement and quality of life after SCI.

---

## CONCLUSION

---

The current review may raise the awareness of the SCI community about the use of exoskeletons in the rehabilitation of persons with SCI. We should strive for an interdisciplinary team approach to provide greater accessibility to this technology and further our knowledge on how to expand its use to the general population of SCI by overcome some of the existing limitations that were highlighted. Exoskeletons may improve several physiologic and psycho-somatic outcomes. Moreover, it is time to establish round table discussions including individuals with SCI (consumers), government and health policy makers, researchers and rehabilitation specialists to develop rigorous plans for the future of exoskeletons. As our knowledge and experience increase, more individuals with SCI should become eligible to gain the benefits of this promising technology.

---

## REFERENCES

---

- 1 Gorgey A, Sumrell R, Goetz L. Exoskeletal assisted rehabilitation

- after spinal cord injury. In: Atlas of Orthoses and Assistive Devices. 5th ed. Canada: Elsevier, 2018: 440-447
- 2 **Miller LE**, Zimmermann AK, Herbert WG. Clinical effectiveness and safety of powered exoskeleton-assisted walking in patients with spinal cord injury: systematic review with meta-analysis. *Med Devices (Auckl)* 2016; **9**: 455-466 [PMID: 27042146 DOI: 10.2147/MDER.S103102]
  - 3 **Federici S**, Meloni F, Bracalenti M, De Filippis ML. The effectiveness of powered, active lower limb exoskeletons in neurorehabilitation: A systematic review. *NeuroRehabilitation* 2015; **37**: 321-340 [PMID: 26529583 DOI: 10.3233/NRE-151265]
  - 4 **Louie DR**, Eng JJ, Lam T; Spinal Cord Injury Research Evidence (SCIRE) Research Team. Gait speed using powered robotic exoskeletons after spinal cord injury: a systematic review and correlational study. *J Neuroeng Rehabil* 2015; **12**: 82 [PMID: 26463355 DOI: 10.1186/s12984-015-0074-9]
  - 5 **Asselin P**, Knezevic S, Kornfeld S, Cirmigliaro C, Agranova-Breyter I, Bauman WA, Spungen AM. Heart rate and oxygen demand of powered exoskeleton-assisted walking in persons with paraplegia. *J Rehabil Res Dev* 2015; **52**: 147-158 [PMID: 26230182 DOI: 10.1682/JRRD.2014.02.0060]
  - 6 **Bach Baunsgaard C**, Vig Nissen U, Katrin Brust A, Frotzler A, Ribeill C, Kalke YB, León N, Gómez B, Samuelsson K, Antepohl W, Holmström U, Marklund N, Glott T, Opheim A, Benito J, Murillo N, Nachtegaal J, Faber W, Biering-Sørensen F. Gait training after spinal cord injury: safety, feasibility and gait function following 8 weeks of training with the exoskeletons from Ekso Bionics. *Spinal Cord* 2018; **56**: 106-116 [PMID: 29105657 DOI: 10.1038/s41393-017-0013-7]
  - 7 **Gorgey AS**, Wade R, Sumrell R, Villadelgado L, Khalil RE, Lavis T. Exoskeleton Training May Improve Level of Physical Activity After Spinal Cord Injury: A Case Series. *Top Spinal Cord Inj Rehabil* 2017; **23**: 245-255 [PMID: 29339900 DOI: 10.1310/sci16-00025]
  - 8 **Evans N**, Hartigan C, Kandilakis C, Pharo E, Clesson I. Acute Cardiorespiratory and Metabolic Responses During Exoskeleton-Assisted Walking Overground Among Persons with Chronic Spinal Cord Injury. *Top Spinal Cord Inj Rehabil* 2015; **21**: 122-132 [PMID: 26364281 DOI: 10.1310/sci2102-122]
  - 9 **Kressler J**, Thomas CK, Field-Fote EC, Sanchez J, Widerström-Noga E, Cilien DC, Gant K, Ginney K, Gonzalez H, Martinez A, Anderson KD, Nash MS. Understanding therapeutic benefits of overground bionic ambulation: exploratory case series in persons with chronic, complete spinal cord injury. *Arch Phys Med Rehabil* 2014; **95**: 1878-1887.e4 [PMID: 24845221 DOI: 10.1016/j.apmr.2014.04.026]
  - 10 **Katzmarzyk PT**, Church TS, Craig CL, Bouchard C. Sitting time and mortality from all causes, cardiovascular disease, and cancer. *Med Sci Sports Exerc* 2009; **41**: 998-1005 [PMID: 19346988 DOI: 10.1249/MSS.0b013e3181930355]
  - 11 **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.0000000245]
  - 12 **Buchholz AC**, Martin Ginis KA, Bray SR, Craven BC, Hicks AL, Hayes KC, Latimer AE, McColl MA, Potter PJ, Wolfe DL. Greater daily leisure time physical activity is associated with lower chronic disease risk in adults with spinal cord injury. *Appl Physiol Nutr Metab* 2009; **34**: 640-647 [PMID: 19767799 DOI: 10.1139/H09-050]
  - 13 **Dolbow DR**, Gorgey AS, Daniels JA, Adler RA, Moore JR, Gater DR Jr. The effects of spinal cord injury and exercise on bone mass: a literature review. *NeuroRehabilitation* 2011; **29**: 261-269 [PMID: 22142760 DOI: 10.3233/NRE-2011-0702]
  - 14 **Qin W**, Bauman WA, Cardozo C. Bone and muscle loss after spinal cord injury: organ interactions. *Ann N Y Acad Sci* 2010; **1211**: 66-84 [PMID: 21062296 DOI: 10.1111/j.1749-6632.2010.05806.x]
  - 15 **Gorgey AS**, Gater DR Jr. Prevalence of Obesity After Spinal Cord Injury. *Top Spinal Cord Inj Rehabil* 2007; **12**: 1-7 [PMID: 29472754 DOI: 10.1310/sci1204-1]
  - 16 **National Spinal Cord Injury Statistical Center**. Spinal cord injury facts and figures at a glance. Available from: URL: [https://www.nscisc.uab.edu/PublicDocuments/fact\\_figures\\_docs/Facts%202012%20Feb%20Final.pdf](https://www.nscisc.uab.edu/PublicDocuments/fact_figures_docs/Facts%202012%20Feb%20Final.pdf)
  - 17 **Tamez-Duque J**, Cobian-Ugalde R, Kilicarslan A, Venkatakrishnan A, Soto R, Contreras-Vidal JL. Real-time strap pressure sensor system for powered exoskeletons. *Sensors (Basel)* 2015; **15**: 4550-4563 [PMID: 25690551 DOI: 10.3390/s150204550]
  - 18 **Birch N**, Graham J, Priestley T, Heywood C, Sakel M, Gall A, Nunn A, Signal N. Results of the first interim analysis of the RAPPER II trial in patients with spinal cord injury: ambulation and functional exercise programs in the REX powered walking aid. *J Neuroeng Rehabil* 2017; **14**: 60 [PMID: 28629390 DOI: 10.1186/s12984-017-0274-6]
  - 19 **Nightingale TE**, Walhin JP, Thompson D, Bilzon JL. Biomarkers of cardiometabolic health are associated with body composition characteristics but not physical activity in persons with spinal cord injury. *J Spinal Cord Med* 2017; **1**-10 [PMID: 28901220 DOI: 10.1080/10790268.2017.1368203]
  - 20 **Martin Ginis KA**, van der Scheer JW, Latimer-Cheung AE, Barrow A, Bourne C, Carruthers P, Bernardi M, Ditor DS, Gaudet S, de Groot S, Hayes KC, Hicks AL, Leicht CA, Lexell J, Macaluso S, Manns PJ, McBride CB, Noonan VK, Pomerleau P, Rimmer JH, Shaw RB, Smith B, Smith KM, Steeves JD, Tussler D, West CR, Wolfe DL, Goosey-Tolfrey VL. Evidence-based scientific exercise guidelines for adults with spinal cord injury: an update and a new guideline. *Spinal Cord* 2018; **56**: 308-321 [PMID: 29070812 DOI: 10.1038/s41393-017-0017-3]
  - 21 **Ginis KA**, Arbour-Nicitopoulos KP, Latimer AE, Buchholz AC, Bray SR, Craven BC, Hayes KC, Hicks AL, McColl MA, Potter PJ, Smith K, Wolfe DL. Leisure time physical activity in a population-based sample of people with spinal cord injury part II : activity types, intensities, and durations. *Arch Phys Med Rehabil* 2010; **91**: 729-733 [PMID: 20434610 DOI: 10.1016/j.apmr.2009.12.028]
  - 22 **Evans N**, Wingo B, Sasso E, Hicks A, Gorgey AS, Harness E. Exercise Recommendations and Considerations for Persons With Spinal Cord Injury. *Arch Phys Med Rehabil* 2015; **96**: 1749-1750 [PMID: 26198424 DOI: 10.1016/j.apmr.2015.02.005]
  - 23 **Leite SA**, Monk AM, Upham PA, Bergenstal RM. Low cardiorespiratory fitness in people at risk for type 2 diabetes: early marker for insulin resistance. *Diabetol Metab Syndr* 2009; **1**: 8 [PMID: 19825145 DOI: 10.1186/1758-5996-1-8]
  - 24 **del-Ama AJ**, Gil-Agudo A, Pons JL, Moreno JC. Hybrid FES-robot cooperative control of ambulatory gait rehabilitation exoskeleton. *J Neuroeng Rehabil* 2014; **11**: 27 [PMID: 24594302 DOI: 10.1186/1743-0003-11-27]
  - 25 **del-Ama AJ**, Koutsou AD, Moreno JC, de-los-Reyes A, Gil-Agudo A, Pons JL. Review of hybrid exoskeletons to restore gait following spinal cord injury. *J Rehabil Res Dev* 2012; **49**: 497-514 [PMID: 22773254 DOI: 10.1682/JRRD.2011.03.0043]
  - 26 **Harvey LA**, Herbert RD. Muscle stretching for treatment and prevention of contracture in people with spinal cord injury. *Spinal Cord* 2002; **40**: 1-9 [PMID: 11821963 DOI: 10.1038/sj.sc.3101241]
  - 27 **Cirnigliaro CM**, Myslinski MJ, La Fontaine MF, Kirshblum SC, Forrest GF, Bauman WA. Bone loss at the distal femur and proximal tibia in persons with spinal cord injury: imaging approaches, risk of fracture, and potential treatment options. *Osteoporos Int* 2017; **28**: 747-765 [PMID: 27921146 DOI: 10.1007/s00198-016-3798-x]
  - 28 **Garland DE**, Adkins RH, Kushwaha V, Stewart C. Risk factors for osteoporosis at the knee in the spinal cord injury population. *J Spinal Cord Med* 2004; **27**: 202-206 [PMID: 15478520 DOI: 10.1080/10790268.2004.11753748]
  - 29 **Garland DE**, Adkins RH, Stewart CA. Five-year longitudinal bone evaluations in individuals with chronic complete spinal cord injury. *J Spinal Cord Med* 2008; **31**: 543-550 [PMID: 19086712 DOI: 10.1080/10790268.2008.11753650]
  - 30 **Johnston TE**, Marino RJ, Oleson CV, Schmidt-Read M, Leib BE, Sendeki J, Singh H, Modlesky CM. Musculoskeletal Effects of 2 Functional Electrical Stimulation Cycling Paradigms Conducted at Different Cadences for People With Spinal Cord Injury: A Pilot Study. *Arch Phys Med Rehabil* 2016; **97**: 1413-1422 [PMID: 26705884]

- DOI: 10.1016/j.apmr.2015.11.014]
- 31 **Saladin LK**, Krause JS. Pressure ulcer prevalence and barriers to treatment after spinal cord injury: comparisons of four groups based on race-ethnicity. *NeuroRehabilitation* 2009; **24**: 57-66 [PMID: 19208958 DOI: 10.3233/NRE-2009-0454]
  - 32 **Groah SL**, Schladen M, Pineda CG, Hsieh CH. Prevention of Pressure Ulcers Among People With Spinal Cord Injury: A Systematic Review. *PM R* 2015; **7**: 613-636 [PMID: 25529614 DOI: 10.1016/j.pmrj.2014.11.014]
  - 33 **Chaudhary U**, Birbaumer N, Ramos-Murguialday A. Brain-computer interfaces for communication and rehabilitation. *Nat Rev Neurol* 2016; **12**: 513-525 [PMID: 27539560 DOI: 10.1038/nrneurol.2016.113]
  - 34 **Piazza S**, Torricelli D, Brunetti F, del-Ama AJ, Gil-Agudo A, Pons JL. A novel FES control paradigm based on muscle synergies for postural rehabilitation therapy with hybrid exoskeletons. *Conf Proc IEEE Eng Med Biol Soc* 2012; **2012**: 1868-1871 [PMID: 23366277 DOI: 10.1109/EMBC.2012.6346316]
  - 35 **Lerner ZF**, Damiano DL, Bulea TC. A lower-extremity exoskeleton improves knee extension in children with crouch gait from cerebral palsy. *Sci Transl Med* 2017; **9**: pii: eaam9145 [PMID: 28835518 DOI: 10.1126/scitranslmed.aam9145]
  - 36 **Lerner ZF**, Damiano DL, Bulea TC. The Effects of Exoskeleton Assisted Knee Extension on Lower-Extremity Gait Kinematics, Kinetics, and Muscle Activity in Children with Cerebral Palsy. *Sci Rep* 2017; **7**: 13512 [PMID: 29044202 DOI: 10.1038/s41598-017-13554-2]

**P- Reviewer:** Elgafy H, Emara KM **S- Editor:** Ji FF  
**L- Editor:** A **E- Editor:** Song H



## Basic Study

**Vascular endothelial growth factor for the treatment of femoral head osteonecrosis: An experimental study in canines**

Zoe H Dailiana, Nikolaos Stefanou, Lubna Khaldi, Georgios Dimakopoulos, James R Bowers, Cristian Fink, James R Urbaniak

Zoe H Dailiana, Nikolaos Stefanou, Department of Orthopaedic Surgery, Faculty of Medicine, University of Thessalia, Larissa 41500, Greece

Zoe H Dailiana, James R Bowers, Cristian Fink, James R Urbaniak, Department of Orthopaedic Surgery, Duke University Medical Center, Durham, NC 27710, United States

Lubna Khaldi, Department of Pathology, "Saint Savvas" Anti-Cancer Hospital, Athens 11522, Greece

Georgios Dimakopoulos, Medical Statistics, Epirus Science and Technology Park Campus of the University of Ioannina, Ioannina 45500, Greece

James R Bowers, Emerge Ortho, Independence Park, Durham, NC 27704, United States

Cristian Fink, Gelenkpunkt, Sports and Joint Surgery, Innsbruck 6020, Austria

Cristian Fink, Research Unit of Orthopedic Sports Medicine and Injury Prevention, Institute for Sports Medicine, Alpine Medicine and Health Tourism (ISAG), UMIT, Tirol 6060, Austria

ORCID number: Zoe H Dailiana (0000-0003-3890-0832); Nikolaos Stefanou (0000-0002-6784-6022); Lubna Khaldi (0000-0002-4189-5029); Georgios Dimakopoulos (0000-0002-2351-7411); James R Bowers (0000-0003-1627-739X); Cristian Fink (0000-0002-8446-2434); James R Urbaniak (0000-0001-9908-5849).

**Author contributions:** Dailiana ZH participated in the inception and design of the study, the acquisition and the interpretation of the data, and wrote the manuscript; Stefanou N critically reviewed the findings and wrote the manuscript; Khaldi L performed the qualitative histological estimation, quantitative bone histomorphometry and the photography of sections, wrote the histological/histomorphometrical materials and methods and the histological figure legends; Dimakopoulos G performed the statistical analysis; Bowers JR and Fink C participated in the acquisition and interpretation of the data and helped draft the

manuscript; Urbaniak JR participated in the inception and design of the study, critically reviewed the findings, and revised the manuscript.

Supported by Piedmont Orthopaedic Foundation, United States.

**Institutional review board statement:** The experimental study was approved from the Institutional Animal Care and Use Committee of Duke University.

**Conflict-of-interest statement:** We have no financial relationships to disclose.

**ARRIVE guidelines statement:** The authors have read the ARRIVE guidelines, and the manuscript was prepared and revised according to the ARRIVE guidelines.

**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:** Zoe H Dailiana, MD, PhD, Professor, Surgeon, Department of Orthopaedic Surgery, Faculty of Medicine, University of Thessalia, 3 Panepistimiou St., Larissa 41500, Greece. [dailiana@med.uth.gr](mailto:dailiana@med.uth.gr)  
**Telephone:** +30-24-13502722  
**Fax:** +30-24-13501011

**Received:** March 29, 2018

**Peer-review started:** March 29, 2018

**First decision:** April 29, 2018

**Revised:** June 20, 2018

**Accepted:** June 26, 2018

**Article in press:** June 27, 2018

Published online: September 18, 2018

## Abstract

### AIM

To evaluate the treatment of osteonecrosis of the femoral head (ONFH) with the use of vascular endothelial growth factor (VEGF).

### METHODS

In 30 mature beagles (6 groups of 5 beagles) ONFH was induced cryosurgically and one of the following solutions was administered locally in the femoral head (FH) in each group: Single injection of 500  $\mu$ g VEGF (t-VEGF $\mu$  group); single injection of 500 ng VEGF (t-VEGFn group); continuous delivery of 500  $\mu$ g VEGF through osmotic micropump (t-VEGFpump- $\mu$  group); continuous delivery of 500 ng VEGF through osmotic micropump (t-VEGFpump-n group); single injection of 0.9% sodium chloride (t-NS group), while one group that served as control group did not receive any local solution (No-t group). FHs were retrieved 12 wk postoperatively, underwent decalcification and hematoxylin/eosin and toluidine blue staining. In two canines per group, one half of FH was processed without decalcification and stained with modified Masson Trichrome. Histological sections were observed by light microscopy and measured with a semi-automatized bone histomorphometry system and Bone Volume/Total Volume (BV/TV), Marrow Volume/Total Volume (MaV/TV), and Trabecular Thickness (TbTh) were assessed. Standard and robust tests (Welch, Brown Forsythe) of analysis of variance along with multiple comparisons, were carried out among the categories.

### RESULTS

The untreated (No-t) group had signs of osteonecrosis, whereas the VEGF groups revealed reversal of the osteonecrosis. Statistical analysis of the decalcified specimens revealed a significantly better BV/TV ratio and a higher TbTh between the VEGF treatment groups (except the t-VEGFn group) and the No-t group or the control t-NS group. Single dose 500  $\mu$ g VEGF group had significantly better BV/TV ratio and higher TbTh when compared to the No-t group ( $50.45 \pm 6.18$  vs  $29.50 \pm 12.27$ ,  $P = 0.002$  and  $151.44 \pm 19.07$  vs  $107.77 \pm 35.15$ ,  $P = 0.161$  respectively) and the control t-NS group ( $50.45 \pm 6.18$  vs  $30.9 \pm 6.67$ ,  $P = 0.004$  and  $151.44 \pm 19.07$  vs  $107.14 \pm 35.71$ ,  $P = 0.151$  respectively). Similar differences were found for the prolonged VEGF delivery/pump groups of 500  $\mu$ g and 500 ng. Analysis of the totality of specimens (decalcified/non-decalcified) enhanced the aforementioned differences and additionally revealed significant differences in the comparison of the TbTh.

### CONCLUSION

In an experimental model of ONFH in canines it was found that local treatment with VEGF leads to bone tissue remodeling and new bone formation.

**Key words:** Osteonecrosis; Vascular endothelial growth factor; Avascular necrosis; Femoral head; Osteogenesis; Animal model

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Osteonecrosis of the femoral head (ONFH) is a painful disorder which usually results in hip joint destruction. Although the pathogenic process is poorly understood, ON is the final condition that completes an already precarious microcirculation of the FH by traumatic and non-traumatic causes. Since vascular endothelial growth factor (VEGF) regulates numerous cellular events associated with angiogenesis and osteogenesis, we evaluated, in an experimental model of ONFH in canines if the local treatment with VEGF leads to bone tissue remodeling and new bone formation at the necrotic site, and subsequently to reversal of ON.

Dailiana ZH, Stefanou N, Khaldi L, Dimakopoulos G, Bowers JR, Fink C, Urbaniak JR. Vascular endothelial growth factor for the treatment of femoral head osteonecrosis: An experimental study in canines. *World J Orthop* 2018; 9(9): 120-129 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/120.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.120>

## INTRODUCTION

Osteonecrosis (ON), also known as avascular necrosis (AVN), is defined as a pathologic process that results from a crucial disruption of blood supply to the bone and elevated intraosseous pressure. Ischemic injury subsequently leads to the degradation of the organic elements of the bone and the marrow and usually results in a collapse of subchondral bone in the femoral head (FH)<sup>[1-3]</sup>. Also, numerous studies have emphasized the association of multiple risk factors, including alcohol consumption, glucocorticoids, trauma, autoimmune diseases, thrombophilia, genetic and metabolic components with secondary ON<sup>[4,5]</sup>. A process of repair is initiated at the necrotic - adjacent intact trabeculae interface by fibrovascular tissue invasion and osteoclasts activation followed by a temporary osteoblastic activity, but unless the lesion is small, this repair procedure is usually ineffective. The structural collapse of the osteonecrotic segment indicates the progressive course of the disease, leads to osteoarthritis of the hip joint in young adults and up to now total hip replacement is predestinate in the long term<sup>[6]</sup>.

Early diagnosis and management aims to suspend the process of joint destruction through enhancement of bone repair and bone renewal. In the early stages of ON there are surgical alternatives to restrain the progressive destruction of the subchondral bone such as core decompression, osteotomy, non-vascularized or vascularized bone grafting, which might be enhanced

with the use of growth and differentiation factors<sup>[6-12]</sup>. Recently, scientists introduced the use of cell-based strategies to enhance osseous regeneration by the application of multipotent mesenchymal stem cells (MSCs), endothelial progenitor cells (EPCs), and osteochondral auto- and allografts in a variety of *in vivo* and *ex vivo* processing<sup>[10-11,13]</sup>. Furthermore, promising osteogenic growth factors, investigated for their bone healing potential, such as bone morphogenetic proteins (BMPs), transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1), hepatocyte growth factor (HGF) and vascular endothelial growth factor (VEGF)<sup>[10,14,15]</sup>, received attention the past decades.

As bone is a highly vascularized tissue, angiogenic cytokines are essential components during the healing process of the necrotic FH. Among them, VEGF has shown its vital role, in a paracrine and autocrine manner, as a specific endothelial cell mitogen and a promoter of angiogenesis<sup>[16,17]</sup>. It is the major endothelial cell survival factor that is required for effective coupling of angiogenesis and osteogenesis in the bone micro-environment. Reconstructing local microcirculation and increasing blood vessel density are essential parameters for effective bone regeneration, the major objective of bone tissue engineering<sup>[18,19]</sup>. Furthermore, it has been suggested that the inhibition of the VEGF downregulates the extracellular matrix remodeling and bone formation in animal models<sup>[20]</sup>. Thus, it is not surprising that a recent meta-analysis clarified an association between VEGF polymorphisms and the risk of the FH necrosis<sup>[21]</sup>.

It seems that several molecular pathways regulate the balance between osteoclasts and osteoblasts and determine the rate of bone remodeling. Thus, considerable effort, using *in vitro* and *in vivo* models including animal models, has been directed towards understanding the effect of growth factors and transcription factors on bone resorption and formation. Through the last decades it was well established that VEGF is a crucial part of the wide network of the molecules regulating osteoinduction on the femoral head like BMPs, leptin, hypoxia - inducible factor (HIF) and their target genes<sup>[22-25]</sup>. Under these considerations, an experimental model of cryosurgically-induced ONFH in canines was used to assess the power of our hypothesis that VEGF could be a crucial therapeutic factor for bone tissue remodeling and reversal of osseous degradation during the treatment of ON.

## MATERIALS AND METHODS

After approval from the Institutional Animal Care and Use Committee, cryosurgically-induced ON of the right FH was established in 30 mature beagles (6 groups with 5 specimens)<sup>[26]</sup>. The canines were sedated with Acepromazine and anesthetized with *iv* injection of Thiopental. Anesthesia was maintained with endotracheal intubation and inhalation of isoflurane, while a Fentanyl patch provided analgesia during the procedure and

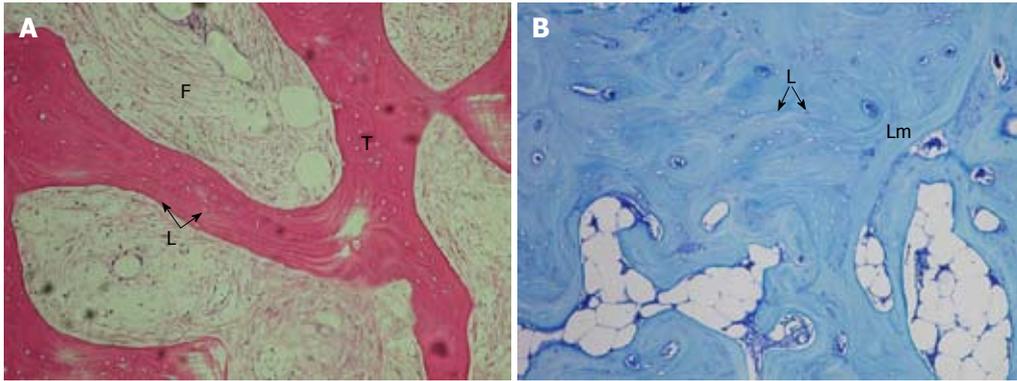
postoperatively. Under absolute aseptic conditions a cryoprobe (CMS Accuprobe 620, Cryomedical Sciences Inc, Rockville, MD) was inserted in the FH through a drill hole extending from the lateral subtrochanteric region to the subchondral bone of the FH. A freezing lesion was created by a freeze (-180 °C) - thaw cycle<sup>[26]</sup>. Subsequently, the necrotic area of the FH was either left untreated or treated with local delivery of VEGF (rhVEGF, Genentech Inc, South San Francisco, CA) or 0.9% sodium chloride (normal saline, NS). NS was injected in a single dose of 1 mL, while VEGF was either injected in a single dose of 500  $\mu$ g (in 1 mL) or 500 ng (in 1 mL) or administered continuously in the necrotic area with the use of an osmotic micropump (ALZET osmotic pumps, ALZA Corporation, Palo Alto, CA), in a dose of 500  $\mu$ g or 500 ng, delivering 5  $\mu$ L/h over a period of 14 d.

The beagles were assigned to 6 groups of 5 canines each: Untreated ONFH (No-t group), ONFH treated with NS (t-NS group), ONFH treated with a single injection of 500  $\mu$ g VEGF (t-VEGF $_{\mu}$  group), ONFH treated with a single injection of 500 ng VEGF (t-VEGF $_n$  group), ONFH treated with 500  $\mu$ g VEGF delivered through a pump (t-VEGF $_{\mu}$ pump- $\mu$  group), ONFH treated with 500 ng VEGF delivered through a pump (t-VEGF $_{\mu}$ pump-n group). The procedure lasted less than one hour and was tolerated very well by the animals which were weight - bearing the first postoperative hours.

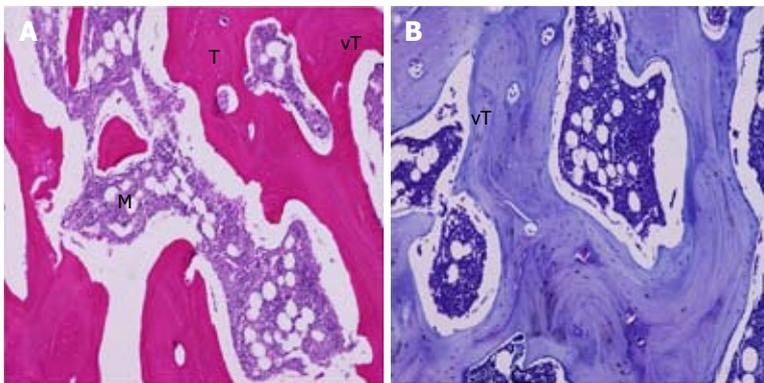
The canines were euthanized at 12 wk. All FHs were retrieved and fixed in 10% neutral buffer formalin for 24 h, cut in half in the frontal level using low-speed diamond sawing machine (IsoMet-Buehler). One half underwent decalcification with neutral EDTA solution pH 7, dehydrated and embedded in paraffin. Sections (5  $\mu$ m thick) were stained with hematoxylin and eosin (H and E) (Figures 1A, 2A and 3A), as well as toluidine blue (TB) (Figures 1B, 2B and 3B). In two canines per group (with the exception of the t-NS group) the other half of the retrieved FH was processed without decalcification, dehydrated, embedded in methylmethacrylate, sectioned with Polycut Model microtome (Leica, Heidelberg, Germany), and stained with modified Masson Trichrome (MT). Histological sections were observed by light microscopy and measured with a semi-automatized bone histomorphometry system using OsteoMeasure software (Interactive measure system for bone histomorphometry, Osteometrics, Atlanta, GA) and the following values were assessed: Bone Volume/Total Volume (BV/TV), Marrow Volume/Total Volume (MaV/TV) and Trabecular Thickness (TbTh), at the subchondral area (above the tip of the tunnel created for the insertion of the cryoprobe)<sup>[27]</sup>. The 4 groups treated with VEGF (t-VEGF $_{\mu}$ , t-VEGF $_n$ , t-VEGF $_{\mu}$ pump- $\mu$ , t-VEGF $_{\mu}$ pump-n) were compared with each other, with the group treated with normal saline (t-NS) and with the untreated group (No-t).

### Statistical analysis

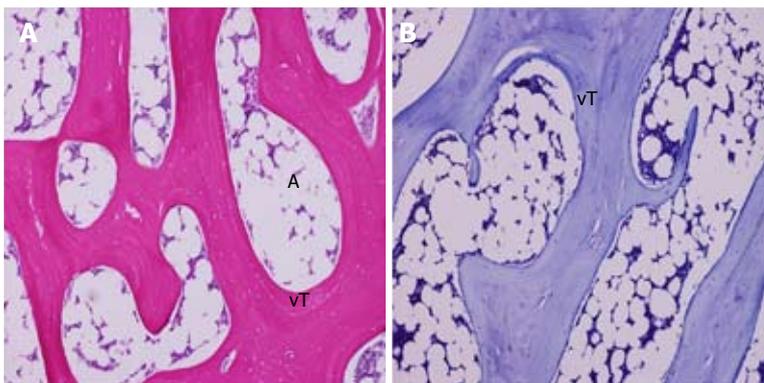
Means and standard deviations were used to describe the values of BV/TV, MaV/TV and TbTh across the categories studied. Standard, as well as robust tests



**Figure 1** Cryosurgically-induced osteonecrosis of the femoral head (No-t group). The specimen was retrieved 12 wk postoperatively. A: Cancellous lamellar bone (T) with empty bone lacunae (L) marked with arrows, and fibrotic/loose connective tissue marrow space (F), indicating osteonecrosis (Obj.  $\times 10$ , H and E); B: Lamellar compact bone (Lm) of cortical type, in between spaces filled with adipose tissue (A). The absence of nuclei in osteocyte's lacunae (L) (marked with arrows) indicates that the bone is necrotic (Obj.  $\times 10$ , TB).



**Figure 2** Osteonecrosis of the femoral head treated with a single injection of 500  $\mu\text{g}$  vascular endothelial growth factor (t-VEGF $_{\mu}$  group); specimen retrieved 12 wk postoperatively. A well-formed cancellous bone network with thickened lamellar trabeculae is visible, while the in between spaces are filled with normal marrow cells (M). A: Newly formed (vT) were noticed on the surface of the trabeculae (T) (Obj.  $\times 10$ , H and E). B: Almost all trabeculae's (T) surface is covered by newly (vT) formed bone (Obj.  $\times 10$ , TB).



**Figure 3** Osteonecrosis of the femoral head treated with prolonged delivery of 500  $\mu\text{g}$  of vascular endothelial growth factor through a pump (t-VEGF $_{\text{pump-}\mu}$  group). At 12 wk postoperatively, a well-formed trabecular network is visible, with slightly thickened lamellar trabeculae, and normal marrow cells and adipose tissue (A) in between. A: Few trabeculae are covered by newly formed bone (vT), the presence of nuclei in lacunae is noticed (Obj.  $\times 10$ , H and E); B: New bone (vT) formation is observed on the surface of some trabeculae (Obj.  $\times 10$ , TB).

(Welch, Brown Forsythe), of analysis of variance along with multiple comparisons under the Tukey's HSD criterion, were carried out to detect statistically significant differences among the categories. Statistical significance was set at 0.05 and the SPSS v21.0 was

used for the analysis of the data.

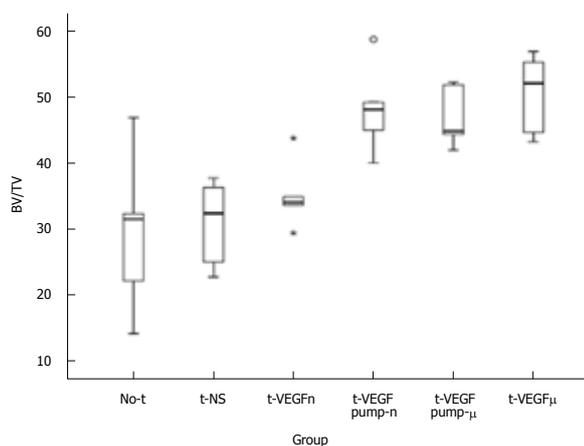
## RESULTS

The untreated group had signs of osteonecrosis (Figure

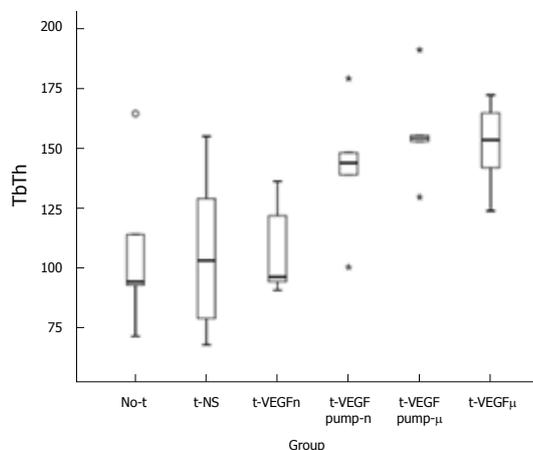
**Table 1 Bone volume/total volume and trabecular thickness mean values across the different groups (decalcified specimens)**

	N	mean	SD	P-value vs No-t	P-value vs t-NS	P-value vs t-VEGF-n
<b>BV/TV</b>						
No-t	5	29497	12265	-	NS	NS
t-NS	5	30902	6672	NS	-	NS
t-VEGF <sub>n</sub>	5	35220	5256	NS	NS	-
t-VEGF <sub>pump-n</sub>	5	48250	6869	0.006	0.013	NS
t-VEGF <sub>pump-μ</sub>	5	47077	4677	0.011	0.023	NS
t-VEGF <sub>μ</sub>	5	50450	6181	0.002	0.004	0.036
Total	30	40233	11039			
<b>TbTh</b>						
No-t	5	107776	35146	-	NS	NS
t-NS	5	107149	35711	NS	-	NS
t-VEGF <sub>n</sub>	5	108195	19986	NS	NS	-
t-VEGF <sub>pump-n</sub>	5	142307	28107	0.380	0.361	NS
t-VEGF <sub>pump-μ</sub>	5	156875	21965	0.088	0.082	NS
t-VEGF <sub>μ</sub>	5	151445	19065	0.161	0.151	0.168
Total	30	128958	33361			

Statistically significant differences for BV/TV are provided as estimated after the Tukey’s HSD criterion while non-significant differences and denoted as “NS” or not shown. The same P-values are reported for TbTh for comparative reasons. BV/TV: Bone volume/total volume; TbTh: Trabecular thickness; VEGF: Vascular endothelial growth factor; NS: Not significant.



**Figure 4 Comparative boxplot of the bone volume/total volume values across the different groups for the decalcified specimens.** BV/TV: Bone volume/total volume; VEGF: Vascular endothelial growth factor.



**Figure 5 Comparative boxplot of the trabecular thickness values across the different groups for the decalcified specimens.** Higher box and whiskers stand for higher TbTh values. TbTh: Trabecular thickness; VEGF: Vascular endothelial growth factor.

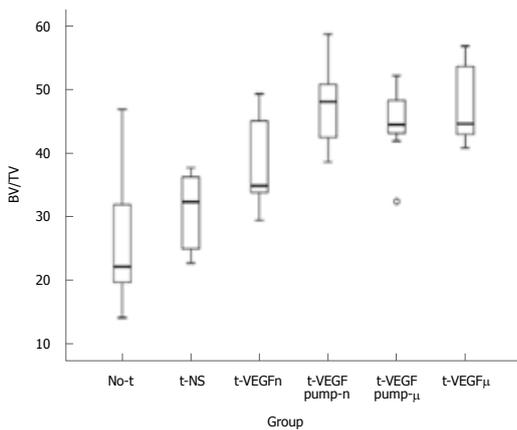
1A and B), whereas the treatment groups revealed reversal of the osteonecrosis (Figures 2A and B, 3A and B) except the group treated with NS, that served as control<sup>[26]</sup>. Statistical analysis was performed in the decalcified specimens (5 samples per group). An additional analysis was performed in the totality of specimens (5 decalcified and 2 non-decalcified; 7 samples per group except of the t-NS group where only 5 decalcified were included). Analysis of the decalcified specimens revealed a significant difference in the BV/TV and MV/TV ratio (BV/TV and MV/TV ratios are complementary between the VEGF treatment groups (apart of the t-VEGF<sub>n</sub> group) and the untreated (No-t) group or the t-NS control group (Table 1). A non-significant difference of the trabecular thickness (TbTh) was observed between the VEGF (apart of the t-VEGF<sub>n</sub>) treatment groups and the untreated (No-t) group or the t-NS control group (Table 1).

Group t-VEGF<sub>μ</sub> had significantly better BV/TV ratio and higher TbTh when compared to the untreated group (No-t) ( $P = 0.002$  and  $P = 0.161$  respectively) and the control t-NS group ( $P = 0.004$  and  $P = 0.151$  respectively) (Table 1, Figure 2A and B). Analogous differences were found for the groups t-VEGF<sub>pump-μ</sub> ( $P = 0.011$  and  $P = 0.088$  respectively for comparison with the No-t group;  $P = 0.023$  and  $P = 0.082$  respectively for comparison with the t-NS group) (Figure 3A and B) and t-VEGF<sub>pump-n</sub> ( $P = 0.006$  and  $P = 0.380$  respectively for comparison with the No-t group;  $P = 0.013$  and  $P = 0.361$  respectively for comparison with the t-NS group). The only group with different behaviour was the t-VEGF<sub>n</sub> group with similar responses to the No-t group for the BV/TV ratio and the TbTh ( $P = 0.823$  and  $P = 1$  respectively) and the control t-NS group ( $P = 0.937$  and  $P = 1$  respectively) (Table 1, Figures 4 and 5). When the different VEGF treatment groups were compared to each other, there was a hierarchic response concerning the BV/TV ratio as following:

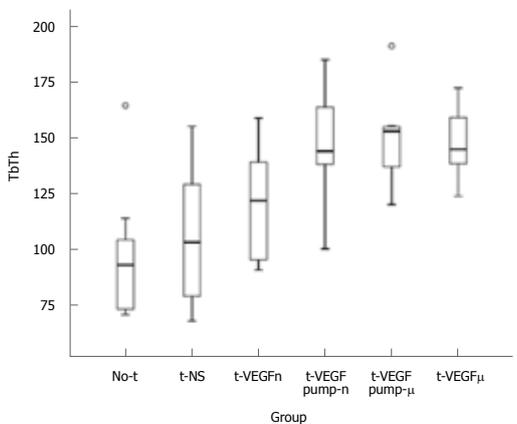
**Table 2** Bone volume/total volume and trabecular thickness mean values across the different groups on the totality of specimens (decalcified and non-decalcified)

	<i>N</i>	mean	SD	<i>P</i> -value vs No-t	<i>P</i> -value vs t-NS	<i>P</i> -value vs t-VEGF-n
<b>BV/TV</b>						
No-t	7	26739	11135	-	NS	NS
t-NS	5	30902	6672	NS	-	NS
t-VEGF <sub>n</sub>	7	38853	7591	NS	NS	-
t-VEGF <sub>pump-n</sub>	7	47485	7009	< 0.001	0.011	NS
t-VEGF <sub>pump-μ</sub>	7	44634	6638	0.002	0.053	NS
t-VEGF <sub>μ</sub>	7	48005	6573	< 0.001	0.008	0.27
Total	40	39863	11013			
<b>TbTh</b>						
No-t	7	97891	33316	-	NS	NS
t-NS	5	107149	35711	NS	-	NS
t-VEGF <sub>n</sub>	7	120315	26799	NS	NS	-
t-VEGF <sub>pump-n</sub>	7	147738	28295	0.020	0.145	NS
t-VEGF <sub>pump-μ</sub>	7	149884	22642	0.014	0.111	NS
t-VEGF <sub>μ</sub>	7	148194	16770	0.018	0.137	0.42
Total	40	129597	33360			

Statistically significant differences are provided as estimated after the Tukey’s HSD criterion while non-significant differences and denoted as NS or not shown. The same *P*-values are reported for TbTh for comparative reasons. BV/TV: Bone volume/total volume; TbTh: Trabecular thickness; VEGF: Vascular endothelial growth factor; NS: Not significant.



**Figure 6** Comparative boxplot of the bone volume/total volume values across the different groups for the decalcified and non-decalcified specimens. BV/TV: Bone volume/total volume; VEGF: Vascular endothelial growth factor.



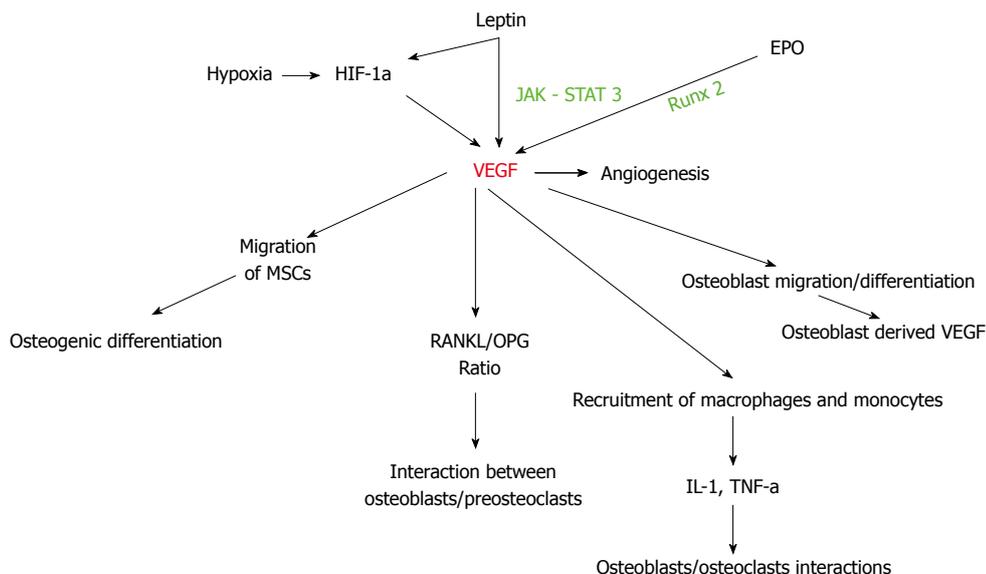
**Figure 7** Comparative boxplot of the trabecular thickness values across the different groups for the decalcified and non-decalcified specimens. Higher box and whiskers stand for higher TbTh values. TbTh: Trabecular thickness; VEGF: Vascular endothelial growth factor.

t-VEGF<sub>μ</sub> > t-VEGF<sub>pump-n</sub> > t-VEGF<sub>pump-μ</sub> > t-VEGF<sub>n</sub>, with a significant difference between the t-VEGF<sub>μ</sub> and t-VEGF<sub>n</sub> groups (*P* = 0.036) (Table 1). Analysis of the totality of specimens enhanced the aforementioned differences and also revealed significant differences also in the comparison of the TbTh (Table 2).

Group t-VEGF<sub>μ</sub> had significantly higher BV/TV ratio and TbTh when compared to the untreated group (No-t) (*P* = 0.000 and *P* = 0.018 respectively). When compared to the control t-NS group the differences were higher or significantly higher (*P* = 0.008 and *P* = 0.137 respectively for the BV/TV and TbTh) (Figure 2A and B). Analogous differences were found for the groups t-VEGF<sub>pump-μ</sub> (*P* = 0.02 and *P* = 0.014 respectively for comparison with the No-t group; *P* = 0.053 and *P* = 0.111 respectively for comparison with the t-NS group) (Figure 3A and B) and t-VEGF<sub>pump-n</sub> (*P* = 0.000 and *P* = 0.020 respectively for comparison with the No-t group; *P* = 0.011 and *P* = 0.145 respectively for comparison with the t-NS group). The t-VEGF<sub>n</sub> group had with similar responses to the No-t group for the BV/TV ratio and the TbTh (*P* = 0.067 and *P* = 0.649 respectively) and the control t-NS group (*P* = 0.520 and *P* = 0.962 respectively) (Table 2, Figures 6 and 7). The hierarchic responses were the same with the decalcified analysis (Table 2).

## DISCUSSION

Osteonecrosis of the FH is a multifactorial disease affecting mostly young individuals (average age 35-50), leading to a subchondral bone infarct and to FH collapse and finally to the destruction of the hip joint. Among all controversial pathogenic mechanisms of ON, ischemic injury, which results from interruption of the blood supply and lack of oxygen, appears to be the most convincing. Decreased blood flow is followed by death of



**Figure 8** Diagram summarizing potential interactions of vascular endothelial growth factor related to bone tissue healing in femoral head osteonecrosis. VEGF: Vascular endothelial growth factor; HIF: Hypoxia-inducible factor; EPO: Erythropoietin; TNF: Tumor necrosis factor; IL: Interleukin.

bone and marrow elements. A process of repair is then initiated by fibrovascular tissue invasion and osteoclasts activation, followed by a temporary osteoblastic activity, but unless the lesion is small, this repair process is usually ineffective leading to eventual collapse of the architectural bony structure of the FH and loss of hip joint function<sup>[1,2,4]</sup>.

Core decompression is considered the gold standard technique for the treatment of pre-collapse, early stage ON (ARCO I - II) of the FH and reveals superior clinical outcome in comparison with non-operative treatment alternatives<sup>[6,10]</sup>. Other surgical options may include rotational osteotomy, non-vascularized and vascularized bone grafting, which might be enhanced with the use of growth and differentiation factors and anterograde osteochondral reconstruction in advanced, post-collapse, stages of ON (ARCO III -IV)<sup>[6-11,28]</sup>. As the treatment of osteochondral defects in advanced stages of ON remains an unresolved issue in orthopedic surgery most young patients usually resulting in the terminal option of the total hip arthroplasty<sup>[6,12]</sup>.

In order to overcome the disadvantages of traditional therapies, scientists promote bone tissue engineering techniques for achieving effective bone regeneration and successful osteoinduction. It has been well established that the growth, development and maintenance of bone are highly regulated processes, which at the cellular level involve the coordinated regulation of osteoblasts and osteoclasts. Several molecular pathways regulate the balance between osteoclasts and osteoblasts and determine the role of bone remodeling. Osteoclastic activity appears to be modulated by cytokines released by osteoblasts. Numerous osteogenic growth factors such as BMPs, TGF-β1, erythropoietin (EPO), platelet-derived growth factor (PDGF) and granulocyte colony-

stimulating factor (G-CSF) have been proposed as target molecules for enhancing the osteoinduction<sup>[10,11,29,30]</sup>.

Blood supply is undoubtedly the absolute goal for any tissue engineering manipulation of the musculoskeletal system and osteonecrotic bone<sup>[22,31]</sup>. It is well understood that the reconstruction of the local microcirculation is prerequisite for effective bone regeneration<sup>[18]</sup>. Since angiogenesis and osteogenesis are highly coupled and VEGF is one of the most important growth factors for the regulation of vascular development we can easily recognize it as a pivotal regulator of bone repair<sup>[32]</sup>. VEGF as a proinflammatory, angiogenic and osteogenic cytokine regulates osteoblastic activity by stimulating crosstalk between endothelial, osteoblastic and hematopoietic cells in a paracrine manner and it directly affects osteoblast functions *via* autocrine mechanisms<sup>[18,33]</sup>. Moreover, the multipotent role of the VEGF in the bone environment includes the regulation of maturation and differentiation of osteoclasts, the recruitment of MSCs and osteoprogenitor cells, the promotion of the osteogenic differentiation of MSCs and finally cartilage formation and resorption<sup>[22,34]</sup>. All these studies demonstrate that the bone regeneration process in the osteonecrotic microenvironment could be affected by manipulation of VEGF levels (Figure 8).

In the present study the influence of the commonly accepted as an angiogenic factor-VEGF on osteogenesis was investigated in an experimental model of ONFH, in mature beagles. Our results indicate that the experimental model of osteonecrosis is reliable and leads to uniform and reproducible osteonecrosis of the FH in the canines<sup>[26]</sup>. The surgical technique is relatively easy and minimally invasive, leading to decreased duration of the procedure and for that is well tolerated by the animals. Other benefits of this canine animal

model are the low costs of rearing, the nature of the species as a representative of mammals, their body size that allows accurate surgical treatment and radiographic guidance or surveillance and the fact that can be achieved histological patterns which are similar to those of humans.

Moreover, we demonstrated that the use of the VEGF affects in a positive and dose dependent manner the necrotic bone and induces the process of osseous regeneration. Since now it is well established by numerous studies that there are strong indications of a cellular and molecular pattern of angiogenic-osteogenic coupling<sup>[18,19,22]</sup>. The restoration of bone vascularity is an absolute parameter in the process of osteoinduction, which is the target of any therapeutic agent against osteonecrosis in the FH. As VEGF acted in a dose dependent manner we conclude that the optimal amounts of VEGF are critical for the therapeutic outcome and probably depend on the size of the necrotic area. The levels of exogenous VEGF for its adequate activity are probably determined by both the type of cells in which it acts and the production of endogenous VEGF in them.

Taking into account that the analysis of the totality of specimens (decalcified and non-decalcified) magnified the differences between the subgroups we conclude that the healing interaction of the VEGF over the osseous tissue refers not only to the organic but to the inorganic fraction of the bone matrix too. This is important as the bone matrix serves as a reservoir for osteogenic growth factors which are pivotal collaborators of VEGF during bone repair<sup>[10,35]</sup>. It is essential for every therapeutic agent against ONFH to achieve a good quality of bone tissue during osseous regeneration.

Traditional administration of growth factors is limited by their relatively short half-lives and potential side effects<sup>[34]</sup>. VEGF has a short half-life of 6-8 h, which means that controlled and more sustained delivery could be required to ensure its efficient activity<sup>[19]</sup>. Under all these considerations we administered VEGF continuously in the necrotic FH with the use of an osmotic micropump over a period of 14 d but without transcendent outcome in comparison with single dose injection. It seems that a high single, initial dose is superior for the bone defect repair in this animal model and that may reveal that VEGF has a nodal role at early stages of the osteonecrotic bone healing procedure. The optimal delivery model of VEGF needs to be further studied. Utilizing a well-designed delivery system, like specific slow release scaffolds or gene delivery projects may better achieve bone regeneration and improve its therapeutic effect by stabilizing it against rapid degradation<sup>[22,35-37]</sup>.

The results of previous studies supported that the vascular network induced by VEGF alone is immature<sup>[29,38]</sup>. There is obviously a wide network of molecules regulating bone regeneration such as BMPs, leptin, HIF, TGF, IGF and EPO. Even if VEGF is sufficient to improve revascularization, recently scientists introduced the

use of a combination of growth factors and manipulated progenitor cells to enhance bone repair and bone renewal<sup>[15,22-24,35,39,40]</sup>.

In summary, in an experimental model of ONFH in mature beagles it was found that the treatment with VEGF leads to bone tissue remodeling and new bone formation at the osteonecrotic site and subsequently to reversal of ON. This study however, has some limitations; it is an experimental study in canines, and in addition, the induction and treatment of ONFH (with local infusion of VEGF) are almost simultaneous procedures. Although local VEGF administration is known to promote angiogenesis and enhanced new bone formation in ONFH in our study, future studies should further investigate, in a variety of experimental conditions, the role of VEGF as a key molecule and essential player for therapeutic strategies targeting bone reconstruction, so that an even transition to clinical trials may be achieved.

## ARTICLE HIGHLIGHTS

### Research background

Numerous studies have emphasized the association of multiple risk factors, including alcohol consumption, glucocorticoids, trauma, autoimmune diseases, thrombophilia, genetic and metabolic components with secondary osteonecrosis (ON). ON of the femoral head (FH) is a debilitating disease that usually leads to osteoarthritis of the hip joint in young adults and up to now total hip replacement is predestinate in the long term.

### Research motivation

Early diagnosis and management aims to suspend the process of joint destruction through enhancement of bone repair and bone renewal. In the early stages of ONFH there are surgical alternatives to restrain the progressive destruction of the subchondral bone such as core decompression, osteotomy, non-vascularized or vascularized bone grafting. This study extended the prospect of use growth and angiogenic factors for the process of repair at the necrotic trabeculae of the FH.

### Research objectives

The main aim of this research project was to evaluate the treatment of ONFH with the use of vascular endothelial growth factor (VEGF).

### Research methods

An experimental model of cryosurgically-induced ONFH in canines was used to assess the power of our hypothesis that VEGF could be a crucial therapeutic factor for bone tissue remodeling and reversal of osseous degradation during the treatment of ON. VEGF (2 different doses of 500 µg and 500 ng) was either injected in a single dose or administered continuously in the necrotic area with the use of an osmotic micropump, while in a control group 0.9% sodium chloride (NS) was injected in the necrotic area.

### Research results

The untreated group had signs of ONFH, whereas the treatment groups with VEGF revealed reversal of the osteonecrosis, except the group treated with NS, that served as control. These findings demonstrate that the bone regeneration process in the osteonecrotic microenvironment could be affected by manipulation of VEGF levels.

### Research conclusions

We demonstrated that the use of the VEGF affects in a positive and dose dependent manner the necrotic bone and induces the process of osseous regeneration. Since now it is well established by numerous studies that there are strong indications of a cellular and molecular pattern of angiogenic-

osteogenic coupling. The restoration of bone vascularity is an absolute parameter in the process of osteoinduction, which is the target of any therapeutic agent against ONFH.

### Research perspectives

In a reproducible experimental model of ONFH in mature beagles it was found that the treatment with VEGF leads to bone tissue remodeling and new bone formation at the osteonecrotic site and subsequently to reversal of ON. Besides that, the optimal delivery model of VEGF needs to be further studied. Utilizing a well-designed delivery system, like specific slow release scaffolds or gene delivery projects, may potentially lead to better bone regeneration and improve VEGFs therapeutic effect by stabilizing it against rapid degradation. Even if VEGF is sufficient to improve revascularization, recently scientists introduced the use of a combination of growth factors and manipulated progenitor cells to enhance bone repair and bone renewal. Although local VEGF administration is known to enhance new bone formation in ONFH in our study, future studies should further investigate, in a variety of experimental conditions, the role of VEGF as a key molecule and essential player for therapeutic strategies targeting bone reconstruction, so that an even transition to clinical trials may be achieved.

## REFERENCES

- 1 **Guerado E**, Caso E. The physiopathology of avascular necrosis of the femoral head: an update. *Injury* 2016; **47** Suppl 6: S16-S26 [PMID: 28040082 DOI: 10.1016/S0020-1383(16)30835-X]
- 2 **Mont MA**, Hungerford DS. Non-traumatic avascular necrosis of the femoral head. *J Bone Joint Surg Am* 1995; **77**: 459-474 [PMID: 7890797 DOI: 10.2106/00004623-199503000-00018]
- 3 **Zalavras C**, Dailiana Z, Elisaf M, Bairaktari E, Vlachogiannopoulos P, Katsaraki A, Malizos KN. Potential aetiological factors concerning the development of osteonecrosis of the femoral head. *Eur J Clin Invest* 2000; **30**: 215-221 [PMID: 10691998 DOI: 10.1046/j.1365-2362.2000.00621.x]
- 4 **Seamon J**, Keller T, Saleh J, Cui Q. The pathogenesis of non-traumatic osteonecrosis. *Arthritis* 2012; **2012**: 601763 [PMID: 23243507 DOI: 10.1155/2012/601763]
- 5 **Aldridge JM 3rd**, Urbaniak JR. Avascular necrosis of the femoral head: etiology, pathophysiology, classification, and current treatment guidelines. *Am J Orthop (Belle Mead NJ)* 2004; **33**: 327-332 [PMID: 15344574]
- 6 **Lieberman JR**, Berry DJ, Mont MA, Aaron RK, Callaghan JJ, Rajadhyaksha AD, Urbaniak JR. Osteonecrosis of the hip: management in the 21st century. *Instr Course Lect* 2003; **52**: 337-355 [PMID: 12690862]
- 7 **Soucacos PN**, Beris AE, Malizos K, Koropiliadis A, Zalavras H, Dailiana Z. Treatment of avascular necrosis of the femoral head with vascularized fibular transplant. *Clin Orthop Relat Res* 2001; **386**: 120-130 [PMID: 11347825 DOI: 10.1097/00003086-20010500-00016]
- 8 **Urbaniak JR**, Coogan PG, Gunneson EB, Nunley JA. Treatment of osteonecrosis of the femoral head with free vascularized fibular grafting. A long-term follow-up study of one hundred and three hips. *J Bone Joint Surg Am* 1995; **77**: 681-694 [PMID: 7744893 DOI: 10.2106/00004623-199505000-00004]
- 9 **Calori GM**, Mazza E, Colombo M, Mazzola S, Mineo GV, Giannoudis PV. Treatment of AVN using the induction chamber technique and a biological-based approach: indications and clinical results. *Injury* 2014; **45**: 369-373 [PMID: 24119830 DOI: 10.1016/j.injury.2013.09.014]
- 10 **Rackwitz L**, Eden L, Reppenhausen S, Reichert JC, Jakob F, Walles H, Pullig O, Tuan RS, Rudert M, Nöth U. Stem cell- and growth factor-based regenerative therapies for avascular necrosis of the femoral head. *Stem Cell Res Ther* 2012; **3**: 7 [PMID: 22356811 DOI: 10.1186/s12928]
- 11 **Papanagiotou M**, Malizos KN, Vlychou M, Dailiana ZH. Autologous (non-vascularised) fibular grafting with recombinant bone morphogenetic protein-7 for the treatment of femoral head osteonecrosis: preliminary report. *Bone Joint J* 2014; **96-B**: 31-35 [PMID: 24395307 DOI: 10.1302/0301-620X.96B1.32773]
- 12 **McGrory BJ**, York SC, Iorio R, Macaulay W, Pelker RR, Parsley BS, Teeny SM. Current practices of AAHKS members in the treatment of adult osteonecrosis of the femoral head. *J Bone Joint Surg Am* 2007; **89**: 1194-1204 [PMID: 17545421 DOI: 10.2106/JBJS.F.00302]
- 13 **Müller I**, Vaegler M, Holzwarth C, Tzaribatchev N, Pfister SM, Schütt B, Reize P, Greil J, Handgretinger R, Rudert M. Secretion of angiogenic proteins by human multipotent mesenchymal stromal cells and their clinical potential in the treatment of avascular osteonecrosis. *Leukemia* 2008; **22**: 2054-2061 [PMID: 18719618 DOI: 10.1038/leu.2008.217]
- 14 **Samara S**, Dailiana Z, Varitimidis S, Chassanidis C, Koromila T, Malizos KN, Kollia P. Bone morphogenetic proteins (BMPs) expression in the femoral heads of patients with avascular necrosis. *Mol Biol Rep* 2013; **40**: 4465-4472 [PMID: 23649763 DOI: 10.1007/s11033-013-2538-y]
- 15 **Yang C**, Yang S, Du J, Li J, Xu W, Xiong Y. Vascular endothelial growth factor gene transfection to enhance the repair of avascular necrosis of the femoral head of rabbit. *Chin Med J (Engl)* 2003; **116**: 1544-1548 [PMID: 14570620]
- 16 **Hoeben A**, Landuyt B, Highley MS, Wildiers H, Van Oosterom AT, De Bruijn EA. Vascular endothelial growth factor and angiogenesis. *Pharmacol Rev* 2004; **56**: 549-580 [PMID: 15602010 DOI: 10.1124/pr.56.4.3]
- 17 **Ferrara N**. Vascular endothelial growth factor: basic science and clinical progress. *Endocr Rev* 2004; **25**: 581-611 [PMID: 15294883 DOI: 10.1210/er.2003-0027]
- 18 **Saran U**, Gemini Piperni S, Chatterjee S. Role of angiogenesis in bone repair. *Arch Biochem Biophys* 2014; **561**: 109-117 [PMID: 25034215 DOI: 10.1016/j.abb.2014.07.006]
- 19 **Kaigler D**, Wang Z, Horger K, Mooney DJ, Krebsbach PH. VEGF scaffolds enhance angiogenesis and bone regeneration in irradiated osseous defects. *J Bone Miner Res* 2006; **21**: 735-744 [PMID: 16734388 DOI: 10.1359/jbmr.060120]
- 20 **Gerber HP**, Vu TH, Ryan AM, Kowalski J, Werb Z, Ferrara N. VEGF couples hypertrophic cartilage remodeling, ossification and angiogenesis during endochondral bone formation. *Nat Med* 1999; **5**: 623-628 [PMID: 10371499 DOI: 10.1038/9467]
- 21 **Hong GJ**, Lin N, Chen LL, Chen XB, He W. Association between vascular endothelial growth factor gene polymorphisms and the risk of osteonecrosis of the femoral head: Systematic review. *Biomed Rep* 2016; **4**: 92-96 [PMID: 26870342 DOI: 10.3892/br.2015.527]
- 22 **Li B**, Wang H, Qiu G, Su X, Wu Z. Synergistic Effects of Vascular Endothelial Growth Factor on Bone Morphogenetic Proteins Induced Bone Formation In Vivo: Influencing Factors and Future Research Directions. *Biomed Res Int* 2016; **2016**: 2869572 [PMID: 28070506 DOI: 10.1155/2016/2869572]
- 23 **Zhou L**, Jang KY, Moon YJ, Wagle S, Kim KM, Lee KB, Park BH, Kim JR. Leptin ameliorates ischemic necrosis of the femoral head in rats with obesity induced by a high-fat diet. *Sci Rep* 2015; **5**: 9397 [PMID: 25797953 DOI: 10.1038/srep09397]
- 24 **Fan L**, Li J, Yu Z, Dang X, Wang K. The hypoxia-inducible factor pathway, prolyl hydroxylase domain protein inhibitors, and their roles in bone repair and regeneration. *Biomed Res Int* 2014; **2014**: 239356 [PMID: 24895555 DOI: 10.1155/2014/239356]
- 25 **Fan L**, Li J, Yu Z, Dang X, Wang K. Hypoxia-inducible factor prolyl hydroxylase inhibitor prevents steroid-associated osteonecrosis of the femoral head in rabbits by promoting angiogenesis and inhibiting apoptosis. *PLoS One* 2014; **9**: e107774 [PMID: 25244080 DOI: 10.1371/journal.pone.0107774]
- 26 **Dailiana Z**, Fink Ch, Baust J, Seaher AV, Urbaniak JR. A new canine model of osteonecrosis with the use of cryosurgery. *JACS* 2000; **191**: S91-S91 [DOI: 10.1016/S1072-7515(00)00658-X]
- 27 **Revell PA**. Histomorphometry of bone. *J Clin Pathol* 1983; **36**: 1323-1331 [PMID: 6361070 DOI: 10.1136/jcp.36.12.1323]
- 28 **Huffman KM**, Bowers JR, Dailiana Z, Huebner JL, Urbaniak JR, Kraus VB. Synovial fluid metabolites in osteonecrosis. *Rheumatology (Oxford)* 2007; **46**: 523-528 [PMID: 17003168 DOI:

- 10.1093/rheumatology/ke1302]
- 29 **Lieberman JR**, Daluiski A, Einhorn TA. The role of growth factors in the repair of bone. Biology and clinical applications. *J Bone Joint Surg Am* 2002; **84-A**: 1032-1044 [PMID: 12063342 DOI: 10.2106/00004623-200206000-00022]
- 30 **Xu T**, Jin H, Lao Y, Wang P, Zhang S, Ruan H, Mao Q, Zhou L, Xiao L, Tong P, Wu C. Administration of erythropoietin prevents bone loss in osteonecrosis of the femoral head in mice. *Mol Med Rep* 2017; **16**: 8755-8762 [PMID: 29039481 DOI: 10.3892/mmr.2017.7735]
- 31 **Jain RK**, Au P, Tam J, Duda DG, Fukumura D. Engineering vascularized tissue. *Nat Biotechnol* 2005; **23**: 821-823 [PMID: 16003365 DOI: 10.1038/nbt0705-821]
- 32 **Coultas L**, Chawengsaksophak K, Rossant J. Endothelial cells and VEGF in vascular development. *Nature* 2005; **438**: 937-945 [PMID: 16355211 DOI: 10.1038/nature04479]
- 33 **Hu K**, Olsen BR. Osteoblast-derived VEGF regulates osteoblast differentiation and bone formation during bone repair. *J Clin Invest* 2016; **126**: 509-526 [PMID: 26731472 DOI: 10.1172/JCI82585]
- 34 **Aldridge SE**, Lennard TW, Williams JR, Birch MA. Vascular endothelial growth factor receptors in osteoclast differentiation and function. *Biochem Biophys Res Commun* 2005; **335**: 793-798 [PMID: 16105658 DOI: 10.1016/j.bbrc.2005.07.145]
- 35 **Almubarak S**, Nethercott H, Freeberg M, Beaudon C, Jha A, Jackson W, Marcucio R, Miclau T, Healy K, Bahney C. Tissue engineering strategies for promoting vascularized bone regeneration. *Bone* 2016; **83**: 197-209 [PMID: 26608518 DOI: 10.1016/j.bone.2015.11.011]
- 36 **Jung YJ**, Kim KC, Heo JY, Jing K, Lee KE, Hwang JS, Lim K, Jo DY, Ahn JP, Kim JM, Huh KM, Park JI. Induction of Angiogenesis by Matrigel Coating of VEGF-Loaded PEG/PCL-Based Hydrogel Scaffolds for hBMSC Transplantation. *Mol Cells* 2015; **38**: 663-668 [PMID: 26159216 DOI: 10.14348/molcells.2015.0142]
- 37 **Zhang C**, Ma J, Li M, Li XH, Dang XQ, Wang KZ. Repair effect of coexpression of the hVEGF and hBMP genes via an adeno-associated virus vector in a rabbit model of early steroid-induced avascular necrosis of the femoral head. *Transl Res* 2015; **166**: 269-280 [PMID: 25843672 DOI: 10.1016/j.trsl.2015.03.003]
- 38 **Blau HM**, Banfi A. The well-tempered vessel. *Nat Med* 2001; **7**: 532-534 [PMID: 11329048 DOI: 10.1038/87850]
- 39 **Kasten P**, Beverungen M, Lorenz H, Wieland J, Fehr M, Geiger F. Comparison of platelet-rich plasma and VEGF-transfected mesenchymal stem cells on vascularization and bone formation in a critical-size bone defect. *Cells Tissues Organs* 2012; **196**: 523-533 [PMID: 22796828 DOI: 10.1159/000337490]
- 40 **Hernigou P**, Trousselier M, Roubinau F, Bouthors C, Chevallier N, Rouard H, Flouzat-Lachaniette CH. Stem Cell Therapy for the Treatment of Hip Osteonecrosis: A 30-Year Review of Progress. *Clin Orthop Surg* 2016; **8**: 1-8 [PMID: 26929793 DOI: 10.4055/cios.2016.8.1.1]

**P- Reviewer:** Cheung WH, Cui Q, Tarnawski AS **S- Editor:** Ji FF  
**L- Editor:** A **E- Editor:** Song H



## Basic Study

**Assessment of palmar subcutaneous tissue vascularization in patients with Dupuytren's contracture**

Nathalia Shchudlo, Tatyana Varsegova, Tatyana Stupina, Tamara Dolganova, Michael Shchudlo, Nathalia Shihaleva, Vadim Kostin

Nathalia Shchudlo, Tamara Dolganova, Michael Shchudlo, Nathalia Shihaleva, Vadim Kostin, Clinics and Experimental Laboratory for Reconstructive Microsurgery and Hand Surgery, Russian Ilizarov Scientific Center "Restorative Traumatology and Orthopaedics", Kurgan 640014, Russia

Tatyana Varsegova, Tatyana Stupina, Laboratory of Morphology of Federal State Budget Institution, Russian Ilizarov Scientific Center "Restorative Traumatology and Orthopaedics", Kurgan 640014, Russia

ORCID number: Nathalia Shchudlo (0000-0001-9914-8563); Tatyana Varsegova (0000-0001-5430-2045); Tatyana Stupina (0000-0003-3434-0372); Tamara Dolganova (0000-0002-0117-3451); Michael Shchudlo (0000-0003-0661-6685); Nathalia Shihaleva (0000-0003-4889-9783); Vadim Kostin (0000-0002-0655-1407).

**Author contributions:** Shchudlo N, Varsegova T, Stupina T, Dolganova T, Shchudlo M, Shihaleva N and Kostin V substantially contributed to the conception and design of the study, acquisition, analysis, and interpretation of data; all authors drafted the article, made critical revisions related to the intellectual content of the manuscript, and approved the final version of the article to be published.

**Supported by** The RF Ministry of Health within Government-Mandated Program for FSBI Russian Ilizarov Scientific Center "Restorative Traumatology and Orthopaedics" (RISC "RTO") for Scientific Research in 2018-2020 Yr./Yrs. No. AAAA-A18-118011190119-5 from 11/01/2018.

**Institutional review board statement:** The article was reviewed by RISC "RTO" Review Board and statement including: (1) The manuscript is not simultaneously being considered by other journals or already published elsewhere; (2) The manuscript has no redundant publication, plagiarism, or data fabrication or falsification; (3) Ethical clearance for this study was obtained from the RISC "RTO" Institutional ethics committee; and (4) Material contained within the manuscript is original, with all information from other sources appropriately referenced.

**Conflict-of-interest statement:** The authors declare 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:** Nathalia Shchudlo, MD, Academic Research, DM, Head, Clinics and Experimental Laboratory for Reconstructive Microsurgery and Hand Surgery, Russian Ilizarov Scientific Center "Restorative Traumatology and Orthopaedics", M. Ulianova Street 6, Kurgan 640014, Russia. [nshchudlo@mail.ru](mailto:nshchudlo@mail.ru)  
Telephone: +7-89-225631752  
Fax: +7-83-522454060

**Received:** March 28, 2018

**Peer-review started:** March 29, 2018

**First decision:** May 9, 2018

**Revised:** May 14, 2018

**Accepted:** May 31, 2018

**Article in press:** May 31, 2018

**Published online:** September 18, 2018

**Abstract****AIM**

To investigate the structural and functional characteristics of palmar hypodermal tissue vascularization in Dupuytren's contracture patients of different age

groups.

### METHODS

Eighty-seven Dupuytren's contracture patients underwent partial fasciectomy. Twenty-two of them were less than 55 years old (Y-group,  $n = 22$ ); the others were 55 and older (O-group,  $n = 65$ ). In surgically excised representative tissue samples, a histomorphometric analysis of the perforating arteries of the palmar aponeurosis and stereologic analysis of hypodermis vascularity were performed. The method of laser flowmetry estimated the microcirculation of the skin of the palm.

### RESULTS

Frequency of cases with rapid development of contracture (less than 5 years) was 13.6% in the Y-group and 40% in the O-group,  $P < 0.05$ . The external and luminal diameters of perforating arteries in palmar fascia were decreased more severely in Y. The thickness of intima increased three times compared with healthy control, and the intima/media relation also increased, especially in O. Increased numerical and volumetric micro-vessel densities in hypodermis, percentage of large vessels (more than  $12 \mu\text{m}$  in diameter), and percentage of vessels with signs of periadventitial inflammatory infiltration were noted in Y. The percentage of vessels with adventitial fibrosis was greater in O than in Y. Base capillary flow in Y was increased compared to healthy control subjects and to O, and peak capillary flow was increased in comparison with control.

### CONCLUSION

Compared to the O-group, Y-group patients exhibited more severe constrictive remodeling of palmar fascia perforating arteries supplying hypodermis but more expressed compensatory changes of its capillarization.

**Key words:** Dupuytren's contracture; Laser Doppler flowmetry; Hypodermis; Histo-morphometry; Palmar fascia

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** This is a retrospective study comparing the incidence of quick development of Dupuytren's contracture (less than 5 years) and peculiarities of palmar hypodermal tissue vascularization and microcirculation in two age groups of patients undergoing partial fasciectomy. The quantitative characteristics of palmar fascia perforating arteries remodeling, the hypodermal adipose tissue vascularization, and skin microcirculatory flow in patients with Dupuytren's contracture depending on age were represented for the first time. In patients younger than 55 years, the incidence of rapidly progressive contracture was two, nine

times less than that in the older group. Both age groups were characterized with constrictive arterial remodeling, especially the younger group, but quantitative signs of compensatory capillaro- and arteriogenesis were more prominent in the younger group.

Shchudlo N, Varsegova T, Stupina T, Dolganova T, Shchudlo M, Shihaleva N, Kostin V. Assessment of palmar subcutaneous tissue vascularization in patients with Dupuytren's contracture. *World J Orthop* 2018; 9(9): 130-137 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/130.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.130>

### INTRODUCTION

Dupuytren's disease (palmar fascial fibromatosis) relates to fibro-proliferative pathology of unknown cause that affects predominantly palmar and digital fasciae, limits finger extension, and causes a progressive contracture of metacarpophalangeal and interphalangeal joints and persistent hand deformity. The prevalence of the disease in different countries varies significantly and is caused by geographic factors, ethnic peculiarities, age, and gender population composition<sup>[1]</sup>. In most of countries, it affects mainly men over 40 years old. Risk factors for Dupuytren's contracture remain a topic of discussion. The independent role of alcohol, smoking and the aggravating effect of their combination, the role of chronic traumatization during manual labor, and effects of vibration have been proven<sup>[2,3]</sup>. The main mechanisms of pathogeny are expression of genes, controlling fibrosis and tissue remodeling<sup>[4]</sup>, vessel narrowing, tissue hypoxia, and formation of free radicals and active forms of oxygen<sup>[5]</sup>, reactive inflammation<sup>[6]</sup>.

Pathologically changed tissues in Dupuytren's contracture represent fibromatosis nodules and chords with different microscopic structures. Nodules are characterized by increased vascularity and abundant fibroblasts, and among them there are plenty of myofibroblasts with contractile properties; cords contain less cellular elements and are relatively avascular but rich in collagen. Transforming growth factor  $\beta$  is considered the main modulator of myofibroblast trans-differentiation<sup>[7]</sup>. Palmar fascial fibromatosis is a kind of reactive proliferation, but not like tumor processes<sup>[8]</sup>, although it was characterized by infiltrative growth<sup>[9]</sup> in hypodermis, dermis, tendons sheaths, and joints capsules. On the other hand, in the skin and hypodermis of Dupuytren's contracture patients, high expression of stem cells markers was revealed<sup>[10]</sup>. Stem cells are considered an additional source of fibroblasts and myofibroblasts proliferation. Laminin-rich blood vessels also act as the centers of myofibroblasts proliferation<sup>[11]</sup>.

Substantial differences in genes expression were noted in the hypodermis but not in skin of Dupuytren's contracture patients compared to healthy individuals<sup>[12]</sup>.

In type 2 diabetes, the severity of insulin resistance is determined by changes in vascularity of hypodermis<sup>[13,14]</sup>. A characteristic feature of Dupuytren's contracture tissues is plenty of young vessels<sup>[9]</sup>, but the influence of tissue vascularization on the course of the disease is unclear. There are contradictory reports regarding the impact of patient's age on disease onset, progression, and recurrence<sup>[15,16]</sup>. Vascularization of hypodermis in Dupuytren's contracture patients of different age groups has not been studied. The aim of our research is to investigate the structural and functional characteristics of palmar hypodermal tissue vascularization in Dupuytren's contracture patients of different age groups.

## MATERIALS AND METHODS

### *Patient's characteristics*

At the FSBI Russian Ilizarov Scientific Center, 236 patients with Dupuytren's contracture were operated on 2013 through 2018. Age of the patients ranged from 27 to 84 years. All of them gave prior informed consent for surgery. The study protocol was approved by the ethics committee of the institution. At the time of surgery, in most cases, the contracture matched the stages 2-3 according to R. Tubiana<sup>[9]</sup> classification, but four patients had stage 4. The inclusion criteria included histologically confirmed clinical diagnosis of Dupuytren's contracture and detailed anamnesis morbi in the case report. The exclusion criterion was the acute trauma of the hand in anamnesis. For clinical characteristics, the following data were taken into account: age, sex, duration of clinical signs of fibromatosis, bilateral affection and number of fingers with impaired function, and comorbid conditions.

### *Histological analysis*

Tissue samples of pathologically changed palmar aponeurosis with hypodermis from 87 patients were fixed in a mixture of 20 g/L solutions of glutaraldehyde and paraformaldehyde in phosphate buffer (pH 7.4) adding 1 g/L picric acid. Then according to standard protocols, samples were embedded in paraffin. For preparation of histological sections (thickness 5-7  $\mu\text{m}$ ), the Reichert microtome (Vienna, Austria) was used. Sections were stained with hematoxylin-eosin, Masson's trichrome method was used for collagen, and Weigert-van Gieson's was used for elastic fibers selective evaluation. Digital images of the fields of view of the photomicroscope "Opton" (Oberkochen, Germany) were obtained using the "DiaMorph" hardware-software complex (Moscow, Russia). Histomorphometry was performed with the PhotoFiltre and "VT-Master-Morphology" programs (VideoTest, St. Petersburg, Russia). From each tissue sample, 30 visual fields were obtained (magnification 200  $\times$ ). Using the electronic version of the test grid for point-counting method the percentage of adipocytes, numerical and volumetric vessels densities were assessed. Numerical density is the number of blood vessels profiles per unit area of histological section; volumetric density is their



Figure 1 Assessment of skin microcirculation in patient with Dupuytren's contracture using laser Doppler flowmetry and local ischemic test.

volume fraction in a series of histological sections. The percentages of vessels with signs of periadventitial inflammatory infiltration and periadventitial fibrosis were determined. In digital images of transverse sections of perforating palmar aponeurosis arteries (magnification 500  $\times$ ), their outside diameters, lumen diameters, wall thickness, intima thickness, and media thickness were measured and intima/media ratio was counted. Patients with acute hand wounds ( $n = 3$ ) were used as the source of small tissue samples from normal palmar aponeurosis.

### *Laser doppler flowmetry*

Assessment of microcirculation of skin tissues was carried out using laser doppler flowmetry (LDF) with a BLF 21 monitor (Transonic System Inc., Ithaca, NY, United States), calibrated according to manufacturer's recommendations. The apparatus was equipped with a standard fiber separation probe (0.25 mm) and laser wavelength of 780 nm with a measurement depth of 0.5-1.0 mm. The method of LDF examines vessels of the microcirculatory bed, located in the dermis and hypodermis. The probe was placed on the palmar surface of the hand (Figure 1) on areas of pronounced fibromatosis (bases of IV-V fingers) and fastened with a double-sided adhesive membrane. Measurements of LDF were expressed in arbitrary units of perfusion (PU). To study the mechanisms involved in the regulation of tissue blood flow, a local ischemic test including the installation of an occlusive cuff on the forearm was performed. After registration of capillary flow at rest (microcirculatory flow base - MFB) and after 3 min of ischemia (microcirculatory flow peak - MFP), the index of peak microcirculatory blood flow was counted:  $\text{IMFP} = \text{MFP}/\text{MFB} \times 100\%$  - percentage of increase in capillary blood flow after cuff release. Time of hyperemic response - from the moment of cuff release to maximal growth of capillary blood flow, velocity of hyperemic response - velocity of growth of microcirculatory flow from the moment of cuff release to maximal capillary blood flow, time of half-recovery, speed of half-recovery, time of full microcirculatory blood flow recovery, duration of hyperemic response, and the intensity (area)

**Table 1** Characteristics of Dupuytren's contracture patients ( $n = 87$ )  $n$  (%)

Parameter	Value
Demographic characteristics	
Age ( $M \pm o$ ) (min-max)	(59 $\pm$ 10) (24-83)
Male:Female relation	8:01
Status localis	
Frequency of bilateral affection	28 (32, 18)
Duration of disease, years - (min-max) - Me (Q1; Q3)	(0.5-20) - 5 (4; 10)
Level of contracture - (min-max) - Me (Q1; Q3)	(2-4) - 2.5 (2; 3)
Number of fingers with impaired function (Min-max) - Me (Q1; Q3)	(1-8) - 2 (1-2)
Comorbid conditions	
Arterial hypertension	41 (47.1)
Ischemic heart disease	5 (5.7)
Chronic cardiac insufficiency	3 (3.4)
Postinfarction cardiosclerosis	2 (2.3)
Diabetes type 2	4 (4.6)
Chronic obstructive pulmonary disease	6 (7.8)
Chronic hepatitis	6 (7.8)
Neuritis of the auditory nerve	4 (4.6)
Urolithiasis disease	2 (2.3)
Obesity	2 (2.3)
Extremal active smoking	7 (8.0)

of the hyperemic response were also defined.

### Statistical analysis

After obtaining the parameters of descriptive statistics, all samples of quantitative data were evaluated for the normality of distribution using the Shapiro-Wilk test. For some samples, the normality hypothesis was not confirmed. The majority of quantitative characteristics were represented in tables in the form of medians and quartiles [Me (Q1; Q3)]. The hypothesis of differences was tested using non-parametric Wilcoxon and Mann-Whitney criteria and exact Barnard test with a significance level of 0.05. For all statistical treatments, the software package Attestat Program (version 9.3.1, developed by Gaidyshev IP, Certificate of Rospatent official registration No. 2002611109) was used.

## RESULTS

### Patient's characteristics

General characteristics of Dupuytren's contracture patients are presented in Table 1. Out of 87 patients, 22 (25.3%) noted the first symptoms of palmar fibromatosis at the age of less than 50 years and were younger than 55 at the time of surgery (Y-group). The remaining 65 patients were aged 50 years and older at disease onset and they were 55 and more years old at the time of surgery (O-group). These groups differed in the frequency of cases, with a rapidly progressive development of contracture (less than 5 years) in Y-group 13.6% and in O-group 40.0% ( $P = 0.029161528$ ). The incidence of cardiovascular diseases in the Y-group was 27.3%, and in the O-group 61.5% ( $P = 0.001772739$ ).

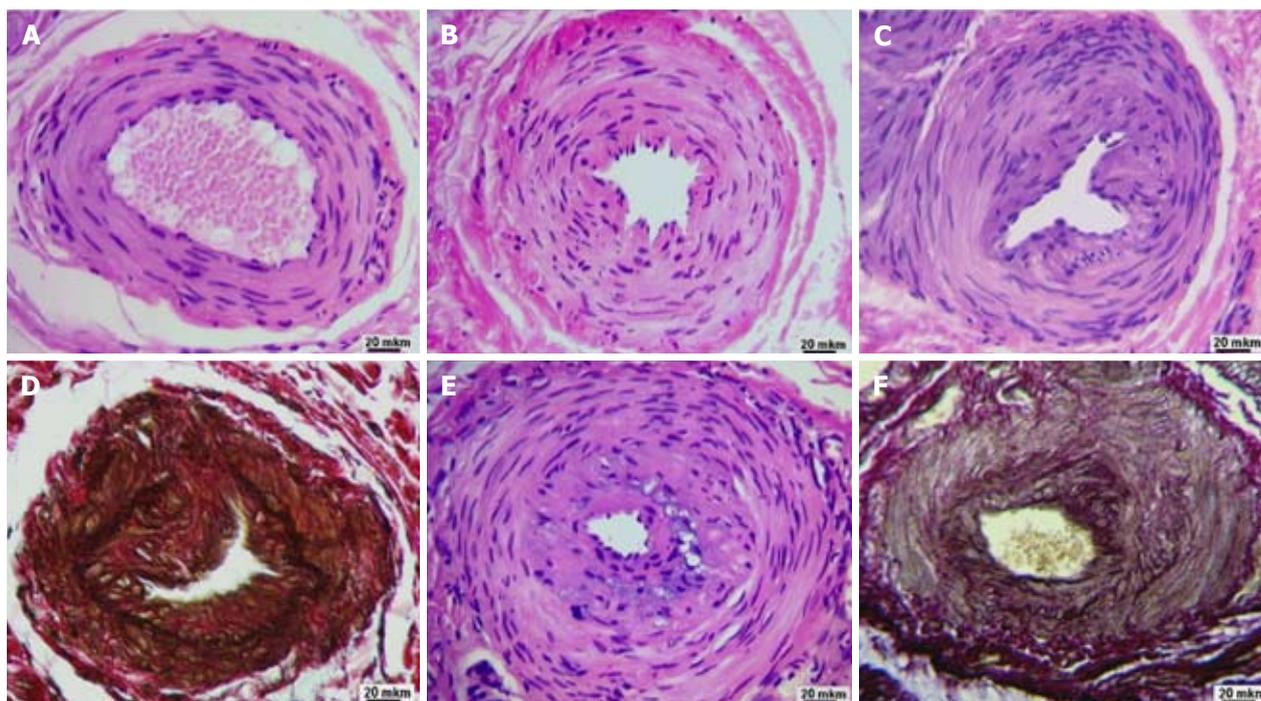
### Histological findings

According to microscopic examination of histological

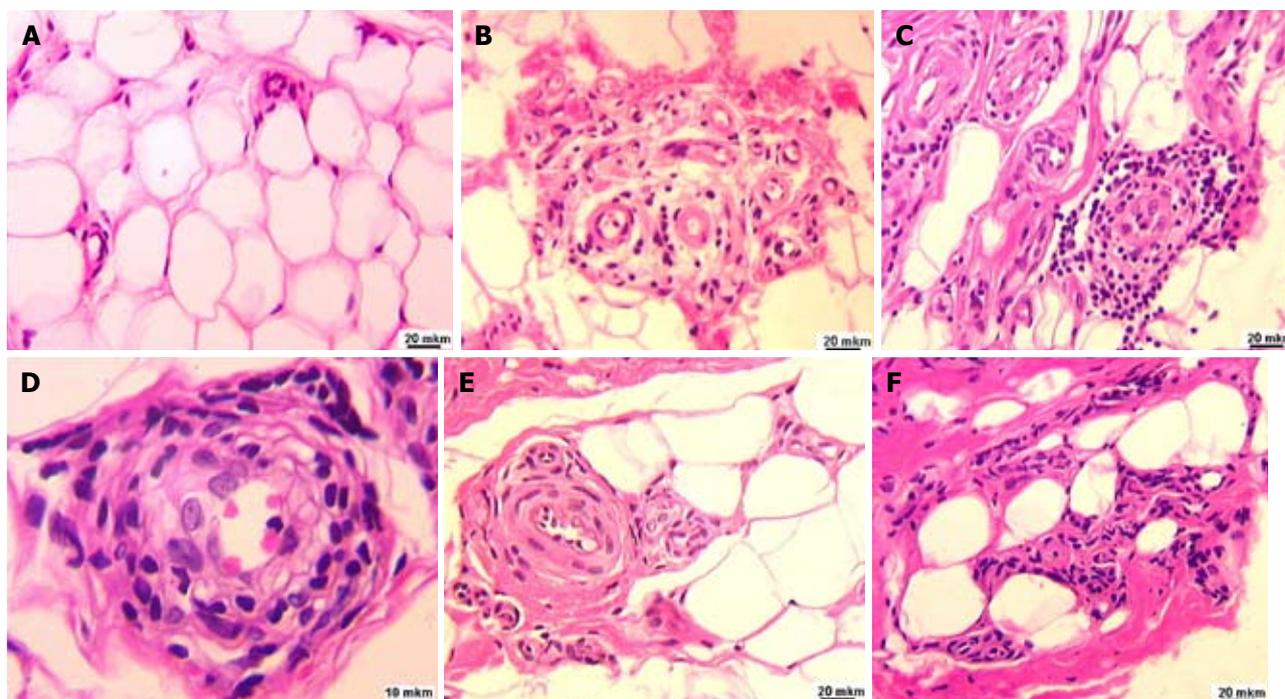
preparations, along with arteries of a typical structure (Figure 2A), there are arteries in the state of constrictive remodeling that differ from normal by a significant narrowing of the lumen. In some cases, such arteries are characterized by pronounced fibrosis of adventitia and contraction of the muscular layer (Figure 2B) but preserved integrity of the internal elastic membrane. In the luminal lining of such arteries, there are only single neo-intimal cells - modified smooth muscle cells. In other cases, the narrowing of the lumen of remodeled arteries is due to the presence of a pronounced polymorphic cell neo-intimal layer (Figures 2C and E). The specific coloration of elastin allowed for visualization of damage to the internal elastic membrane (Figure 2D), which were residual fragments of the old (pre-existing) internal elastic membrane, and a network of newly formed elastic fibers in the thickness of the neo-intima (Figure 2F).

The hypodermal tissue adjacent to the surface layer of the palmar aponeurosis was characterized by increased vascularization. Thick-walled capillaries were located singly (Figure 3A) or in the form of clusters. Perivascular spaces were often infiltrated with inflammatory cells (Figure 3B), which in some cases formed continuous multicellular cuffs (Figure 3C and D). In some loci of the hypodermis, pronounced perivascular fibrosis (Figures 3C, E and F), replacement of fat cells with collagen deposits, and perivascular clusters of fibroblasts were evident (Figure 3F).

With morphometric analysis, it was established that the outer diameter and diameter of the lumen of the perforating arteries of the palmar aponeurosis were reduced in comparison with the control in both Dupuytren's contracture groups, but this reduction was greater in the Y-group than the O-group (Table 2). The thickness of the artery wall was also increased in comparison with the control, but this increase was greater



**Figure 2** Transverse paraffin sections of palmar fascia perforating arteries from Dupuytren's contracture patients. A: Almost normal structure of perforating artery; B: Adventitial fibrosis, constriction of media and deformity of artery lumen; C: Artery with thick neointimal layer; D: The same artery with breakdown of internal elastic laminae evident due to specific elastin staining (dark brown); E: Extreme lumen narrowing due to neointimal thickening; F: Residual fragments of old internal elastic laminae newly formed elastic fibers in the neointimal layer. Staining: Hematoxylin-eosin (A, B, C, E); Weigert - van Gieson (D, E). Magnification 200 ×.



**Figure 3** Fragments of hypodermis paraffin sections from Dupuytren's contracture patients. A: Thick-walled capillaries in adipose tissue of hypodermis; B: Inflammatory infiltration of vascular pool; C: Multilayered round-cellular cuff outside the narrowed vessel; D: Perivascular and intramural infiltration with lymphocytes and macrophages; E: Pronounced perivascular fibrosis; F: Collagen deposits and perivascular clusters of fibroblasts. Staining: Hematoxylin-eosin. Magnification 200 ×.

extent in the O-group. Both groups are characterized by a reliable approximately three-fold increase in intimal thickness, statistically insignificant thinning of the medial layer, and an increased intima/media thickness ratio

compared to control. Intima thickness and intima/media thickness ratio were significantly greater in the O-group than in the Y-group.

The Y-group was characterized by a higher content

**Table 2 Morphometric characteristics of palmar fascia perforating arteries in healthy control and Dupuytren's contracture groups [Me (Q1/Q3)]**

Group/parameters	Healthy control <i>n</i> = 3	Y-group (< 55 yr of age) <i>n</i> = 8	O-group ( $\geq$ 55 yr of age) <i>n</i> = 19
Diameter of artery ( $\mu\text{m}$ )	412.8 (351.43/506.31)	31566 (306.96/326.91) <sup>a,c</sup> $P_2 = 0.000332; P_3 = 0.136006$	334.85 (309.06/441.19) <sup>a</sup> $P_1 = 0.010485$
Lumen diameter ( $\mu\text{m}$ )	243.15 (223.07/326.52)	151.56 (94.72/153.90) <sup>a,c</sup> $P_2 = 0.000736; P_3 = 0.249671$	178.19 (113.78/246.52) <sup>a</sup> $P_2 = 0.007253$
Wall thickness ( $\mu\text{m}$ )	89.03 (65.97/88.88)	92.16 (80.88/106.12) <sup>c</sup> $P_2 = 0.49959; P_3 = 0.010846$	117.98 (98.37/133.13) <sup>a</sup> $P_2 = 0.004483$
Thickness of intima ( $\mu\text{m}$ )	8.41 (7.80/0.82)	22.26 (14.79/33.42) <sup>a</sup> $P_2 = 0.004998; P_3 = 0.355126$	25.37 (21.16/41.75) <sup>a</sup> $P_2 = 0.000463$
Thickness of media ( $\mu\text{m}$ )	58.45 (44.01/60.28)	46.52 (38.08/60.30) $P_2 = 0.37436; P_3 = 0.924826$	46.77 (38.26/64.03) $P_2 = 0.17192$
Intima/media thickness ratio	0.18 (0.12/0.24)	0.53 (0.25/0.55) <sup>a</sup> $P_2 = 0.001992; P_3 = 0.282078$	0.68 (0.33/0.96) <sup>a</sup> $P_2 = 0.000198$

<sup>a</sup> $P < 0.05$  vs Healthy control; <sup>c</sup> $P < 0.05$  vs O-group.

**Table 3 Stereologic characteristics of hypodermis from Dupuytren's contracture patients**

Group/parameters	Y-group (< 55 yr of age) <i>n</i> = 15	O-group ( $\geq$ 55 yr of age) <i>n</i> = 14
Percentage of adipocytes in serial sections of Dupuytren's tissue sample [Me (Q1/Q3), %]	35.05 (23.40/40.09) <sup>a</sup> $P_1 = 0.000338$	27.79 (19.37/32.82)
Numerical microvessels density [Me (Q1/Q3), $\mu\text{m}^{-2}$ ]	5 (4/7) <sup>a</sup> $P_2 = 0$	3 (2/4)
Volumetric microvessels density [Me (Q1/Q3), %]	2.48 (1.44/4.13) <sup>a</sup> $P_2 = 8.88 \times 10^{-16}$	1.16 (0.52/2.12)
Relative number of microvessels with signs of periadventitial inflammatory infiltration	21.84 <sup>a</sup> $P_2 = 1.69 \times 10^{-5}$	12.93
Relative number of microvessels with signs of adventitial fibrosis	4.48 <sup>a</sup> $P_2 = 0.002358$	8.19
Microvessels diameters [Me (Q1/Q3), $\mu\text{m}$ ]	12.55 (9.26/18.05) <sup>a</sup> $P_2 = 0.019425$	11.58 (8.67/16.84)

<sup>a</sup> $P < 0.05$  vs O-group.

of adipocytes in the hypodermis and aponeurosis tissue than the O-group (Table 3). The numerical and volumetric density of the vessels in the hypodermis, as well as the percentage of vessels with signs of periadventitial inflammatory infiltration, was also larger in the Y-group. The O-group was characterized by a greater degree of perivascular fibrosis. The average diameter of the vessels was significantly higher in the Y-group. The percentage of vessels with a diameter greater than 12  $\mu\text{m}$  in the Y-group was 47.1%, and in the O-group it was 41.2% ( $P = 0.039384$ ).

### Investigation of microcirculation

The base microcirculatory flow in the Y-group was significantly increased in comparison with the norm and the O-group (Table 4). Peak microcirculatory flow in the Y-group was also increased but only in comparison with corresponding norm. In the O-group, the index of peak microcirculatory flow was increased compared to norm and the Y-group. Both patients' groups differed from healthy controls, with more pronounced variability of post-occlusive hyperemia as well as a more pronounced difference in their right and left arms.

## DISCUSSION

The role of adipose tissue in the pathogenesis of Dupuytren's contracture has been extensively studied. The prevalence of the disease in older age groups was associated with less content of adipose tissue in fascial structures and hypodermis and corresponding reduction of its protective-amortization role during chronic hand traumatization<sup>[17,18]</sup>. Besides peculiarities of the lipid composition in adipose tissue, the similarity of gene expression in adipose tissue and in fibromatous nodes was established in patients with Dupuytren's contracture<sup>[12]</sup>. The role of adipose tissue in angiogenesis is known<sup>[19]</sup>, and the presence of markers of angiogenesis in Dupuytren's contracture palmar aponeurosis was proved<sup>[20]</sup>. The composition of the luminal lining of microvessels revealed potential precursors of myofibroblasts<sup>[21]</sup>.

In this study, the quantitative characteristics of the hypodermal adipose tissue vascularization in patients with Dupuytren's contracture were represented for the first time. It has been established that the perforating arteries of the palmar aponeurosis, which give rise to the vascular plexus of the hypodermis, are in a state

**Table 4 Parameters of microcirculatory flow and post-occlusive hyperemia test in Dupuytren's contracture patients in younger (DCY) and older (DCO) groups and healthy controls (Norm) in different age groups [Me (Q1/Q3)]**

Parameters	Norm (25-54 yr of age) <i>n</i> = 22	DCY (< 55 yr of age) <i>n</i> = 6	Norm (55-70 yr of age) <i>n</i> = 6	DCO ( $\geq$ 55 yr of age) <i>n</i> = 18
Age	33 (23/54)	52 (45/54)	59 (55/63)	66 (59/69)
Microcirculatory flow base (PU)	4 (3.5/5.7)	15.45 <sup>c</sup> (8.4/20.6) $P_3 = 0.020$	3.5 (2.55/4.7)	4.15 <sup>a</sup> (3.1/7.8) $P_2 = 0.019$
Microcirculatory flow peak (PU)	14.7 (11.8/18.3)	27.5 <sup>c</sup> (22.2/44.4) $P_3 = 0.002$	18.2 (8.15/18.7)	20.1 (16.7/24.6)
Microcirculatory flow peak index (%)	340 (232/443)	218.5 (125/488)	373 (223/449)	508 (336/544) $P_2 = 0.045$
Time of hyperemic response (s)	15 (10/25)	17.5 (10/30)	20 (20/25)	20 (15/90)
Velocity of hyperemic response (PU/s)	0.62 (0.50/0.81)	0.56 (0.14/1.19)	0.52 (0.15/0.55)	0.81 (0.21/1.09)
Time of half-recovery (s)	45 (15/75)	30 (5/60)	35 (20/70)	40 (30/130)
Speed of half-recovery (PU/s)	0.18 (0.14/0.34)	0.96 (0.16/1.54)	0.2 (0.11/0.28)	0.28 (0.09/0.49)
Time of full recovery (s)	247 (205/380)	212 (40/600)	147 (125/190)	400 (90/600)
Duration of hyperemic response (s)	270 (180/300)	242 (55/660)	165 (150/210)	515 (120/700)
Intensity (area) of hyperemic response (relative units)	1127 (705/1830)	2799 (193/6216)	1575 (474/2202)	3804 (1110/5084)

<sup>a</sup> $P < 0.05$  vs DCY; <sup>c</sup> $P < 0.05$  vs corresponding norm. DCY: Dupuytren's contracture patients in younger; DCO: Dupuytren's contracture patients in older.

of constrictive remodeling. Such a remodeling was characterized by a reduction of arteries outside and luminal diameters, and in patients older than 55 years it was accompanied with thickening of the arterial wall.

In both age groups, the thickness of the intima and intima/media thickness ratio were increased compared to control. In the older age group, a significantly higher incidence of arterial hypertension and other cardiovascular diseases were noted. A more pronounced decrease in the external diameter and lumen of the perforating arteries in the younger age group suggests that constrictive remodeling of arteries is mainly associated with the development of fascial fibromatosis rather than cardiovascular diseases. This assumption is consistent with the results of a study of normotensive patients with another rheumatic disease - systemic lupus erythematosus<sup>[22]</sup>.

A limitation of our study was the small sample size of patients in the post-occlusive hyperemia test. However, the increased variability of its characteristics in comparison with the norm and the large difference in the parameters of the right and left hands suggest that this sample, and in particular the area of the hyperemic response, may reflect the severity of pathological and compensatory-adaptive changes. In patients with ischemic heart disease, the area of hyperemic response was relevant to endothelial dysfunction<sup>[23]</sup>. We assumed that a study with a large sample of patients with Dupuytren's contracture before and after the operation will clarify the role of microcirculation in the development of individually oriented treatment protocols.

The larger numerical and volumetric densities of microvessels in the hypodermal tissue in patients younger than 55 years of age compared to those in the older age group are consistent with larger microcirculatory blood flow. These data, combined with a significantly greater proportion of vessels with a diameter of more than 12  $\mu\text{m}$ , indicate more pronounced processes of capillary and arteriogenesis. We have not, however, used angiogenesis markers, and this is another limitation of our study. The incidence of quick

progression of contracture was higher in the older group. The secondary hypothesis of our study is that the use of therapeutic angiogenesis in patients operated on for Dupuytren's contracture will slow the recurrence and spread of fibromatosis.

In conclusion, more severe constrictive remodeling of palmar fascia perforating arteries supplying the hypodermis was revealed in patients younger than 55, but the increased vascularization of the hypodermis serves as a compensatory-adaptive mechanism that slows the development of fibromatosis and contracture.

## ARTICLE HIGHLIGHTS

### Research background

Patients with Dupuytren's contracture are numerous in hand clinics. In most cases, conservative treatment is not curable. Surgical excision of diseased tissue and correction of contracture are effective but the risks of recurrence and extension of pathological changes are high. Measures of successful influence on course of the disease are absent.

### Research motivation

Multiple studies of Dupuytren's disease deal with transformations of connective tissue, its molecular mechanisms, peculiarities of cells immuno-histochemical phenotypes, and gene expression. Though vascular remodeling mediates pathogenesis of various diseases, little is known about changes in palmar fascia and hypodermis vascularity in Dupuytren's contracture patients - especially its quantitative characteristics.

### Research objectives

We wanted to analyze histological morphometric parameters of palmar fascia arteries and microvasculature of palmar hypodermis of Dupuytren's contracture patients and to assess the functional parameters of microcirculation of palmar skin tissues. The main purpose was to present peculiarities of structural and functional characteristics of palmar hypodermal tissue vascularization in different age groups and to determine whether these groups differ in the rate of progression of the hand deformity.

### Research methods

We identified clinical characteristics of Dupuytren's contracture patients ( $n = 87$ ), morphometric characteristics of palmar fascia perforating arteries ( $n = 30$ ), stereologic characteristics of hypodermis, parameters of microcirculatory flow, and post-occlusive hyperemia test ( $n = 52$ ) in Dupuytren's contracture patients in younger and older groups and healthy controls in different age groups. Methods were standard, but to the best of our knowledge, they had not been

used for Dupuytren's contracture research.

### Research results

Cases with rapid progression of hand deformity (less than 5 years) were more common in older patients (55 and more years old). Signs of arterial constrictive remodeling were more prominent in the younger group. Adipocytes content, microvessel density, and per cent of microvessels with signs of inflammatory infiltration were bigger in the younger group. Vessels with adventitial fibrosis were seen more often in the older group. Base capillary flow in the younger group was bigger than the healthy control subjects and the older group; peak capillary flow was increased in comparison with control.

### Research conclusions

Constrictive remodeling of palmar fascia arteries in studied groups of patients was associated with the development of fascial fibromatosis rather than cardiovascular disease. In patients younger than 55 years, old compensatory changes of the microcirculatory bed in palmar hypodermis contributed to more benign course of the disease.

### Research perspectives

Further analysis of functional and structural characteristics of blood vessels in different age and comorbidity groups of Dupuytren's contracture patients are necessary for development of effective vasogenic therapy, which may effectively influence disease progression and extending.

## ACKNOWLEDGEMENTS

The authors would like to thank the members of the engineering group for their technical support and Gaidyshev IP for his help with statistical analysis.

## REFERENCES

- 1 **Rayan GM.** Dupuytren's disease: anatomy, pathology, presentation, and treatment. *Instr Course Lect* 2007; **56**: 101-111 [PMID: 17472297]
- 2 **Godtfredsen NS,** Lucht H, Prescott E, Sørensen TI, Grønbaek M. A prospective study linked both alcohol and tobacco to Dupuytren's disease. *J Clin Epidemiol* 2004; **57**: 858-863 [PMID: 15485739 DOI: 10.1016/j.jclinepi.2003.11.015]
- 3 **Descatha A,** Jauffret P, Chastang JF, Roquelaure Y, Leclerc A. Should we consider Dupuytren's contracture as work-related? A review and meta-analysis of an old debate. *BMC Musculoskelet Disord* 2011; **12**: 96 [PMID: 21575231 DOI: 10.1186/1471-2474-12-96]
- 4 **Forrester HB,** Temple-Smith P, Ham S, de Kretser D, Southwick G, Sprung CN. Genome-wide analysis using exon arrays demonstrates an important role for expression of extra-cellular matrix, fibrotic control and tissue remodelling genes in Dupuytren's disease. *PLoS One* 2013; **8**: e59056 [PMID: 23554969 DOI: 10.1371/journal.pone.0059056]
- 5 **Murrell GA.** The role of the fibroblast in Dupuytren's contracture. *Hand Clin* 1991; **7**: 669-680; discussion 681 [PMID: 1769989]
- 6 **Mayerl C,** Del Frari B, Parson W, Boeck G, Piza-Katzer H, Wick G, Wolfram D. Characterisation of the inflammatory response in Dupuytren's disease. *J Plast Surg Hand Surg* 2016; **50**: 171-179 [PMID: 26852784 DOI: 10.3109/2000656X.2016.1140054]
- 7 **Rehman S,** Goodacre R, Day PJ, Bayat A, Westerhoff HV. Dupuytren's: a systems biology disease. *Arthritis Res Ther* 2011; **13**: 238 [PMID: 21943049 DOI: 10.1186/ar3438]
- 8 **Wang L,** Zhu H. Clonal analysis of palmar fibromatosis: a study whether palmar fibromatosis is a real tumor. *J Transl Med* 2006; **4**: 21 [PMID: 16696857 DOI: 10.1186/1479-5876-4-21]
- 9 **Warren RF.** The pathology of Dupuytren's contracture. *Br J Plast Surg* 1953; **6**: 224-230 [PMID: 13093970 DOI: 10.1016/S0007-1226(53)80030-5]
- 10 **Hindocha S,** Iqbal SA, Farhatullah S, Paus R, Bayat A. Characterization of stem cells in Dupuytren's disease. *Br J Surg* 2011; **98**: 308-315 [PMID: 21104823 DOI: 10.1002/bjs.7307]
- 11 **Viiil J,** Maasalu K, Mäemets-Allas K, Tamming L, Lõhmussaar K, Tooming M, Ingerpuu S, Märtson A, Jaks V. Laminin-rich blood vessels display activated growth factor signaling and act as the proliferation centers in Dupuytren's contracture. *Arthritis Res Ther* 2015; **17**: 144 [PMID: 26018562 DOI: 10.1186/s13075-015-0661-y]
- 12 **Shih B,** Brown JJ, Armstrong DJ, Lindau T, Bayat A. Differential gene expression analysis of subcutaneous fat, fascia, and skin overlying a Dupuytren's disease nodule in comparison to control tissue. *Hand (NY)* 2009; **4**: 294-301 [PMID: 19184239 DOI: 10.1007/s11552-009-9164-0]
- 13 **Spencer M,** Unal R, Zhu B, Rasouli N, McGehee RE Jr, Peterson CA, Kern PA. Adipose tissue extracellular matrix and vascular abnormalities in obesity and insulin resistance. *J Clin Endocrinol Metab* 2011; **96**: E1990-E1998 [PMID: 21994960 DOI: 10.1210/jc.2011-1567]
- 14 **Robciuc MR,** Kivelä R, Williams IM, de Boer JF, van Dijk TH, Elamaa H, Tigistu-Sahle F, Molotkov D, Leppänen VM, Käkälä R, Eklund L, Wasserman DH, Groen AK, Alitalo K. VEGFB/VEGFR1-Induced Expansion of Adipose Vasculature Counteracts Obesity and Related Metabolic Complications. *Cell Metab* 2016; **23**: 712-724 [PMID: 27076080 DOI: 10.1016/j.cmet.2016.03.004]
- 15 **Reilly RM,** Stern PJ, Goldfarb CA. A retrospective review of the management of Dupuytren's nodules. *J Hand Surg Am* 2005; **30**: 1014-1018 [PMID: 16182060 DOI: 10.1016/j.jhssa.2005.03.005]
- 16 **Hindocha S,** Stanley JK, Watson JS, Bayat A. Revised Tubiana's staging system for assessment of disease severity in Dupuytren's disease-preliminary clinical findings. *Hand (NY)* 2008; **3**: 80-86 [PMID: 18780081 DOI: 10.1007/s11552-007-9071-1]
- 17 **Tubiana R.** Dupuytren's disease of the radial side of the hand. *Hand Clin* 1999; **15**: 149-159 [PMID: 10050250]
- 18 **Flint M.** The genesis of the palmar lesion. In: Mcfarlane RM, McGrouther DA, Flint MH, editors. Dupuytren's disease: biology and treatment. New York: Churchill Livingstone, 1990: 140-145
- 19 **Hausman GJ,** Richardson RL. Adipose tissue angiogenesis. *J Anim Sci* 2004; **82**: 925-934 [PMID: 15032451 DOI: 10.2527/2004.823925x]
- 20 **Holzer LA,** Cör A, Pfandlsteiner G, Holzer G. Expression of VEGF, its receptors, and HIF-1 $\alpha$  in Dupuytren's disease. *Acta Orthop* 2013; **84**: 420-425 [PMID: 23992143 DOI: 10.3109/17453674.2013.814011]
- 21 **On N,** Koh SP, Brasch HD, Dunne JC, Armstrong JR, Tan ST, Itinteang T. Embryonic Stem Cell-Like Population in Dupuytren's Disease Expresses Components of the Renin-Angiotensin System. *Plast Reconstr Surg Glob Open* 2017; **5**: e1422 [PMID: 28831359 DOI: 10.1097/GOX.0000000000001422]
- 22 **Morreale M,** Mulè G, Ferrante A, D'ignoto F, Cottone S. Early Vascular Aging in Normotensive Patients With Systemic Lupus Erythematosus: Comparison With Young Patients Having Hypertension. *Angiology* 2016; **67**: 676-682 [PMID: 26535012 DOI: 10.1177/0003319715613917]
- 23 **Stiefel P,** Moreno-Luna R, Vallejo-Vaz AJ, Beltrán LM, Costa A, Gómez L, Ordóñez A, Villar J. Which parameter is better to define endothelial dysfunction in a test of postocclusive hyperemia measured by laser-Doppler flowmetry? *Coron Artery Dis* 2012; **23**: 57-61 [PMID: 22133924 DOI: 10.1097/MCA.0b013e32834e4f34]

**P- Reviewer:** Shao R **S- Editor:** Ji FF  
**L- Editor:** Filipodia **E- Editor:** Song H



## Prospective Study

**Single rod instrumentation in patients with scoliosis and co-morbidities: Indications and outcomes**

Athanasios I Tsirikos, Peter R Loughenbury

Athanasios I Tsirikos, Peter R Loughenbury, Scottish National Spine Deformity Centre, Royal Hospital for Sick Children, Edinburgh EH9 1LF, United Kingdom

ORCID number: Athanasios I Tsirikos (0000-0003-2339-5327); Peter R Loughenbury (0000-0002-0208-2623).

**Author contributions:** Tsirikos AI treated the patients included in this series, and analyzed the data and wrote the paper; Loughenbury PR collected, analyzed the data, and wrote the initial draft of the paper; both authors reviewed the final manuscript including the present revision and agreed to proceed with the submission.

**Institutional review board statement:** The study was reviewed and approved by the Royal Hospital for Sick Children Institutional Review Board.

**Informed consent statement:** Patients were not required to give informed consent to the study because the analysis used anonymous data that were obtained after each patient agreed to treatment by written consent.

**Conflict-of-interest statement:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. No conflict of interest is to be declared

**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:** Athanasios I Tsirikos, FRCS (Hon), MD, PhD, Senior Lecturer, Senior Scientist, Surgeon, Scottish National Spine Deformity Centre, Royal Hospital for Sick Children, Sciennes Road, Edinburgh EH9 1LF, United Kingdom. [atsirikos@hotmail.com](mailto:atsirikos@hotmail.com)

Telephone: +44-131-5360784

Fax: +44-131-6621265

Received: February 9, 2018

Peer-review started: February 10, 2018

First decision: March 9, 2018

Revised: May 20, 2018

Accepted: May 23, 2018

Article in press: May 23, 2018

Published online: September 18, 2018

**Abstract****AIM**

To present our results on the use of a single rod instrumentation correction technique in a small number of patients with major medical co-morbidities.

**METHODS**

This study was a prospective single surgeon series. Patients were treated with single rod hybrid constructs and had a minimum 2-year follow-up. Indications included complex underlying co-morbidities, conversion of growing rods to definitive fusion, and moderate adolescent idiopathic primarily thoracic scoliosis with severe eczema and low body mass index (BMI).

**RESULTS**

We included 99 consecutive patients. Mean age at surgery was 12.8 years (SD 3.5 years). Mean scoliosis correction was 62% (SD 15%) from 73° (SD 22°) to 28° (SD 15°). Mean surgical time was 153 min (SD 34 min), and blood loss was 530 mL (SD 327 mL); 20% BV (SD 13%). Mean clinical and radiological follow-up was 3.2 years (range: 2-12) post-operatively. Complications included rod failure, which occurred in three of our complex patients with severe syndromic or congenital kyphoscoliosis (3%). Only one of these three patients

required revision surgery to address a non-union. Our revision rate was 2% (including a distal junctional kyphosis in a Marfan's syndrome patient).

### CONCLUSION

The single rod technique has achieved satisfactory deformity correction and a low rate of complications in patients with specific indications and severe underlying medical conditions. In these children with significant co-morbidities, where the risks of scoliosis surgery are significantly increased, this technique has achieved low operative time, blood loss, and associated surgical morbidity.

**Key words:** Pediatric scoliosis; Indications; Spinal deformity; Surgery; Spinal fusion; Single rod technique; Outcomes

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** We reviewed 99 pediatric patients treated for scoliosis with a single-rod hybrid technique. They belonged in three groups: Group A included 62 patients with complex deformities and low body mass index (BMI) associated with medical co-morbidities increasing the risk of cardiac, respiratory, neurological complications and intra-operative blood loss; group B included 21 patients treated with growing rod lengtheners who underwent spinal fusion; group C included 16 patients with moderate adolescent idiopathic scoliosis, low BMI, and severe eczema at risk of wound or systemic infection. The single-rod technique has achieved and maintained at follow-up good deformity correction with low surgical time, blood loss, and surgical morbidity.

Tsirikos AI, Loughenbury PR. Single rod instrumentation in patients with scoliosis and co-morbidities: Indications and outcomes. *World J Orthop* 2018; 9(9): 138-148 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/138.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.138>

## INTRODUCTION

Dual rod instrumentation has become the standard of care for scoliosis correction. The use of bilateral segmental pedicle screw fixation over two rods can produce effective coronal and axial deformity correction and a stable construct whilst fusion occurs<sup>[1-3]</sup>. In most surgical techniques, the majority of curve correction occurs during placement of the first rod with the second rod providing additional stability in the post-operative period while the bone grafts are healing. Use of a single rod construct may offer theoretical advantages, including shorter surgical time, lesser blood loss, lower rates of infection, technically easier procedures, simpler pre-operative planning, lower instrumentation profile,

and reduced implant cost. There is only one direct comparison of single and double rod instrumentation in the treatment of adolescent idiopathic scoliosis (AIS). This demonstrates superiority of the double rod technique and a higher rate of rod breakage with single rods (21% compared to 4% with double rods)<sup>[4]</sup>. Mechanical testing of single-rod and double-rod segmental hook fixation constructs with hooks at every level except the apex in a long-segment animal model (calf spines) indicated that over 12 vertebral segments the single rod instrumentation allowed more neutral zone rotation than the double rod construct<sup>[5]</sup>. There remains interest in using a single rod technique in high-risk patients, such as children with Duchenne muscular dystrophy (DMD), in order to minimize duration and morbidity of surgery<sup>[6]</sup>.

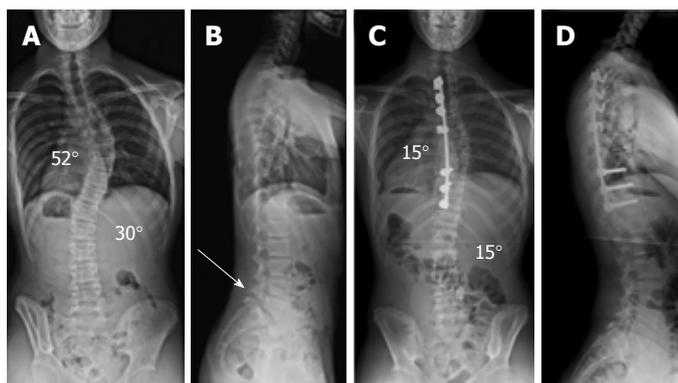
This study reports a prospective series of patients treated by a single surgeon with a single rod hybrid technique in an effort to reduce peri-operative morbidity. The indications for use of this technique are discussed and the post-operative clinical, radiological, and functional outcomes are reported.

## MATERIALS AND METHODS

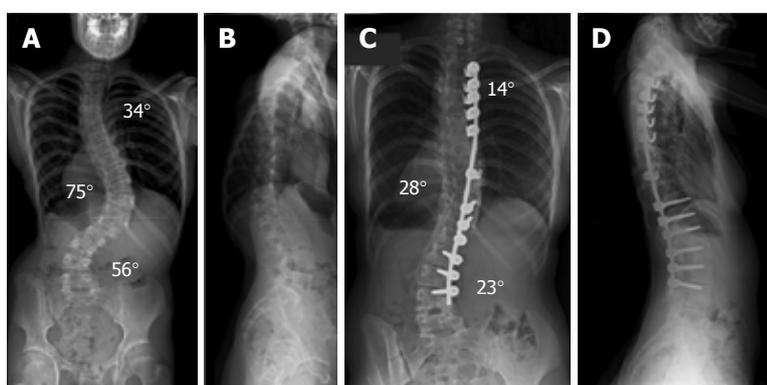
We reviewed 99 patients who underwent surgical correction of scoliosis using a single rod hybrid technique between 2005 and 2015. Indications for this technique over the traditional dual rod construct which is the standard of care in our practice, included high risk of neurological/cardiac complications and intra-operative bleeding, low body mass index (BMI), previous partial fusion due to long-term use of growing rods, and pre-existing severe eczema. Eighty-seven patients underwent posterior and 12 patients with early onset scoliosis (10 idiopathic - 2 syndromic) combined one-stage anterior/posterior spinal fusion. Operative data included surgical time, blood loss (recorded as a volume and percentage of body weight [percentage by volume - blood volume]), and problems related to intra-operative neuro-monitoring. Radiographs were examined pre-operatively to include curve severity (using the Cobb method<sup>[7]</sup>), skeletal maturity (Risser grade<sup>[8]</sup>), and location of curve apex<sup>[9]</sup>. Clinical and radiological review was performed post-operatively at mean follow-up 3.2 years (range: 2-12). Patient reported outcomes (Scoliosis Research Society-22 questionnaire) were available for patients with AIS before and after surgery. Statistical analysis was made using standard descriptive terms and the Microsoft Excel for Mac 2016 (Microsoft, Redmond, WA, United States).

### Surgical technique

Anesthetic management included non-invasive monitoring, use of an arterial line, and urinary catheter. A warming blanket was also used, and our patients received prophylactic cefuroxime on induction and two further doses post-operatively. Blood loss was reduced



**Figure 1 Patient with adolescent idiopathic scoliosis (patient 13; Table 4).** A: Preoperative postero-anterior spinal radiograph shows a primary thoracic and compensatory lumbar AIS; B: Preoperative lateral spinal radiograph shows thoracic hypokyphosis and isthmic spondylolysis at L5 (white arrow) with associated grade 1 lumbosacral spondylolisthesis; C: Postero-anterior spinal radiograph shows very satisfactory scoliosis correction across both curves and a globally balanced spine following a selective posterior thoracic fusion; D: Lateral spinal radiograph shows restoration of thoracic kyphosis and a normal sagittal balance of the spine with no change in the grade 1 lumbosacral spondylolisthesis. AIS: Adolescent idiopathic scoliosis.



**Figure 2 Patient with neuromuscular kyphoscoliosis.** A: Preoperative postero-anterior spinal radiograph shows a triple thoracic and lumbar scoliosis; B: Preoperative lateral spinal radiograph shows a thoracolumbar rotatory kyphosis producing positive global sagittal balance of the spine; C: Postero-anterior spinal radiograph shows excellent scoliosis correction and a balanced spine in the coronal plane; D: Lateral spinal radiograph shows restoration of thoracic kyphosis and a normal sagittal balance of the spine.

with intra-operative tranexamic acid and transfusion of autologous blood using cell salvage. Multimodal spinal cord monitoring was applied recording cortical and cervical somatosensory (SSEPs), as well as transcranial motor evoked potentials (MEPs) that remained stable in all patients throughout the procedure. Anterior release was performed through a convex thoracotomy in 12 patients. All patients underwent posterior correction across the thoracic or thoracic/lumbar spine short of the sacrum and pelvis through a midline incision with bilateral subperiosteal exposure to the tips of the transverse processes. Soft tissue release and facetectomies were performed, and correction was achieved with a single rod. This was secured using distal pedicle screws, proximal pedicle hooks, and transverse process hooks or sublaminar wires at the apex of the curve. Scoliosis correction was achieved either through concave rod derotation and apical translation towards the midline (Figure 1) or through apical translation and convex rod cantilever maneuver from proximal to distal (Figure 2). The Universal Spinal System (USS) instrumentation was used (DePuy/

Synthes, West Chester, Pennsylvania, United States) in all patients. Decortication of the posterior elements and use of autologous local and allograft bone (fresh frozen femoral heads) aimed to achieve a solid fusion. Autologous rib graft was used when an anterior release was performed. In six patients who underwent posterior surgery, additional iliac crest graft was used. Topical vancomycin (1 g) was applied prior to closure. The wound was closed in layers without wound drains. Mobilization commenced on the first post-operative day and patients were fitted with a custom-molded removable underarm spinal jacket to wear when out of bed for 6 mo after surgery.

### Cost analysis

The cost of our typical construct used in AIS was considered for both a thoracic (mean 10 instrumented levels) and a double thoracic/lumbar fusion (mean 15 instrumented levels). For a thoracic fusion, our single rod construct included three proximal pedicle screw hooks, three distal pedicle screws, one transverse process hook, and a single rod (Figure 1). For a thoracic

**Table 1** Operative and postoperative data among our patient groups

Group	Type of scoliosis	No. of patients	Mean age at surgery (yr)	Procedure (No. of patients)	Operating time (min)	Blood loss (mL)	Blood loss (BV)	Mean follow-up (yr)	Complications
A - Complex deformity	Syndromic	21	13	PSF: 19; A/PSF: 2	164	727	27	3.0	2 rod breakages-one revision required due to non-union; 1 distal junctional kyphosis-distal fusion extension required
	Early onset idiopathic	17	11	PSF: 11; A/PSF: 6	185	519	25	2.9	None
	Congenital	13	11	PSF: 13	138	368	13	4.8	One rod breakage-no revision required
	Neuromuscular	5	14	PSF: 5	125	662	24	3.0	None
	Intraspinal anomalies	6	13	PSF: 6	145	525	22	4.5	None
B - Conversion of growing rods to definitive fusion	Early onset	21	12	PSF: 17; A/PSF: 4	159	497	20	2.8	None
C - AIS	Adolescent idiopathic	16	15.8	PSF: 16	128	406	9	2.8	None
Summary of data		99	13	PSF: 87; A/PSF: 12	153	530	20	3.2	4

PSF: Posterior spinal fusion; A/PSF: Anterior and posterior spinal fusion; BV: Blood volume; AIS: Adolescent idiopathic scoliosis.

and lumbar fusion, our single rod construct included maximum five proximal pedicle screw hooks, six distal pedicle screws, one transverse process hook, and a single rod (Figure 2). This was then compared to a double rod construct using bilateral segmental pedicle screws (implant density: 2) and a double rod construct using the authors' preferred technique with reduced implant density 1.38<sup>[10]</sup>. All costs were calculated using standard prices for USS instrumentation and reported as percentage decrease in cost.

## RESULTS

Mean age at surgery was 12.8 years [standard deviation (SD) 3.5 years]. Mean surgical time was 153 min (SD 34 min), and mean blood loss was 530 mL (SD 327 mL); 20% blood volume (BV) (SD 13%). Three patient groups were included:

### Group A - Patients with complex deformities

This group included 62 complex patients with severe deformities and associated co-morbidities (Tables 1-3 and Figure 2). Underlying scoliosis diagnosis included syndromic (21 patients, Table 3), early onset idiopathic (17 patients; juvenile: 9, infantile: 8), congenital (13 patients), neuromuscular (5 patients; congenital myopathy: 1, cerebral palsy: 1, demyelinating neuropathy: 1, Friedreich's ataxia: 1, congenital hypotonia: 1), and scoliosis associated with intraspinal anomalies (6 patients; Chiari I malformation with syringomyelia: 4, astrocytoma: 1, glioglioma: 1). Indications to use the single rod technique were high risk of neurological/cardiac complications, complex congenital vertebral anomalies, increased intra-

operative bleeding, and low BMI. In the syndromic patients, mean scoliosis correction was 65% for upper thoracic, 62% for main thoracic, and 56% for lumbar curves ( $P < 0.001$ ), surgical time was 164 min (SD 47 min), and blood loss was 27% BV (SD 13%). In the congenital patients, mean scoliosis correction was 54% for upper thoracic, 50% for main thoracic, and 48% for lumbar curves ( $P < 0.001$ ), surgical time was 138 min (SD 29 min), and blood loss was 13% BV (SD 3%). In the early onset idiopathic group, mean scoliosis correction was 62% for upper thoracic, 60% for main thoracic, and 61% for lumbar curves ( $P < 0.001$ ), surgical time was 185 min (SD 101 min), and blood loss was 25% BV (SD 16%). In the neuromuscular patients, mean scoliosis correction was 66% for main thoracic and 57% for lumbar curves ( $P < 0.001$ ), surgical time was 125 min (SD 13 min), and blood loss was 24% BV (SD 11%). In the intraspinal anomalies group, all patients had a thoracic scoliosis. Mean curve correction was 56% ( $P < 0.001$ ), surgical time was 145 min (SD 17 min), and blood loss was 22% BV (SD 11%).

### Group B - Conversion of growing rods to the definitive spinal fusion

There were 21 patients where a single rod was used to achieve final correction and definitive fusion at the end of treatment with growing rod lengthenings (Tables 1-3 and Figure 3). Underlying cause of scoliosis included syndromic (10 patients), infantile idiopathic (6 patients), congenital (4 patients), and neuromuscular (horizontal gaze palsy: 1 patient). Indications for using the single rod technique were the presence of partial fusion and inherent stiffness of the spine due to the long-standing deformity, anterior apical convex epiphysiodesis

**Table 2** Type and size of deformity among our patients in groups A and B

Group	Type of scoliosis	No. of patients	Thoracic scoliosis (mean preop/postop; degrees); (%correction)	Double thoracic scoliosis (mean preop/postop; degrees); (%correction)	Thoracic/lumbar scoliosis (mean preop/postop; degrees); (%correction)	Triple thoracic/lumbar scoliosis (mean preop/postop; degrees); (%correction)	Thoracic kyphoscoliosis (mean preop/postop; degrees); (%correction)
A - Complex deformity	Syndromic	21	78/30 (62%); 8 patients	Upper TH: 46/19 (59%); main TH: 60/24 (60%); 5 patients	TH: 55/18 (67%); L: 43/15 (65%); 4 patients	Upper TH: 32/6 (81%); main TH: 61/28 (54%); L: 52/25 (52%); 2 patients	Scoliosis: 120/48 (60%); kyphosis: 103/60 (42%); 2 patients
	Early onset idiopathic	17 (infantile: 9; juvenile: 8)	99/34 (66%); 4 patients	Upper TH: 53/25 (53%); main TH: 81/47 (42%); one patient	TH: 89/36 (60%); L: 70/27 (61%); 6 patients	Upper TH: 49/15 (69%); main TH: 84/30 (64%); L: 52/20 (62%); 5 patients	Scoliosis: 56/31 (45%); kyphosis: 122/65 (47%); one patient
	Congenital	13	58/36 (38%); 6 patients	Upper TH: 39/22 (44%); main TH: 76/40 (47%); 2 patients	TH: 75/38 (49%); L: 68/36 (47%); 3 patients	Upper TH: 41/15 (63%); main TH: 55/25 (55%); L: 44/22 (50%); one patient	Scoliosis: 70/31 (56%); kyphosis: 75/35 (53%); one patient
B - Conversion of growing rods to definitive fusion	Neuromuscular	5	66/19 (71%); 2 patients	-	TH: 79/31 (61%); L: 65/28 (57%); 3 patients	one patient	-
	Associated with intraspinal anomalies	6	82/36 (56%); 6 patients	-	-	-	-
	Syndromic	10	91/39 (57%); 6 patients	-	TH: 93/52 (44%); L: 69/37 (46%); 4 patients	-	-
B - Conversion of growing rods to definitive fusion	Infantile idiopathic	6	74/28 (62%); 2 patients	Upper TH: 59/34 (42%); main TH: 100/55 (45%); one patient	TH: 61/38 (38%); L: 101/52 (49%); one patient	-	Scoliosis: 63/32 (49%); kyphosis: 104/61 (41%); 2 patients
	Congenital Neuromuscular	4 1	77/38 (51%); 4 patients	-	-	-	Scoliosis: 65/25 (62%); kyphosis: 78/50 (36%); one patient

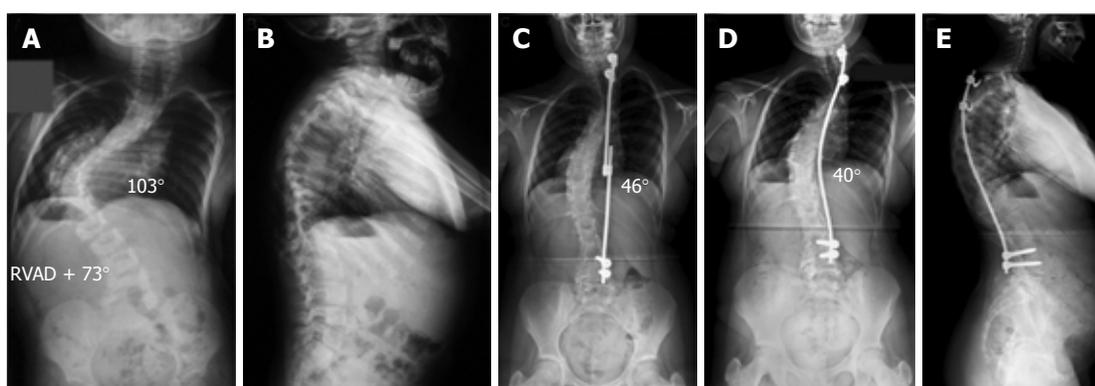
(9 patients), and several previous growing rod lengthenings in order to achieve a globally balanced spine, low BMI, and a high risk of complications due to existing comorbidities. Twelve patients had single thoracic, five had thoracic and lumbar, and one had double thoracic scoliosis while three patients had thoracic kyphoscoliosis. Mean scoliosis correction was 42% for upper thoracic, 52% for main thoracic, and 47% for lumbar curves ( $P < 0.001$ ), surgical time was 159 min (SD 86 min), and blood loss was 20% BV (SD 13%).

**Group C - Patients with AIS**

The single rod technique was used in 16 patients with AIS (Tables 1 and 4). Indications for the single rod technique were pre-existing severe eczema increasing significantly the risk of wound infection and low BMI. Fifteen patients had moderate single or double thoracic scoliosis with compensatory lumbar curves (12 patients), and one patient had a double thoracic and lumbar scoliosis. Mean flexibility index {FI, % = [(pre-operative Cobb angle - supine maximum lateral bending Cobb angle)/preoperative Cobb angle] × 100} as calculated before surgery was 25% (range: 22%-35%) for upper thoracic, 30% (range: 10%-59%) for main thoracic, and 50% (range: 35%-62%) for lumbar curves. Mean correction was 64% for upper thoracic, 70% for main thoracic, and 67% for lumbar curves ( $P < 0.001$ ), surgical time was 128 min (SD 20 min), and blood loss

**Table 3 Patients with syndromic conditions included in our study**

Group A – Complex deformity ( <i>n</i> = 21 patients)	Group B - Conversion of growing rods to definitive fusion ( <i>n</i> = 10 patients)
Neurofibromatosis type 1 (2)	Skeletal dysplasia (2)
Osteogenesis imperfecta (1)	Oculo-auriculo-fronto-nasal syndrome (1)
Rubinstein-Taybi type 2 (1)	Chromosome abnormality (7)
Cystic Fibrosis (1)	
Arthrogryposis multiplex congenital (1)	
Ehlers-Danlos (1)	
Angelman's (1)	
Marfan's (1)	
Prader-Willi (1)	
Down's syndrome (1)	
Chromosome abnormality (4)	
Undiagnosed syndromic condition (6)	



**Figure 3 Patient with a severe infantile idiopathic thoracic scoliosis.** A: Initial postero-anterior spinal radiograph at age 2 years shows a very severe thoracic scoliosis; B: Initial lateral spinal radiograph at age 2 years shows increased thoracic kyphosis. The patient was treated with placement of a concave growing rod construct followed by 21 consecutive lengthening procedures; C: Postero-anterior spinal radiograph at age 13 years when she underwent the definitive posterior spinal fusion with the use of a single concave rod construct; D: Postero-anterior spinal radiograph at latest follow-up (end of spinal growth) shows no evidence of recurrence of the deformity and no crankshaft effect with a globally balanced spine; E: Lateral spinal radiograph shows good global balance in the sagittal plane at skeletal maturity.

was 9% BV (SD 5%). When compared to our previous AIS series of segmental bilateral (mean surgical time: 320 min; mean blood loss: 50% BV)<sup>[10]</sup>, segmental unilateral (mean surgical time: 240 min; mean blood loss: 30% BV)<sup>[10]</sup>, or segmental convex (mean surgical time: 183 min; mean blood loss: 22% BV)<sup>[11]</sup> pedicle screw correction techniques, both surgical time and intra-operative blood loss in the single rod technique was significantly reduced ( $P < 0.001$ ). Excellent correction of global coronal and sagittal balance, including thoracic kyphosis and lumbar lordosis, was also achieved. This was associated with high patient satisfaction (4.8 at latest follow-up) and good functional outcomes (Figure 4).

We compared the single-rod and dual-rod techniques in our practice and did not record significant difference in the degree of scoliosis correction for main thoracic curves, which was the primary deformity among the patients included in our single rod series of 16 AIS patients ( $P > 0.05$ )<sup>[10,11]</sup>. However, the degree of preoperative thoracic scoliosis was significantly greater ( $P < 0.001$ ) among the patients included in our cohorts treated with segmental pedicle screws and a dual rod construct (bilateral technique-mean scoliosis: 68°, range: 40°-98°; unilateral

technique-mean scoliosis: 65°, range: 38°-95°; convex technique-mean scoliosis: 70.2°, range: 55°-110°) when compared to our single rod AIS group (mean scoliosis: 54°, range: 45°-69°)<sup>[10,11]</sup>. SRS-22 individual domain and total scores, as well as patients' satisfaction at 2-year follow-up between single-rod and dual-rod constructs, was also no different ( $P > 0.05$ )<sup>[10,11]</sup>.

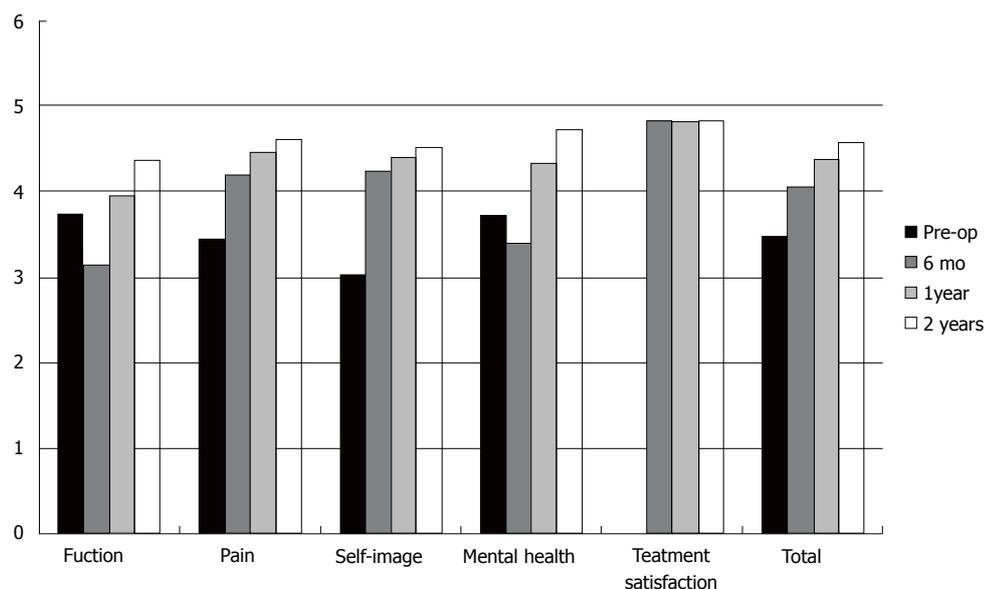
### Complications

We recorded four post-operative complications (4%) that occurred in three patients with syndromic kyphoscoliosis and in a patient with a congenital kyphoscoliosis (group A). Three of these complications involved rod failure. The first was the result of a non-union presenting with rod breakage occurring 17 mo after surgery. This patient had chromosomal abnormality, complex cardiac disease, poor skin healing, and severe behavioral problems. She had a thoracic scoliosis corrected from 120° to 35° through a combined anterior/posterior fusion and associated thoracic hyperkyphosis. Revision posterior surgery was performed to address a hairline non-union using a new rod and the existing fixation points. The fusion was augmented with autologous rib and allograft bone with

**Table 4** Type and size of deformity before and after surgery among our patients with adolescent idiopathic scoliosis and severe eczema (group C)

Patient number	Gender	Risser grade	Scoliosis type (No. of patients) <sup>(1)</sup>	Procedure (posterior spinal fusion/levels)	Upper thoracic scoliosis (pre-op/post-op; degrees); (% correction)	Main thoracic scoliosis (pre-op/post-op; degrees); (% correction)	Lumbar scoliosis (pre-op/post-op; degrees); (% correction)	Kyphosis (pre-op/post-op); (degrees)	Lordosis (pre-op/post-op); (degrees)	Coronal balance (pre-op/post-op); (cm)	Sagittal balance (pre-op/post-op); (cm)
1	F	5	2A	PSF T2-T10	52/23 (56%)	49/22 (55%)	-	19/52	49/52	0/0	-3.5/0
2	F	5	1B	PSF T3-T11	-	48/15 (69%)	35/17 (51%-spontaneous correction)	27/52	47/53	0.3/0	-2.8/0
3	M	2	2A	PSF T2-L1	32/11 (66%)	47/11 (77%)	-	35/44	40/42	0.8/0	-0.8/0
4	F	4	1A	PSF T2/T9	-	45/0 (100%)	-	45/55	55/58	2.3/0	-0.3/0
5	M	5	2A	PSF T2-T11	32/12 (62.5%)	52/16 (69%)	30/6 (80%-spontaneous correction)	23/44	59/45	0.8/0	-3.1/0
6	F	5	3C	PSF T2-L4	-	55/12 (78%)	48/10 (79%)	25/50	40/50	1.2/0	-2.8/0
7	F	5	2B	PSF T3-T12	35/12 (66%)	55/21 (62%)	36/11 (69%-spontaneous correction)	28/48	50/50	1/0	-3.0/0
8	M	4	1A	PSF T2-T12	-	60/15 (75%)	39/10 (74%-spontaneous correction)	16/38	43/42	0/0	1.5/0
9	F	3	2A	PSF T3-T12	29/9 (69%)	48/14 (71%)	30/2 (93%-spontaneous correction)	17/38	33/38	0.6/0	-1.2/0
10	F	3	1A	PSF T2-T11	-	52/20 (61.5%)	36/15 (58%-spontaneous correction)	24/46	61/51	0/0	-2.5/0
11	M	5	1B	PSF T2-T11	-	55/16 (71%)	30/15 (50%-spontaneous correction)	20/48	47/50	3.5/0	4.1/0
12	F	4	2A	PSF T3-T12	32/11 (66%)	59/17 (71%)	32/13 (59%-spontaneous correction)	46/48	57/46	0.8/0.2	-3.5/-1
13	M	4	1A	PSF T2-T11	-	52/15 (71%)	30/15 (50%-spontaneous correction)	20/47	48/46	3/0	3.5/0
14	F	5	2B	PSF T2-T11	42/15 (64.3%)	60/25 (58.3%)	40/14 (65%-spontaneous correction)	31/48	46/47	1.2/0.5	-2.3/0
15	F	4	2A	PSF T3-T12	39/14 (64%)	69/23 (67%)	37/14 (62%-spontaneous correction)	31/47	45/50	0.5/0	-0.5/0
16	F	3	2A	PSF T3-L2	22/8 (64%)	59/20 (66%)	28/9 (68%-spontaneous correction)	56/54	54/53	2.5/0.3	2.2/0
Summary of data	11 F; 5 M	Mean: 4.1	Scoliosis type 1 (1); 2 (2); 3 (6); 4 (7)	15 TH fusions; one TH/L fusion	Mean values: 35/12.7 (64%)	Mean values: 54/16 (70.4%)	Mean values: 35/11.6 (67%)	Mean values: 29/47.4 (63.4%)	Mean values: 48/48 no change	Mean values: 1.16/0.06 (95%)	Mean values: 2.35/0.06 (97.4%)

F: Female; M: Male; PSF: Posterior spinal fusion; TH: Thoracic; L: Lumbar.



**Figure 4 Scoliosis Research Society (SRS-22) in our adolescent idiopathic scoliosis patient population.** Mean scores are presented pre-operatively, at 6-mo, one-year, and two-years post-operatively including postoperative patient satisfaction. There was statistically significant improvement of individual domain scores with regards to function, pain, self-image, mental health, and total score between preoperative and 2-year values ( $P < 0.001$ ).

a good outcome at skeletal maturity. The other two rod failures occurred in a patient with syndromic and another with congenital kyphoscoliosis and presented 3 years after index surgery. Both patients were asymptomatic, and there was no radiographic evidence of recurrence of the deformity. The two opposing ends of the rod were undisplaced at the point of failure, and a computed tomography (CT) scan confirmed a solid fusion across the previously instrumented levels. Therefore, revision surgery was not required, and the patients remained pain-free with a full range of activities and a stable residual deformity at subsequent follow-up. The fourth patient had Marfan's syndrome, intraspinal anomalies, and severe cardiac disease. Following index posterior correction, she developed distal junctional kyphosis. Revision surgery to extend the fusion by two caudal levels resulted in a good outcome at end of skeletal growth. Our revision rate was 2% (1% each for rod breakage and distal junctional kyphosis).

### Cost analysis

Analysis of the instrumentation costs used to treat thoracic and thoracic/lumbar AIS is shown in Table 5. Considering thoracic scoliosis correction and fusion over 10 levels, use of the single rod technique in our series would reduce implant cost by 65% compared to a double rod construct with bilateral segmental screws and by 51% compared to a construct using the authors' reported lesser screw density technique<sup>[10]</sup>. If this was extended to correction and fusion of 15 levels (such as in double major curves) use of the single rod technique would result in 64% reduction in cost compared to a double rod construct with bilateral segmental screws and 49% compared to a construct using the authors' reduced screw density.

## DISCUSSION

The use of double rod constructs in the treatment of scoliosis is associated with satisfactory clinical and radiographic outcomes, and this has always been the standard of care in the vast majority of our patients. Bilateral pedicle screw instrumentation has become the standard of care to provide powerful correction and stable fixation until a solid fusion is achieved. However, the use of bilateral segmental pedicle screws leads to greater neurological risks, longer operative times and blood loss, potential for instrumentation prominence, and an increase in the risk of deep infection due to high implant density. There is an ongoing interest in limiting the risks of instrumentation placement by reducing the number of implants used during correction<sup>[10,12]</sup>.

There may be a number of patients where it is valid to use a single rod construct in order to minimize surgical morbidity. Cawley *et al.*<sup>[6]</sup> reported 41 patients with DMD, where early correction using limited fixation with one rod proximal to the pelvis allowed adequate sitting posture with low peri-operative morbidity. Unilateral rod fixation is also commonly used in growing rod constructs with good reported outcomes<sup>[13]</sup>. Reduced operative morbidity is especially attractive for pediatric patients who require repetitive surgeries. Whilst it is apparent that the potential advantages of a limited surgical technique may be useful in select patient groups, clear indications have not been established.

This study presents our experience of the single rod technique and describes the limited indications for its use in our practice. The decision to use such surgical approach is tailored to the individual patient. This includes high risk of neurological or cardiac complications; risk of increased intra-operative blood loss due to severe

**Table 5 Cost analysis and comparison between the single and double rod constructs in the treatment of adolescent idiopathic scoliosis based on the Universal Spinal System instrumentation**

No. of levels included	Type of construct	Instrumentation	Comparative cost
10 (thoracic fusion)	Double rod construct with bilateral segmental pedicle screws (implant density: 2)	20 pedicle screws 20 sleeves and nuts 2 rods	100%
	Double rod construct using the authors' preferred technique (implant density: 1.38) <sup>[10]</sup>	14 pedicle screws 14 sleeves and nuts 2 rods	29% reduction compared to bilateral segmental pedicle screw construct
	Single rod hybrid construct	3 pedicle screws 3 pedicle screw hooks 1 transverse process hook 7 sleeves and nuts 1 rod	65% reduction compared to bilateral segmental pedicle screw construct; 51% reduction compared to authors' preferred technique
	Double rod construct with bilateral segmental pedicle screws (implant density: 2)	30 pedicle screws 30 sleeves and nuts 2 rods	100%
	Double rod construct using authors preferred technique (implant density: 1.38) <sup>[10]</sup>	21 pedicle screws 21 sleeves and nuts 2 rods	29% reduction compared with bilateral segmental pedicle screw construct
	Single rod construct	6 pedicle screws 5 pedicle screw hooks 1 transverse process hook 12 sleeves and nuts 1 rod	64% reduction compared to bilateral segmental pedicle screw construct; 49% reduction compared to authors' preferred technique
15 (Thoracic and Lumbar fusion)	Double rod construct with bilateral segmental pedicle screws (implant density: 2)	30 pedicle screws 30 sleeves and nuts 2 rods	100%
	Double rod construct using authors preferred technique (implant density: 1.38) <sup>[10]</sup>	21 pedicle screws 21 sleeves and nuts 2 rods	29% reduction compared with bilateral segmental pedicle screw construct
	Single rod construct	6 pedicle screws 5 pedicle screw hooks 1 transverse process hook 12 sleeves and nuts 1 rod	64% reduction compared to bilateral segmental pedicle screw construct; 49% reduction compared to authors' preferred technique

underlying co-morbidities; low BMI leading to problems related to instrumentation prominence; early onset deformity and repetitive surgery with partial fusion due to the use of growing rods and often initial apical convex growth arrest; and pre-existing severe eczema. One or more of these indications has been present in our patients, and we have used the single rod technique in three groups: (1) complex deformity - high risk of cardiac/pulmonary/neurological complications and intra-operative blood loss as well as low BMI; (2) Conversion of growing rod to definitive fusion - a balanced correction is required; the patients often have low BMI and significant medical co-morbidities; and (3) Adolescent idiopathic scoliosis - in patients with moderate curves, low BMI, and severe eczema that increase the risk of either wound or systemic infection. The first two groups represent a mixture of underlying diagnoses and include syndromic, early onset idiopathic, neuromuscular, and congenital scoliosis associated with intraspinal anomalies<sup>[14,15]</sup>.

The outcomes from the use of the single rod technique in our AIS patients with moderate primarily thoracic curves were satisfactory, and we did not record any complications. In AIS patients with no severe eczema, we select a dual pedicle screw/rod technique that is more effective to correct the deformity and has produced optimum outcomes<sup>[10,11]</sup>. In severe AIS we also find that the dual rod segmental pedicle screw techniques have greater ability to correct the deformity without the need for anterior release to increase curve flexibility when compared to the single rod hybrid technique<sup>[10,11]</sup>. Our results of the single rod technique are in contrast to those reported by Wattenbarger *et al.*<sup>[4]</sup> who identified a higher rate of rod breakage with single (21%) than double rods (4%) in AIS. Rod failure occurred in

three of our complex patients with severe syndromic or congenital kyphoscoliosis (3%). Our revision rate was 2% (including a distal junctional kyphosis in a Marfan's syndrome patient). Cawley *et al.*<sup>[6]</sup> recorded 7.3% rod breakage when they used the single rod technique in DMD patients. The use of post-operative immobilization (spinal jacket) may have contributed to our reduced instrumentation failure rates. Post-operative orthotic support can protect the rod construct and provide additional stability until fusion is achieved.

Due to the multitude of underlying diagnoses in groups A and B, a direct comparison to previous studies cannot be made. The number of patients where we felt a single rod construct would be preferable to dual instrumentation is small and represents less than 10% of the senior author's practice in the same chronological period. However, our results demonstrate that the single rod correction technique within the above limited indications can achieve satisfactory deformity correction with low complication rates in patients with severe underlying co-morbidities. In our experience, this technique has reduced surgical time and intra-operative blood loss resulting in lower peri-operative morbidity in medically compromised patients with considerably less implant related complications than previously reported<sup>[4]</sup>. Instrumentation cost has also been significantly reduced when compared to a double pedicle screw/rod technique.

## ARTICLE HIGHLIGHTS

### Research background

Scoliosis surgery is a major spinal procedure that is associated with significant risks of neurological and medical complications, producing permanent patient disability and increasing surgical morbidity. Surgical techniques have been

developed in an attempt to standardize patient treatment and reduce the rate of operative complications. In recent decades, dual-rod instrumentation has become the standard of care for scoliosis correction. The introduction of segmental pedicle screws has allowed better coronal and axial deformity correction but has increased surgical risks. Single-rod correction techniques have been used in patients with adolescent idiopathic scoliosis (AIS) and Duchenne muscular dystrophy with controversial results in two previous series.

### Research motivation

Single-rod correction techniques may offer advantages over dual-rod pedicle screw constructs, including reduced operative time and blood loss, lower risk of infection and instrumentation profile, easier surgical planning and operative technique, as well as reduced implant cost. In patients with major co-morbidities, such techniques may improve surgical safety and reduce associated morbidity and mortality of the procedure.

### Research objectives

In this study, we reviewed demographic, radiographic, surgical, as well as quality of life data of 99 children and adolescents with scoliosis who underwent surgical correction using a single rod hybrid technique under the senior author. We report on the effectiveness of this technique in correcting the spinal deformity and focus on the rate of complications. We also analyzed the instrumentation costs in AIS and compared the single rod construct to previous series of patients treated in our practice with segmental pedicle screw dual instrumentation.

### Research methods

We prospectively collected data on 99 pediatric patients including review of patient records and spinal radiographs as well as assessment of quality of life questionnaires (SRS-22) in AIS patients both before and after surgery. We applied statistical analysis of our results where appropriate and compared the outcomes of the single rod technique to those that we had previously reported in the treatment of AIS using dual segmental pedicle screw constructs.

### Research results

We included three groups of patients: Group A had 62 patients with complex deformities and low BMI associated with medical co-morbidities increasing the risk of cardiac, respiratory, and neurological complications, and intra-operative blood loss; group B had 21 patients previously treated with growing rod lengthenings who underwent definitive spinal fusion; group C had 16 patients with moderate AIS, low BMI, and severe eczema at risk of wound or systemic infection. Mean age at surgery was 12.8 years (SD 3.5 years). Mean scoliosis correction for the 99 patients was 62% (SD 15%) from 73° (SD 22°) to 28° (SD 15°). Mean surgical time was 153 min (SD 34 min), and blood loss was 530 mL (SD 327 mL); 20% blood volume (SD 13%). Mean clinical and radiological follow-up was 3.2 years (range: 2-12) post-operatively. Complications included rod failure, which occurred in three of our complex patients (group A) with severe syndromic or congenital kyphoscoliosis (3%). Only one of these three patients required revision surgery to address a non-union. Our revision rate was 2% (including a distal junctional kyphosis in a Marfan's syndrome patient that required distal extension of the fusion).

### Research conclusions

The single-rod technique has achieved and maintained at follow-up good deformity correction associated with low surgical time, blood loss, and surgical morbidity. The use of lesser implants may reduce the instrumentation related risks, such as pedicle screw malposition, producing neurological, vascular, or visceral injury. The risk of wound infection may also be reduced as the volume of implants used in single rod instrumentation is much less than that in a dual rod/segmental pedicle screw construct. In our practice, this technique has a role primarily in pediatric patients with severe underlying co-morbidities and high surgical risks. The single rod technique has also reduced significantly the instrumentation cost compared to dual rod pedicle screw techniques, which is an important consideration at a time when health economics play an essential role in provision of patient care. Our complication rate is markedly lower than that reported in the two previous series of AIS or Duchenne muscular dystrophy patients with a low rate of re-operation (2%). We recorded high patient satisfaction among AIS patients and good functional outcomes that are

comparable to our previous series of patients treated with dual rod/segmental pedicle screw instrumentation.

### Research perspectives

Despite the fact that the longest postoperative follow-up in our study was 12 years (mean follow-up: 3.2 years), we are monitoring our patients beyond skeletal maturity and well into adult life in order to confirm that no long-term complications occur. We believe that in light of this study the single rod technique is a reasonable alternative to dual rod techniques, especially in the treatment of complex patients with associated high morbidity. Further studies comparing outcomes of different techniques would be useful to determine the best option in different clinical scenarios and types of deformity.

## REFERENCES

- 1 Lee SM, Suk SI, Chung ER. Direct vertebral rotation: a new technique of three-dimensional deformity correction with segmental pedicle screw fixation in adolescent idiopathic scoliosis. *Spine (Phila Pa 1976)* 2004; **29**: 343-349 [PMID: 14752361 DOI: 10.1097/01.BRS.0000109991.88149.19]
- 2 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]
- 3 Suk SI, Kim JH, Kim SS, Lim DJ. Pedicle screw instrumentation in adolescent idiopathic scoliosis (AIS). *Eur Spine J* 2012; **21**: 13-22 [PMID: 21874625 DOI: 10.1007/s00586-011-1986-0]
- 4 Wattenbarger JM, Richards BS, Herring JA. A comparison of single-rod instrumentation with double-rod instrumentation in adolescent idiopathic scoliosis. *Spine (Phila Pa 1976)* 2000; **25**: 1680-1688 [PMID: 10870143 DOI: 10.1097/00007632-200007010-00011]
- 5 Wattenbarger JM, Herring JA, Bronson D, Ashman RB. Mechanical testing of a single rod versus a double rod in a long-segment animal model. *J Spinal Disord* 2001; **14**: 232-236 [PMID: 11389374 DOI: 10.1097/00002517-200106000-00008]
- 6 Cawley DT, Carmody O, Dodds MK, McCormack D. Early limited instrumentation of scoliosis in Duchenne muscular dystrophy: is a single-rod construct sufficient? *Spine J* 2015; **15**: 2166-2171 [PMID: 26070283 DOI: 10.1016/j.spinee.2015.06.008]
- 7 Cobb JR. Outline for the study of scoliosis. The American Academy of Orthopedic Surgeons Instructional Course Lectures. *Instr Course Lect* 1948; **5**: 261-275
- 8 Risser JC. The Iliac apophysis; an invaluable sign in the management of scoliosis. *Clin Orthop* 1958; **11**: 111-119 [PMID: 13561591]
- 9 Lenke LG, Betz RR, Hafer TR, Lapp MA, Merola AA, Harms J, Shufflebarger HL. Multisurgeon assessment of surgical decision-making in adolescent idiopathic scoliosis: curve classification, operative approach, and fusion levels. *Spine (Phila Pa 1976)* 2001; **26**: 2347-2353 [PMID: 11679820 DOI: 10.1097/00007632-200111010-00011]
- 10 Tsirikos AI, Subramanian AS. Posterior spinal arthrodesis for adolescent idiopathic scoliosis using pedicle screw instrumentation: does a bilateral or unilateral screw technique affect surgical outcome? *J Bone Joint Surg Br* 2012; **94**: 1670-1677 [PMID: 23188910 DOI: 10.1302/0301-620X.94B12.29403]
- 11 Tsirikos AI, Mataliotakis G, Bounakis N. Posterior spinal fusion for adolescent idiopathic scoliosis using a convex pedicle screw technique: a novel concept of deformity correction. *Bone Joint J* 2017; **99-B**: 1080-1087 [PMID: 28768786 DOI: 10.1302/0301-620X.99B8.BJJ-2016-1351.R1]
- 12 Quan GM, Gibson MJ. Correction of main thoracic adolescent idiopathic scoliosis using pedicle screw instrumentation: does higher implant density improve correction? *Spine (Phila Pa 1976)* 2010; **35**: 562-567 [PMID: 20118842 DOI: 10.1097/BRS.0b013e3181b4af34]
- 13 Farooq N, Garrido E, Altaf F, Dartnell J, Shah SA, Tucker SK, Noordeen H. Minimizing complications with single submuscular

- growing rods: a review of technique and results on 88 patients with minimum two-year follow-up. *Spine* (Phila Pa 1976) 2010; **35**: 2252-2258 [PMID: 21102301 DOI: 10.1097/BRS.0b013e3181ecf41a]
- 14 **Bounakis N**, Karampalis C, Sharp H, Tsirikos AI. Surgical treatment of scoliosis in Rubinstein-Taybi syndrome type 2: a case report. *J Med Case Rep* 2015; **9**: 10 [PMID: 25596810 DOI: 10.1186/1752-1947-9-10]
- 15 **Mataliotakis GI**, Tsirikos AI, Pearson K, Urquhart DS, Smith C, Fall A. Scoliosis Surgery in Cystic Fibrosis: Surgical Considerations and the Multidisciplinary Approach of a Rare Case. *Case Rep Orthop* 2016; **2016**: 7186258 [PMID: 27413564 DOI: 10.1155/2016/7186258]

**P- Reviewer:** Cheuk DKL, Lykissas MG **S- Editor:** Ji FF

**L- Editor:** Filipodia **E- Editor:** Song H



## Prospective Study

# Outcomes of mobile bearing unicompartmental knee arthroplasty in medial osteoarthritis knee with and without preoperative genu recurvatum

Boonchana Pongcharoen, Krit Boontanapibul

Boonchana Pongcharoen, Orthopedics, Faculty of medicine, Thammasat University, Klongluang 12120, Thailand

Krit Boontanapibul, Orthopedics, Thammasat University, Klongluang 12120, Thailand

ORCID number: Boonchana Pongcharoen (0000-0001-6907-0024); Krit Boontanapibul (0000-0001-8525-8577).

**Author contributions:** The authors contributed equally to this study, in all aspects of its design, performance, interpretation and write-up.

**Institutional review board statement:** The study was reviewed and approved for publication by the Institutional Reviewer of Thammasat University.

**Clinical trial registration statement:** The clinical trial is registered with ClinicalTrials.gov, using identifier NCT02854189. Details can be found at <https://clinicaltrials.gov/ct2/show/NCT02854189?term=NCT02854189&rank=1>.

**Informed consent statement:** All study participants or their legal guardian provided informed written consent prior to study enrolment for the collection and publication of their anonymized personal and medical data.

**Conflict-of-interest statement:** The authors have no conflict of interest related to the manuscript.

**CONSORT 2010 statement:** The authors have read the CONSORT 2010 Statement, and the manuscript was prepared and revised according to the CONSORT 2010 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/>

**Manuscript source:** Unsolicited manuscript

**Correspondence to:** Boonchana Pongcharoen, MD, Associate Professor, Orthopedics, Faculty of Medicine, Thammasat University, 95 Paholyothin Road, Klongluang 12120, Thailand. [pobounch@tu.ac.th](mailto:pobounch@tu.ac.th)  
Telephone: +66-89-7472423

**Received:** March 2, 2018

**Peer-review started:** March 2, 2018

**First decision:** March 18, 2018

**Revised:** July 3, 2018

**Accepted:** July 14, 2018

**Article in press:** July 15, 2018

**Published online:** September 18, 2018

## Abstract

### AIM

To compare clinical outcomes of patients with and without preoperative genu recurvatum (GR) following mobile bearing unicompartmental knee arthroplasty (UKA).

### METHODS

We prospectively followed 176 patients for at least 24 mo who had been treated by unilateral, minimally invasive, Oxford UKA. Patients with medial osteoarthritis (OA) knee and preoperative GR (Group I) accounted for 18% ( $n = 32$ ) and patients without preoperative GR (Group II) accounted for the remaining 82% ( $n = 144$ ). Knee score, pain scores, and functional scores were assessed for each patient and compared between the two groups. The incidence of postoperative GR

and the postoperative hyperextension angles also were recorded and analyzed.

## RESULTS

The pain score, knee score and functional score were not significantly different between the two groups. Similarly, the incidence of postoperative GR and the measured hyperextension angles were not significantly different between the two groups. The incidence of postoperative GR was 1/32 (3.12%) in Group I and 1/144 (0.69%) in Group II ( $P = 0.34$ ). The mean postoperative hyperextension angles were  $2.40^\circ \pm 2.19^\circ$  (range:  $1^\circ$ - $7^\circ$ ) for Group I and  $1.57^\circ \pm 3.51^\circ$  (range:  $1^\circ$ - $6^\circ$ ) for Group II ( $P = 0.65$ ).

## CONCLUSION

Medial OA of the knee and concomitant GR is not a contraindication for the mobile bearing UKA.

**Key words:** Unicompartmental knee; Genu recurvatum; Osteoarthritis; Hyperextension knee; Knee arthroplasty; Oxford knee

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** There is no previous study addressing the results of mobile bearing unicompartmental knee arthroplasty (UKA) in medial osteoarthritis (OA) knees with preexisting genu recurvatum (GR). This study determined the clinical outcomes and incidence of postoperative GR of medial OA knees with and without preexisting GR following mobile bearing UKA. Clinical outcomes, postoperative GR and hyperextension angle were evaluated at minimal 2 years of follow-up. Medial OA knees with and without GR showed no difference in clinical outcomes, incidence of postoperative GR or hyperextension angle. Therefore, medial OA knee with preoperative GR is not a contraindication for mobile bearing UKA.

Pongcharoen B, Boontanapibul K. Outcomes of mobile bearing unicompartmental knee arthroplasty in medial osteoarthritis knee with and without preoperative genu recurvatum. *World J Orthop* 2018; 9(9): 149-155 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/149.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.149>

## INTRODUCTION

The mobile bearing unicompartmental knee arthroplasty (UKA) has yielded excellent results in patients with medial osteoarthritis (OA) of the knees<sup>[1-6]</sup>. However, some patients who do not have neuromuscular disorders may develop medial OA of the knees and concomitant genu recurvatum (GR). Moreover, some patients have developed postoperative GR and shown poor clinical

outcomes following fixed bearing UKA and total knee arthroplasty (TKA)<sup>[7-9]</sup>. The optimal prosthesis to use in patients with OA of the knees and GR remains controversial.

To the best of our knowledge, there have not been any studies reporting the clinical outcomes of mobile bearing UKA in medial OA knees with concomitant preoperative GR. The purpose of this study was, therefore, to determine the clinical outcome of the knee, as reflected by pain score, knee score and functional score, following the mobile bearing UKA and performing a comparison of the results between two groups of patients with medial OA knees, namely those with and without preoperative GR. The incidence of postoperative GR and the hyperextension angles were also compared.

## MATERIALS AND METHODS

### Study design and patients

We conducted a prospective cohort study of patients undergoing medial Oxford UKAs (Zimmer Biomet, Bridgend, United Kingdom), performed by a single surgeon, between January 2011 and November 2014 at the Thammasat University Hospital. The study was approved by the Human Research Ethics Committee of the Faculty of Medicine at Thammasat University. The clinical trial is registered at ClinicalTrials.gov (NCT02854189).

The patients were divided into two groups, with Group I consisting of 32 patients (32 knees) with preoperative GR and Group II consisting of 144 patients (144 knees) without preoperative GR. The Group I patients had hyperextension angle of more than  $5^\circ$ <sup>[7]</sup>. We enrolled patients with medial OA knees of moderate to severe Alhback class (grades 2, 3 and 4)<sup>[10]</sup>. The inclusion criteria were age older than 40 years, range of motion (ROM) greater than  $90^\circ$ , varus deformity less than  $25^\circ$ , and flexion contractures less than  $20^\circ$ . The exclusion criteria were diagnosis with spontaneous osteonecrosis of the knee (SONK), intraoperative anterior cruciate ligament insufficiency, posttraumatic arthritis, gouty arthritis, inflammatory joint disease, or history of a previous bilateral Oxford UKA. OA of the patellofemoral joint, young age and obesity were not considered contraindications for this procedure<sup>[1-3]</sup>.

We recorded demographic data on a standard case record form, including age, sex, site, body mass index, preoperative ROM (measured with a long-arm goniometer), preoperative Knee Society Score<sup>®</sup> (KSS)<sup>[11]</sup>, and preoperative tibiofemoral angle from standing anteroposterior knee radiograph (Table 1). The patients attended follow-up at 6 wk, 3 mo, 6 mo, 1 year, and annually thereafter. At each follow-up, a blinded research assistant recorded each patient's KSS (pain score, knee score, and functional score). Incidence of postoperative GR and the hyperextension angles

**Table 1** Demographic data

Variable	Group I (patients with preoperative genu recurvatum), <i>n</i> = 32 knees	Group II (patients without preoperative genu recurvatum), <i>n</i> = 144 knees	<i>P</i> -value
Age	65.10 ± 8.02 (57-76)	65.67 ± 7.40 (44-88)	0.71
Sex, male/female	1/31	14/130	0.31
Site, right/left	16/17	70/74	0.91
BMI	26.76 ± 3.69 (20.81-33.21)	26.26 ± 3.05 (20-42.22)	0.47
Knee score	34.10 ± 2.47 (27-44)	34.35 ± 2.62 (30-40)	0.61
Pain score	11.52 ± 4.42 (0-20)	11.75 ± 4.94 (0-20)	0.23
Functional score	54.69 ± 9.75 (30-65)	52.03 ± 10.13 (35-65)	0.18
ROM (°)	122.58 ± 4.17 (110-125)	119.37 ± 10.92 (90-130)	0.10
Tibiofemoral angle (°)	Varus 5.45 ± 3.86 (0-20)	Varus 5.68 ± 3.99 (0-15)	0.77

BMI: Body mass index; ROM: Range of motion.



**Figure 1** The extension gap will be tight when the knee moves beyond full extension according to use of the larger-sized femoral component (dashed lines).

were also recorded. The patients were subjected to anteroposterior standing, lateral standing, skyline view and long-leg radiographs and the component alignment and tibiofemoral angles were recorded. Complications such as infection, component loosening, fractures and bearing dislocations were recorded.

### Statistical analysis

The sample-size was calculated based on postoperative KSS, to ensure detection of a clinical relevant difference of 6 points using a standard deviation of 3.0<sup>[12]</sup>. It was determined that having 30 knees in Group I and 140 knees in Group II would allow for 80% power at the significance of 5%. Intergroup differences in age, knee score, pain score, functional score, body mass index, ROM, tibiofemoral angle, flexion contractures and GR were assessed using the Student's *t*-test. Intergroup differences in incidence of GR, sex, ratio of sex and ratio of operative site were assessed using the chi-square or the Fisher's exact test, as appropriate.

### Surgical technique

All patients were anesthetized *via* spinal block with morphine (0.1-0.2 mg). Prior to skin incision, all patients were fitted with a thigh tourniquet (inflated to 300

mmHg) and received 1 g cefazolin (intravenously). The size of the femoral component was chosen preoperatively using the X-ray template with a true lateral radiograph. For the Group I patients, there was an option of operation using a larger femoral component when the femoral component was between standard sizes or the hyperextension angle was between 10°-20°. Use of a larger femoral component will change the position at the superior part of the distal femoral condyle and tighten the extension gap, possibly preventing postoperative GR (Figure 1).

An anteromedial skin incision was made from the upper pole of the patella to the medial aspect of the tibial tubercle. A mini-midvastus approach was applied to all patients for prevention of patellar maltracking<sup>[13]</sup>. The patella was slightly subluxated laterally but was not everted. Minimally invasive instrumentation was used for all patients. The shaft of the tibial saw guide was parallel to the long axis of the tibia to create 7° tibial slope. The depth of the tibial bone cut was 2 mm below the deepest part of the medial tibial plateau and perpendicular to the mechanical axis. The posterior condyle of the femur was then cut using intramedullary femoral-guided instrumentation that connected the femoral drill guide with the intramedullary (IM) link.

The flexion gap was set at 100° of flexion, then the extension gap was set at 20° of flexion. The distal condyle of the femur was cut by the milling technique, to create equal flexion-extension gap. However, in Group I patients, the distal condyle of the femur were removed at 1 mm less length than that of the Group II patients, to tighten the extension gap. If patients in Group I showed slight flexion contracture (< 10°) intraoperatively after applying the trial prosthesis, the slight flexion contracture would have been accepted; however, if the knee showed flexion contracture more than 10°, the distal femur would have been recut to create equal gap.

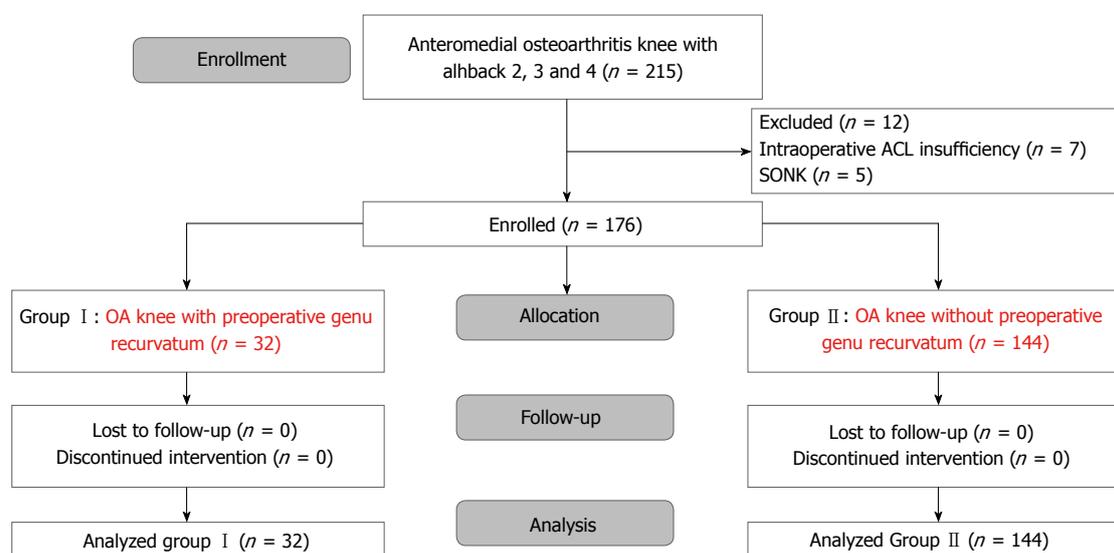
All operations used the same instrumentation to finish the tibia and femur. Thirty millimeters of bupivacaine was injected prior to closing the incision, with one intraarticular drain (10-G) having been inserted before closing. The operative time, blood loss volume and occurrence of intraoperative fracture were recorded.

**Table 2 Pain score, knee score and functional score at 2-yr follow-up**

Variable	Group I (patients with preoperative genu recurvatum), n = 32 knees	Group II (patients without preoperative genu recurvatum), n = 144 knees	P-value
Knee score, points	97.97 ± 2.49 (94-100)	96.91 ± 4.44 (81-100)	0.19
Pain score, points	48.94 ± 2.36 (45-50)	48.71 ± 2.63 (40-50)	0.64
Functional score, points	82.12 ± 4.85 (80-100)	82.55 ± 5.10 (65-100)	0.66

**Table 3 Incidence of postoperative genu recurvatum and postoperative hyperextension angle**

Variable	Group I (patients with preoperative genu recurvatum), n = 32 knees	Group II (patients without preoperative genu recurvatum), n = 144 knees	P-value
Incidence of postoperative genu recurvatum (%)	3.13 (1/32)	0.69 (1/144)	0.34
Hyperextension angle (°)	2.40 ± 2.19 (1-7)	1.57 ± 3.51 (1-6)	0.65



**Figure 2 Flow chart protocol of this study.** ACL: Anterior cruciate ligament; OA: Osteoarthritis; SONK: Spontaneous osteonecrosis of knee.

## RESULTS

Medial OA knees with and without preoperative GR less than 19° have similar clinical outcome and incidence of postoperative GR. A total of 176 patients (15 males and 161 females) underwent unilateral mobile bearing UKAs, and the total 176 knees were evaluated for study entry (Trial profile, Figure 2). The patients' ages ranged from 43-88 years (mean: 65.30 years). Thirty-two patients had preoperative GR and one hundred and forty-four patients did not have preoperative GR. All demographic and preoperative characteristics were similar between the two groups.

The mean hyperextension angle of Group I patients was 7.03° ± 3.19° (5°-19°). The mean hyperextension angle and flexion contracture of Group II patients were 0.02° ± 0.19° (1°-2°) and 6.99° ± 5.03° (1°-18°), respectively. Follow-up extended from 24 mo to 70 mo, for an overall mean of 37.66 mo; no patients were lost to follow-up. The pain scores, knee scores and functional scores were not significantly different

between the two groups (Table 2). The mean KSS of patients in Group I improved from 34.10 ± 2.47 (27-44) to 97.97 ± 2.49 (94-100), and the KSS of patients in Group II improved from 34.35 ± 2.62 (30-40) to 96.91 ± 4.44 (81-100) (Tables 1 and 2). The incidence of postoperative GR was 3.13% in Group I compared to 0.7% in Group II (P = 0.34), and the mean postoperative hyperextension angle was 2.40° ± 2.19° (1°-7°) for Group I compared to 1.57° ± 3.51° (1-6) in Group II (P = 0.65) (Table 3). No patient in Group I showed flexion contracture.

The postoperative ROM, postoperative tibiofemoral angles, femoral component alignment, tibial component alignment, posterior slope of the tibial component, and operative times were not different between the two groups (Table 4). This study did not observe any postoperative complications, such as patellar crepitation, infections, mobile bearing dislocation or component loosening. However, one patient in Group II did suffer a medial tibial plateau fracture at 3 mo postoperatively and was excluded from the study; this patient

**Table 4 Postoperative range of motion, component alignment, postoperative tibiofemoral angle and operative time**

Variable	Group I (patients with preoperative genu recurvatum), <i>n</i> = 32 knees	Group II (patients without preoperative genu recurvatum), <i>n</i> = 144 knees	<i>P</i> -value
Postoperative ROM (°)	126.21 ± 5.30 (115-135)	123.30 ± 9.88 (90-145)	0.14
Postoperative tibiofemoral angle (°)	5.82 ± 1.55 (valgus 3-valgus 8)	5.66 ± 1.77 (valgus 2-valgus 10)	0.65
Femoral component alignment (°)	6.06 ± 1.43 (valgus 2-valgus 8)	5.99 ± 1.56 (valgus 2-valgus 10)	0.82
Tibia component alignment (°)	Varus 0.97 ± 0.92 (varus 3-valgus 1)	Varus 0.77 ± 1.19 (varus 3-valgus 2)	0.37
Posterior slope of tibial component (°)	6.73 ± 1.92 (4-10)	6.31 ± 2.04 (2-10)	0.28
Operative time in min	88.94 ± 10.59 (75-120)	93.01 ± 13.64 (65-130)	0.11

ROM: Range of motion.

underwent a revision TKA, with good result.

## DISCUSSION

To the best of our knowledge, no previous study in the publicly available literature has addressed the clinical outcomes of the mobile bearing UKA in medial OA of the knees in patients with preexisting GR. In the study, the OA knees with and without preexisting GR showed good clinical outcome following mobile bearing UKA. The postoperative pain score, knee score and functional score were no different between the two groups (*i.e.*, with and without preexisting GR). The incidence of postoperative GR and hyperextension angles were also essentially the same for the two groups.

Previous studies have found that patients who had preoperative GR tended to develop GR postoperatively, and showed poor clinical outcome following TKA and fixed bearing UKA applied using the standard surgical technique<sup>[7-9]</sup>. Only one study has determined the hyperextension angle of this group of patients following TKA and fixed bearing UKA<sup>[7]</sup>. In that study, the hyperextension angles decreased from 6° ± 2° to 2° ± 4° after TKA and 7° ± 2° to 1° ± 3° after fixed bearing UKA<sup>[7]</sup>. Therefore, Mullaji *et al.*<sup>[14]</sup> set a slightly tight extension gap for medial OA knee with preoperative GR, with the aim of preventing recurrent hyperextension deformity following TKA. The patients with preexisting GR were reported to have good clinical results and no development of recurrent hyperextension deformity with the tight extension gap<sup>[14]</sup>.

In the present study, the patients who had preoperative hyperextension angle up to 19° showed excellent clinical outcome and did not develop postoperative GR at 3 years of follow-up (Figure 3). The different results in our study compared to those from the previous studies may be due to several issues. First, the medial mobile bearing UKA has shown normal or nearly normal biomechanics and kinematics, with the knee joint stability, ligament tension and knee alignment returning to predisease stage levels<sup>[15-17]</sup>. Second, our study used a larger femoral component when between sizes. The extension gap was tight, even when knees were extended beyond full extension (Figure

1). It is important to note, however, that an abnormally large femoral component may also cause problems with the patellofemoral joint; nonetheless, our study showed no anterior knee pain, patellar crepitation or patellar dislocation in the Group I patients. Moreover, the phases I and II of the Oxford mobile bearing UKA used only a single size for the femoral component, being applied to all patients, and no patients to date have had to undergo surgical revision because of patellofemoral joint problems<sup>[1,18]</sup>. Third, our study set a tighter extension gap or slight flexion contracture in some of the patients in Group I, for prevention of GR. However, no patients have presented flexion contracture postoperatively, even after 2 years of follow-up. Moreover, no patients have developed overcorrection of the tibiofemoral joint. The tibiofemoral angle of Group I patients showed a greater valgus alignment than that of Group II patients, but this was within normal limits. Fourth, all patients were encouraged to perform quadricep exercises to improve quadricep muscle power before and after the operation. Meding *et al.*<sup>[19]</sup> showed that weakness of the quadricep muscles can cause GR.

Our study has some limitations that should be considered when interpreting our findings. Firstly, the hyperextension angle may represent an underestimation. The pain may be uncomfortable for patients, resulting in some reduction of knee hyperextension. Therefore, both groups of patients might present higher hyperextension angles. Secondly, our study showed that the patients with preoperative GR of up to 19° have good clinical outcomes following mobile bearing UKA; patients with preoperative GR of more than 19° are now needed to compare the clinical outcome with primary TKA or constrained TKA. Thirdly, although the mean age of both groups was similar, the age range was different for the two groups (57-76 years for Group I patients and 44-88 years for Group II patients). Thus, the Group II patients may have presented better clinical outcome than the generally older Group I patients. However, the clinical outcome of the Group I patients was not different than that of the Group II patients. In conclusion, combined GR and medial OA of the knee is not a contraindication



**Figure 3** The preoperative and postoperative radiographic images of a patient with preoperative genu recurvatum. A: A hyperextension angle of 19°; B: A hyperextension angle of 18°; C: A hyperextension angle of 14°.

for mobile bearing UKA, and good outcomes may be expected.

## ARTICLE HIGHLIGHTS

### Research background

Postoperative genu recurvatum (GR) has a tendency to develop in the medial osteoarthritis (OA) knee with preexisting GR following total knee arthroplasty (TKA) and unicompartmental knee arthroplasty (UKA). The prosthesis of choice for medial OA knee with preexisting GR is controversial. Constrained TKA has been chosen by some surgeons for prevention of postoperative GR, even though the patients could develop early loosening of the prosthesis, require early reoperation, and experience bone loss during revision TKA. The present study found that the medial OA knee with preoperative GR (< 19°) and without preoperative GR have similar clinical outcomes and determined the incidence of postoperative GR following mobile bearing UKA. Use of the normal biomechanical and kinematic parameters, while adjusting some steps of the surgical technique, including a tighter extension gap with and without application of larger femoral component, could prevent postoperative GR following mobile bearing UKA.

### Research motivation

Medial OA knees with and without preexisting GR have shown good clinical outcomes and no difference in incidence of postoperative GR following mobile bearing UKA. However, the causes of OA knee with preexisting GR are unclear. Quadriceps muscle weakness from spondylosis or abnormal ligament tension

might underlie the occurrence of OA knee with preexisting GR. Therefore, the future research should focus on this yet unresolved issue.

### Research objectives

The main objectives of this study were to determine the clinical outcomes and the incidence of postoperative GR in medial OA knees with and without preexisting GR.

### Research methods

In this prospective cohort study, we used pain score, functional score and knee score to compare patients having medial OA knees with and without preexisting GR. The occurrence of postoperative GR and hyperextension angle were also recorded. Follow-up extended from 24 mo to 70 mo, for a mean of 37.66 mo. No patients were lost to follow-up.

### Research results

Medial OA knees with and without preexisting GR showed similar clinical outcomes and incidence of postoperative GR following mobile bearing UKA. The mean Knee Society Score<sup>®</sup> was 97.97 for patients with preexisting GR and 96.91 for patients without GR. The incidences of postoperative GR were 3.13% and 0.7% for patients with preexisting GR and patients without preexisting GR, respectively.

### Research conclusions

Medial OA knee with preoperative GR is not a contraindication for mobile

bearing UKA.

### Research perspectives

Mobile bearing UKA with a little tight extension gap with and without use of a larger femoral component could prevent postoperative GR in the medial OA knee with preexisting GR. However, the causes of GR in OA knee patients without neuromuscular disorder remain unclear and should be identified by future studies.

## REFERENCES

- 1 **Murray DW**, Goodfellow JW, O'Connor JJ. The Oxford medial unicompartmental arthroplasty: a ten-year survival study. *J Bone Joint Surg Br* 1998; **80**: 983-989 [PMID: 9853489 DOI: 10.1302/0301-620X.80B6.0800983]
- 2 **Price AJ**, Waite JC, Svard U. Long-term clinical results of the medial Oxford unicompartmental knee arthroplasty. *Clin Orthop Relat Res* 2005; (**435**): 171-180 [PMID: 15930935 DOI: 10.1097/0003086-200506000-00024]
- 3 **Pongcharoen B**, Reutiwarangkoon C. The comparison of anterior knee pain in severe and non severe arthritis of the lateral facet of the patella following a mobile bearing unicompartmental knee arthroplasty. *Springerplus* 2016; **5**: 202 [PMID: 27026898 DOI: 10.1186/s40064-016-1914-1]
- 4 **Faour-Martín O**, Valverde-García JA, Martín-Ferrero MA, Vega-Castrillo A, de la Red Gallego MA, Suárez de Puga CC, Amigo-Liñares L. Oxford phase 3 unicompartmental knee arthroplasty through a minimally invasive approach: long-term results. *Int Orthop* 2013; **37**: 833-838 [PMID: 23503637 DOI: 10.1007/s00264-013-1830-8]
- 5 **Clarius M**, Hauck C, Seeger JB, Pritsch M, Merle C, Aldinger PR. Correlation of positioning and clinical results in Oxford UKA. *Int Orthop* 2010; **34**: 1145-1151 [PMID: 19813012 DOI: 10.1007/s00264-009-0881-3]
- 6 **Xue H**, Tu Y, Ma T, Wen T, Yang T, Cai M. Up to twelve year follow-up of the Oxford phase three unicompartmental knee replacement in China: seven hundred and eight knees from an independent centre. *Int Orthop* 2017; **41**: 1571-1577 [PMID: 28488164 DOI: 10.1007/s00264-017-3492-4]
- 7 **Jiang L**, Chen JY, Chong HC, Chia SL, Lo NN, Yeo SJ. Early Outcomes of Unicompartmental Knee Arthroplasty in Patients With Preoperative Genu Recurvatum of Non-neurological Origin. *J Arthroplasty* 2016; **31**: 1204-1207 [PMID: 26775838 DOI: 10.1016/j.arth.2015.12.029]
- 8 **Siddiqui MM**, Yeo SJ, Sivaiah P, Chia SL, Chin PL, Lo NN. Function and quality of life in patients with recurvatum deformity after primary total knee arthroplasty: a review of our joint registry. *J Arthroplasty* 2012; **27**: 1106-1110 [PMID: 22153947 DOI: 10.1016/j.arth.2011.10.013]
- 9 **Koo K**, Silva A, Chong HC, Chin PL, Chia SL, Lo NN, Yeo SJ. Genu Recurvatum versus Fixed Flexion after Total Knee Arthroplasty. *Clin Orthop Surg* 2016; **8**: 249-253 [PMID: 27583106 DOI: 10.4055/cios.2016.8.3.249]
- 10 **Ahlbäck S**. Osteoarthritis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh)* 1968; **Suppl 277**: 7-72 [PMID: 5706059]
- 11 **Insall JN**, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. *Clin Orthop Relat Res* 1989; (**248**): 13-14 [PMID: 2805470 DOI: 10.1097/00003086-198911000-00004]
- 12 **Lee WC**, Kwan YH, Chong HC, Yeo SJ. The minimal clinically important difference for Knee Society Clinical Rating System after total knee arthroplasty for primary osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 3354-3359 [PMID: 27324635 DOI: 10.1007/s00167-016-4208-9]
- 13 **Pongcharoen B**, Yakampor T, Charoencholvanish K. Patellar tracking and anterior knee pain are similar after medial parapatellar and midvastus approaches in minimally invasive TKA. *Clin Orthop Relat Res* 2013; **471**: 1654-1660 [PMID: 23361929 DOI: 10.1007/s11999-012-2778-5]
- 14 **Mullaji A**, Lingaraju AP, Shetty GM. Computer-assisted total knee replacement in patients with arthritis and a recurvatum deformity. *J Bone Joint Surg Br* 2012; **94**: 642-647 [PMID: 22529084 DOI: 10.1302/0301-620X.94B5.27211]
- 15 **Whittle MW**, Jefferson RJ. Functional biomechanical assessment of the Oxford Meniscal Knee. *J Arthroplasty* 1989; **4**: 231-243 [PMID: 2795030 DOI: 10.1016/S0883-5403(89)80019-1]
- 16 **Miller RK**, Goodfellow JW, Murray DW, O'Connor JJ. In vitro measurement of patellofemoral force after three types of knee replacement. *J Bone Joint Surg Br* 1998; **80**: 900-906 [PMID: 9768906 DOI: 10.1302/0301-620X.80B5.8460]
- 17 **Price AJ**, Rees JL, Beard DJ, Gill RH, Dodd CA, Murray DM. Sagittal plane kinematics of a mobile-bearing unicompartmental knee arthroplasty at 10 years: a comparative in vivo fluoroscopic analysis. *J Arthroplasty* 2004; **19**: 590-597 [PMID: 15284980 DOI: 10.1016/j.arth.2003.12.082]
- 18 **Goodfellow JW**, Kershaw CJ, Benson MK, O'Connor JJ. The Oxford Knee for unicompartmental osteoarthritis. The first 103 cases. *J Bone Joint Surg Br* 1988; **70**: 692-701 [PMID: 3192563 DOI: 10.1302/0301-620X.70B5.3192563]
- 19 **Meding JB**, Keating EM, Ritter MA, Faris PM, Berend ME. Total knee replacement in patients with genu recurvatum. *Clin Orthop Relat Res* 2001; (**393**): 244-249 [PMID: 11764354 DOI: 10.1097/0003086-200112000-00027]

**P- Reviewer:** Fernandez-Fairen M, Kuru T, Liu J  
**S- Editor:** Ji FF **L- Editor:** A **E- Editor:** Song H



Randomized Clinical Trial

## Acute effects of partial-body vibration in sitting position

Yannik Faes, Nora Banz, Nathalie Buscher, Angela Blasimann, Lorenz Radlinger, Patric Eichelberger, Achim Elfering

Yannik Faes, Nora Banz, Nathalie Buscher, Achim Elfering, Department of Work and Organizational Psychology, University of Bern, Bern 3012, Switzerland

Angela Blasimann, Lorenz Radlinger, Patric Eichelberger, Department of Health Professions, Bern University of Applied Sciences, Bern 3008, Switzerland

ORCID number: Yannik Faes (0000-0002-0062-9058); Angela Blasimann (0000-0003-0934-8284); Lorenz Radlinger (0000-0002-0326-6264); Achim Elfering (0000-0003-4274-0261).

**Author contributions:** Faes Y, Banz N and Buscher N designed the study, performed the experiment, did the analyses and wrote the manuscript; Blasimann A and Radlinger L provided support at the physiological measurements; Eichelberger P constructed the vibration platform and provided technical support in relation to the vibration platform; Elfering A supervised the design of the study and analyses and wrote the manuscript.

**Institutional review board statement:** This study was reviewed and approved by the ethical committee of the responsible University faculty (University of Bern; Nr. 2016-5-000004).

**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 written 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.

**CONSORT 2010 statement:** The guidelines of the CONSORT 2010 statement had adopted.

**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, MSc, PhD, Professor, Department of Work and Organizational Psychology, University of Bern, Fabrikstrasse 8, Bern 3012, Switzerland. [achim.elfering@psy.unibe.ch](mailto:achim.elfering@psy.unibe.ch)  
**Telephone:** +41-31-6313639

**Received:** March 28, 2018

**Peer-review started:** March 29, 2018

**First decision:** May 2, 2018

**Revised:** May 20, 2018

**Accepted:** May 23, 2018

**Article in press:** May 23, 2018

**Published online:** September 18, 2018

### Abstract

#### AIM

To investigate the acute effects of sinusoidal and stochastic resonance partial-body vibration in sitting position, including muscle activity, heart rate variability, balance and flexibility.

#### METHODS

Fifty healthy participants were assigned randomly to two training conditions: A sinusoidal partial-body vibration (SIN, 8 Hz) or a stochastic resonance partial-body vibration (STOCH,  $8 \pm 2$  Hz). For baseline assessment participants sat on the vibration platform without vibration. Both training conditions consisted of five series of a one-minute vibration training and a one-minute

break between them. In this experimental study surface electromyography (EMG) of the erector spinae (ES), one of the back muscles, and heart rate variability (HRV) was measured at baseline and during training. Balance and flexibility were assessed at baseline and immediately after training. Balance was measured with the modified star excursion balance test (mSEBT) and flexibility was assessed through the modified fingertip-to-floor method (mFTF).

## RESULTS

Paired sample *t*-test showed a significant increase in balance that was restricted to STOCH ( $t = -2.22$ ,  $P = 0.018$ ; SIN:  $t = -0.09$ ,  $P = 0.466$ ). An increase in flexibility was also restricted to STOCH ( $t = 2.65$ ,  $P = 0.007$ ; SIN:  $t = 1.41$ ,  $P = 0.086$ ). There was no significant change of muscle activity in the ES-EMG in STOCH or SIN conditions. In both training conditions, HRV decreased significantly, but remained in a low-load range (STOCH:  $t = 2.89$ ,  $P = 0.004$ ; SIN:  $t = 2.55$ ,  $P = 0.009$ ).

## CONCLUSION

In sitting position, stochastic resonance partial-body vibration can improve balance and flexibility while cardiovascular load is low. STOCH can be a valuable training option to people who are unable to stand (*e.g.*, people, who are temporarily wheelchair-bound).

**Key words:** Partial-body vibration; Balance; Flexibility; Sinusoidal; Stochastic resonance

© The Author(s) 2018. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** This experimental study shows an immediate improvement of balance and flexibility after one training session of stochastic resonance partial-body vibration (STOCH) in sitting position. STOCH in sitting position is a promising complement to stochastic resonance whole-body vibration (SR-WBV) in standing position, especially for individuals who are unable to do SR-WBV (*e.g.*, people who are temporarily wheelchair-bound).

Faes Y, Banz N, Buscher N, Blasimann A, Radlinger L, Eichelberger P, Elfering A. Acute effects of partial-body vibration in sitting position. *World J Orthop* 2018; 9(9): 156-164 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/156.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.156>

## INTRODUCTION

Musculoskeletal diseases (MSD) are among the most common global health problems<sup>[1]</sup>. Wieser, Tomonaga<sup>[2]</sup> calculated the direct costs of MSD for the Swiss health system to be between CHF 8.7 and 11.4 billion per year. Together with cardiovascular diseases (10.3 billion),

these are the highest costs for non-communicable diseases. Long-lasting vibration exposure at work has shown to be a risk factor for musculoskeletal diseases (MSD)<sup>[3]</sup>, whereas a brief vibration experience may lead to beneficial training effects<sup>[4]</sup>.

Thereby, stochastic resonance whole-body vibration (SR-WBV) is especially promising<sup>[5,6]</sup>. Compared to sinusoidal vibration which common vibration platforms are working with, stochastic vibration is random and uses lower frequency vibration exposure up to 12 Hz<sup>[7,8]</sup>.

Effects of SR-WBV at the worksite are auspicious, especially in those with chronic MSD<sup>[9]</sup>. As cardiovascular load during SR-WBV is low<sup>[10]</sup>, no sweating occurs during the training, making it especially promising for workplace interventions. Musculoskeletal well-being increased after a 4-wk SR-WBV training in workers of a steel manufacturing company<sup>[11]</sup>. The same was reported for employees that engaged in sedentary work. With those who suffered from back pain prior to SR-WBV profiting the most<sup>[12]</sup>. These positive effects of SR-WBV also appeared in employees of a university hospital after a 8-wk randomized controlled trial, having the highest impact on those with baseline health restraints<sup>[13]</sup>. SR-WBV is practiced in standing position. However, some older individuals and individuals in a wheel-chair may not be able to stand. As suggested by Eichelberger<sup>[14]</sup> in a single-case study vibration training in sitting position might be "advantageous in deconditioned persons, who suffer from frailty, musculoskeletal complaints, Parkinson's disease, multiple sclerosis or after a stroke". Therefore, this experimental study investigates partial-body vibration in sitting position and its related acute effects.

## Partial-body vibration in sitting position

Thereby, this study tests both, sinusoidal partial-body vibration (SIN) and stochastic resonance partial-body vibration (STOCH). We use the same vibration device as Eichelberger<sup>[14]</sup>. In standing, as well as in sitting position, especially stochastic vibration provoked muscle activity<sup>[14,15]</sup> while cardiovascular activation was low<sup>[10,16]</sup>. Low cardiovascular activation makes stochastic vibration an appropriate training tool for older individuals and people with health problems<sup>[5]</sup>.

According to previous research with whole-body vibration in standing position, we expect an increased muscle activity of the erector spinae (ES), one of the back muscles, during partial-body vibration in sitting position (H1). In addition, we expect low or absent cardiovascular activation during partial-body vibration in sitting position. Hence, heart rate variability (HRV) during training is expected to be unchanged or only slightly lower than during baseline measurement (H2).

## Better balance, better flexibility

In Switzerland, every fourth accident is due to a slip, trip and fall incident<sup>[17]</sup>. They are also the most frequent accidents among office workers<sup>[18]</sup>. Better balance

prevents slip, trip and fall incidents<sup>[19]</sup>. Aside from promising effects on musculoskeletal wellbeing, positive effects of SR-WBV were also found on surefootedness and balance in white-collar employees<sup>[12]</sup> and in health-care professionals<sup>[13]</sup>. Hence, we expect balance to be better after partial-body vibration training compared to baseline (H3).

Previous studies showed an increase of flexibility due to whole-body vibration training in the elderly<sup>[20]</sup>, in healthy, young adults<sup>[21]</sup> as well as in young gymnasts<sup>[21]</sup>. In consequence, we expect flexibility after partial-body vibration training to be better than at baseline (H4).

### **How stochastic vibration works**

While vibration frequency at sinusoidal vibration is constant, stochastic vibration changes randomly within a frequency range. 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”<sup>[22]</sup>. During stochastic vibration, upcoming vibration movements can not be anticipated by the human body, so it is constantly challenged to adapt its neural and muscular reactions. Moreover, the human body shows no muscular fatigue during the application<sup>[8,23-25]</sup>. It seems that an interaction of different types of neurophysiologic sensors is provoked by stochastic vibration while afferent and efferent signals are adjusted. This probably acts as exercise for the sensorimotor system<sup>[8]</sup>.

In the current experimental study, we randomly assigned participants to SIN and STOCH. We expect both, SIN and STOCH to have acute effects on activity of surface electromyography (EMG), HRV, balance, and flexibility. Differences in training effectiveness between SIN and STOCH are likely to emerge only after longer training periods. However, based on previous findings on sinusoidal versus stochastic vibration in whole-body vibration training, we expect changes in muscle activity, HRV, balance, and flexibility to be more distinct in stochastic training condition than in sinusoidal training condition.

## **MATERIALS AND METHODS**

### **Ethics**

The study was performed in consensus with all requirements defined by the Swiss Society of Psychology and was conducted with the understanding and the consent of the human subject. The Ethical Committee of the responsible University faculty (University of Bern) has approved the study (No. 2016-5-000004).

### **Participants**

Expecting a moderate effect size ( $d = 0.5$ ) for the  $t$ -test analysis between two dependent means and a requirement of 80% power to detect an existing difference, the required sample size was 26 partici-

pants for each training condition SIN and STOCH. The inclusion criterion for the participants was to be in good health. The exclusion criteria were being pregnant, having osteosynthesis material (such as implants, screws, etc.) in the body, musculoskeletal disorders, joint problems (especially regarding the knee, hip and back), herniated discs, rheumatism (such as spondylitis, gout, osteoporosis, osteoarthritis), cardiovascular complaints and disorders related to the sense of balance (such as a hearing loss). Twenty-six participants took part in each training condition, so overall 52 participants participated in the study. Due to a broken cable, EMG measurements of two participants were not recorded. Therefore, these data sets were removed for data analysis. Participants who were students at the associated university were rewarded with two of 15 mandatory hours as a participant in studies.

### **Vibration platform**

The vibration platform used in this study is a functional prototype consisting of a plate with a hydraulic vibration, constructed specifically for vibration training in sitting position. The device provides a range of motion of  $\pm 13^\circ$  around each of the three rotation axes and frequencies up to 15 Hz. Stochastic vibration can be introduced through random variation of frequency, amplitude or rotation axis. The chosen amplitude and frequency of the vibration was recommended by one of the co-authors (PE<sup>[14]</sup>). During SIN, an amplitude of  $0.5^\circ$  was applied in medial-lateral direction during a vibration frequency of 8 Hz. During STOCH, amplitude as well as frequency varied over a spectrum of 25%.

### **Muscle activity**

Measurements of the muscle activity of the ES during MVC, baseline and training session were recorded for each participant. Therefore, surface electrodes were used (Ambu<sup>®</sup> BlueSensor N, Synmedic AG, Zürich) and “placed at 2 finger width lateral from the proc. spin. of L1” according to the SENIAM recommendation (Surface Electromyography for the Non-Invasive Assessment of Muscles)<sup>[26]</sup>. EMG signals were forwarded from a transmitter (TeleMyoTM 2400T G2, Noraxon Inc. United States, Velamed GmbH, Medizintechnik und Biomechanische Konzepte, Köln, Germany) to a receiver (TeleMyoTM 2400R Receiver, Noraxon Inc. United States, Velamed GmbH, Medizintechnik und Biomechanische Konzepte, Köln, Germany), which transformed these digital signals into analogue outputs. For recording and processing the data, the software ADS (analog and digital signal processing<sup>®</sup>, uk-labs, Kempen, Germany) was used.

### **Heart rate variability**

The measurement of the R-R intervals (the interval from the onset of one R wave to the onset of the next one<sup>[27]</sup>) was taken while the participant was sitting on the vibration platform during baseline and training

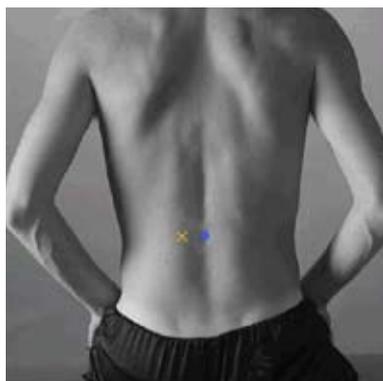


Figure 1 Placement of the electrodes according to SENIAM<sup>[27]</sup>.



Figure 2 Sitting position on the vibration platform. HRV: Heart rate variability; EMG: Electromyography.

session. HRV was measured with Polar V800 and heart rate sensor Polar H7 (©Polar Electro 2016). Giles, Draper<sup>[28]</sup> showed that R-R intervals and HRV do not differ between recordings from Polar V800 and electrocardiography (ECG).

### Balance

Balance was measured using the modified star excursion balance test (mSEBT) from Hertel, Braham<sup>[29]</sup> once after baseline condition and once after training session. The mSEBT measures dynamic balance into the three directions anterior, posteromedial and posterolateral. According to Gribble, Kelly<sup>[30]</sup> and Hertel, Miller<sup>[31]</sup> intra-test reliability ( $r = 0.84$  to  $0.93$ ) and test-retest reliability ( $r = 0.89$  to  $0.93$ ) are high. To exclude effects related to gender, it was important to normalize excursion distances to individual leg length of each participant<sup>[32]</sup>.

### Flexibility

The modified fingertip-to-floor method (mFTF) was used to assess flexibility. It was measured once after baseline condition and once after training session. Compared to the fingertip-to-floor method (FTF), the mFTF has the advantage that the participant stands on a box, so that measurements can be taken of participants who are able to touch the floor or reach beyond the level

of the floor<sup>[33]</sup>. Therefore, negative values indicate a better flexibility than positive values. This test measures unspecific flexibility because spine, pelvis, hip joint and arms are involved<sup>[34]</sup>. Gauvin, Riddle<sup>[33]</sup> report high test-retest reliability ( $r = 0.98$ ), as well as high inter-tester reliability ( $r = 0.95$ ) of the mFTF. Stiffness is reported to be higher in the morning and a maximum of flexibility occurs between midday and midnight<sup>[35]</sup>. In order to partly control for stiffness and provide similar test conditions, every participant was tested in the afternoon or early evening.

### Procedure

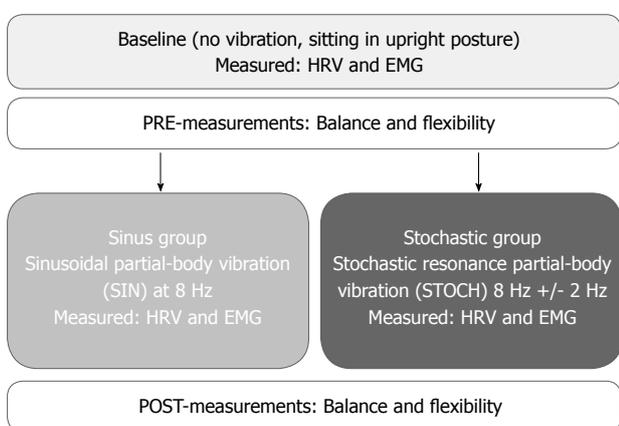
The study was conducted at the movement laboratory of Bern University of Applied Sciences, Applied Research and Development Physiotherapy. To make sure the procedure was standardized, a case report form (CRF) was prepared. The measurements for one participant lasted approximately 90 min. During this time two of three examiners (YF, NB, NB) needed to be present. The first examiner took the lead with the measurements, while the second examiner acted as his assistant. To prevent error due to monotony and routine, the role of the first and second examiner was changed regularly between the three examiners. After reading the study-information, participants signed a consent form. While a surface EMG electrode was placed on the ES (Figure 1), participants answered a demographical and behavioral questionnaire using Qualtrics (©2016 Qualtrics LLC), installed on an iPad Air2 (©2015 Apple Inc.). With an impedance meter (Digitimer model D175, Digitimer Ltd. Welwyn Garden City, United Kingdom) the skin resistance was tested and rated as sufficient being equal or lower as  $5 \text{ k}\Omega$ . Afterwards, a measurement of a maximum voluntary contraction (MVC) of the ES was made in order to be used as reference value for the EMG measurements, rated as 100%<sup>[36]</sup>. While lying prone on a bench, participants were asked to extend their back against one examiner's resistance. With this standardized test<sup>[36]</sup>, MVC values of the ES were captured. For the MVC measurements, the participants were asked to hold the MVC 3 times for 5 s.

For the following baseline measurements, the participants had to sit on the vibration platform in an upright position (Figure 2). They were asked to keep calm and to focus on a black point on the wall at a distance of 2.5 m while no vibration occurred for one minute. During this time muscle activity and HRV were recorded. Then, participants were asked to complete the modified star excursion balance test (mSEBT) of Hertel, Braham<sup>[29]</sup> to assess balance. They were instructed to start with arms akimbo, then stand on one leg and stretch out the other leg as far as possible to touch the floor with the tip of their toes. The maximum distance reached without losing balance or lifting the supporting leg was measured and noted. The same procedure was repeated five times in three directions (anterior, posteromedial and posterolateral) with both legs.

**Table 1** Descriptive and inferential statistics

Variable	STOCH (n = 25)		SIN (n = 25)		t	P
	M	SD	M	SD		
Sex (m, f)	7m, 18f		10m, 15f		-0.89	0.381
Age (yr)	25.12	2.89	25.40	4.38	0.27	0.791
BMI (kg/m <sup>2</sup> )	22.81	3.81	23.54	3.50	0.70	0.487
Sport (1 "rarely" - 6 "prof.")	2.25	1.11	2.36	1.08	0.35	0.727
Smoking (s, ns)	7s, 18ns		8s, 17ns		0.30	0.763
Last time nicotine (h)	25.86	21.71	7.75	16.35	-1.84	0.089
Last time caffeine (h)	7.65	8.25	9.40	9.08	0.64	0.527
EMG ES (%MVC)	29.67	22.43	25.17	18.50	-0.77	0.443
HRV (RMSSD, ms)	35.21	16.77	35.69	19.52	0.09	0.926
Balance-test (cm)	73.34	8.23	77.77	6.75	2.08	0.043
Flexibility-test (cm)	-2.02	9.2	-2.01	9.54	0.001	0.999

EMG: Electromyography, muscular activation expressed as percentage of peak activation measured at maximal voluntary contraction (%MVC) of the lower back muscle erector spinae (ES); HRV: Heart rate variability was measured with the square root of the mean of the sum of the squares of the differences (RMSSD). Balance was measured using the modified star excursion balance test (mSEBT) and expressed in centimeter; Flexibility was assessed with the fingertip-to-floor method (mFTF) and expressed in centimeter.



**Figure 3** Flowchart of the procedure. EMG: Electromyography, muscular activation of the lower back muscle erector spinae (ES); HRV: Heart rate variability was measured with Polar V800. Balance was measured using the modified star excursion balance test (mSEBT) and expressed in centimeter; Flexibility was assessed with the fingertip-to-floor method (mFTF) and measured in centimeter.

As reported by Blasimann<sup>[37]</sup>, flexibility was assessed through the modified fingertip-to-floor method (mFTF). For this test participants stood on a box with both ankles touching each other. They were then instructed to keep their legs and arms straight and bend over as far as possible to push down a control bar in front of them. After one trial run, the same procedure was performed three times. While the first examiner gave verbal instructions, the second examiner wrote down the finger-floor distance in mm and put the control bar back to the starting position. After these tests, the baseline measurement was over and the training session began.

Participants were randomly assigned to SIN (8 Hz) or STOCH (8 ± 2 Hz). As the sequence of the two training conditions was alternated across trials in the movement laboratory, randomization was achieved through time of participation, which means that the first

participant attended in SIN, the second in STOCH and so forth. Participants were blinded with respect to their training condition. However, a blinding of the examiners was not feasible.

The session consisted of five series, which lasted one minute each, with a one-minute break in between. This training regime with five series of a one-minute vibration training was based more on empirical experience from other studies about stochastic vibration training<sup>[11,12]</sup> than on scientific evidence, because the training parameters of stochastic vibration training show a wide range of applications that are not as well known as they are for strength or endurance training<sup>[38]</sup>. A vibration frequency of 8 ± 2 Hz was recommended for the STOCH condition, so acceleration exposure on the body was low<sup>[14]</sup>. For a better comparison, 8 Hz were selected for the SIN condition, too. During the training session, the participant was again sitting in an upright position on the vibration platform focusing on a point on the wall at a distance of 2.5 m while muscle activity and HRV were recorded. After the training session, the same measurements of balance and flexibility as described above were repeated. The whole procedure is shown in Figure 3.

**Statistical analysis**

Muscle activity, HRV as well as balance and flexibility were analyzed in a dependent sample t-test to examine differences between baseline and training conditions. Since all the hypotheses were directed, P-values were one-tailed with an α-level set at 5%. HRV, balance and flexibility were approximately normally distributed (P > 0.05), whereas EMG was not approximately normally distributed as assessed by the Kolmogorov-Smirnov-Test, P < 0.05. However, according to Field<sup>[39]</sup> the analyses of the hypotheses can be considered robust against violations of the normal distribution due to the same group size. Pearson's descriptive statistics for the collected variables are shown in Table 1.

**Table 2** Results of *t*-tests for each training condition

	STOCH ( <i>n</i> = 25)				SIN ( <i>n</i> = 25)			
	BL		T		BL		T	
	mean ± SD	mean ± SD	<i>t</i>	<i>P</i>	mean ± SD	mean ± SD	<i>t</i>	<i>P</i>
EMG ES (%MVC)	29.67 ± 22.43	32.32 ± 24.03	-0.96	0.174	25.17 ± 18.50	26.07 ± 14.73	-0.51	0.307
HRV (RMSSD, msec)	35.21 ± 16.77	29.10 ± 12.64	2.89	0.004	35.69 ± 19.52	29.60 ± 12.90	2.55	0.009
Balance-test (cm)	73.34 ± 8.23	75.28 ± 9.35	-2.22	0.018	77.77 ± 6.75	77.82 ± 6.12	-0.09	0.466
Flexibility-test (cm)	-2.02 ± 9.20	-2.53 ± 9.08	2.65	0.007	-2.01 ± 9.54	-2.55 ± 9.75	1.41	0.086

Left: Stochastic resonance partial-body vibration (STOCH) at Baseline (BL) and Training condition (T); Right: Sinusoidal partial-body vibration (SIN) at BL and T; EMG: Electromyography, activation expressed as percentage of activation measured at maximal voluntary contraction (%MVC) of the lower back muscle erector spinae (ES); HRV: Heart rate variability was measured with the square root of the mean of the squares of the differences (RMSSD); Balance was measured using the modified star excursion balance test (mSEBT) and flexibility with fingertip-to-floor method (MFTF).

## RESULTS

### Participant characteristics

Data of 50 healthy participants (33 females and 17 males, mean age = 25.3 years, SD = 3.7 years; BMI = 23.17 ± 3.64), assigned evenly to STOCH, SIN respectively, were analyzed in this study. Datas of twenty-five participants for each group STOCH and SIN were analyzed. The two groups showed no significant differences in any demographic characteristics or in baseline muscle activity, HRV or flexibility. However, balance in the SIN group was significantly better (longer distance reached) at baseline than in the STOCH group. *T*-test results and descriptive statistics for both training conditions are shown in Table 2.

### Higher muscle activity of the ES during STOCH and SIN (H1)

Overall, vibration training had no significant effect on muscle activity of the ES ( $t = -1.09$ ,  $P = 0.140$ ,  $n = 50$ ). Although not significantly, muscle activity of the ES tended to be slightly higher during vibration training (29.20 ± 19.98 %MVC) than during baseline measurement (27.42 ± 20.47 %MVC).

Focusing on both training conditions, there was also no significant effect of STOCH ( $t = -0.96$ ,  $P = 0.174$ ,  $n = 25$ ) and SIN ( $t = -0.51$ ,  $P = 0.307$ ,  $n = 25$ ) on muscle activity of the ES found. Although not significantly, muscle activity of the ES tended to be slightly higher during STOCH (32.32 ± 24.03 %MVC) than during baseline measurement (29.67 ± 22.43 %MVC) and also higher during SIN (26.07 ± 14.73 %MVC) than during baseline measurement (25.17 ± 18.50 %MVC). According to Cohen<sup>[40]</sup>, effect sizes are described as small ( $d = 0.2$ ), medium ( $d = 0.5$ ), and large ( $d \geq 0.8$ ). Effect sizes using Cohen's  $d^{[40]}$  for muscle activity of the ES for overall vibration was  $d = -0.087$ , for the STOCH group  $d = -1.136$  and for the SIN group  $d = -0.490$ .

### Lower HRV during STOCH and SIN (H2)

A significant effect on HRV was found during overall vibration training ( $t = 3.86$ ,  $P = 0.0003$ ,  $n = 50$ ) compared to baseline measurement. HRV was signi-

ficantly lower during vibration training (29.34 ± 12.65 ms) than during baseline measurement (35.45 ± 18.01 ms).

Focusing on both training conditions, STOCH ( $t = 2.89$ ,  $P = 0.004$ ,  $n = 25$ ) and SIN ( $t = 2.55$ ,  $P = 0.009$ ,  $n = 25$ ) have a significant effect on HRV. HRV during STOCH (29.10 ± 12.64 ms) as well as during SIN (29.60 ± 12.90 ms) were both significantly lower compared to baseline measurements (35.21 ± 16.77 ms) and (35.69 ± 19.52 ms) accordingly. Effect sizes using Cohen's  $d^{[40]}$  on HRV for overall vibration was  $d = 0.355$ , for STOCH  $d = 0.342$  and  $d = 0.320$  for SIN, respectively.

### Increase in balance after STOCH and SIN (H3)

A significant effect on balance was found after overall vibration training ( $t = -1.83$ ,  $P = 0.037$ ,  $n = 50$ ). Compared to baseline measurement (75.55 ± 7.77 cm), overall values for balance were significantly higher after vibration training (76.55 ± 7.92 cm).

Specifically, a significant effect was found after STOCH ( $t = -2.22$ ,  $P = 0.018$ ,  $n = 25$ ) but not after SIN ( $t = -0.09$ ,  $P = 0.466$ ,  $n = 25$ ). Balance was significantly increased after STOCH (75.28 ± 9.35 cm) compared to baseline measurement (73.34 ± 8.23), but not after SIN (77.82 ± 6.12 cm) compared to baseline measurement (77.77 ± 6.75 cm). Effect size using Cohen's  $d^{[40]}$  on balance for overall vibration was  $d = -0.127$ , for STOCH  $d = -0.216$  and for SIN  $d = -0.008$ .

### Increase in flexibility after STOCH (H4)

Overall, vibration training had a significant effect on flexibility ( $t = 2.49$ ,  $P = 0.008$ ,  $n = 25$ ). Flexibility was significantly increased after overall vibration training (-2.54 ± 9.33 cm) compared to baseline measurement (-2.02 ± 9.27 cm). Specifically, a significant effect on flexibility could only be found after STOCH ( $t = 2.65$ ,  $P = 0.007$ ,  $n = 25$ ), but not after SIN ( $t = 1.41$ ,  $P = 0.086$ ,  $n = 25$ ). Flexibility was significantly increased after STOCH (-2.53 ± 9.08 cm) compared to baseline measurement (-2.02 ± 9.20 cm), but not after SIN (-2.55 ± 9.75 cm) compared to baseline measurement (-2.01 ± 9.54 cm). Effect size using Cohen's  $d^{[40]}$  on flexibility for overall vibration was  $d = 0.057$ , for STOCH

$d = 0.058$  and  $d = 0.055$  for SIN, respectively.

## DISCUSSION

In the current experimental study, we expected both, SIN and STOCH to have acute effects on muscle activity, HRV, balance, and flexibility. Although differences in training effectiveness between the two groups are only likely to emerge after longer training periods, we expected changes in measured variables to be more distinct in stochastic training condition than in sinusoidal training condition.

Activity of the ES muscle did not increase with vibration training (H1). This finding goes against our expectation. A possible explanation could be, that the ES was already active during sitting position with upright posture at baseline measurement, so there was no significant increase of muscle activity during vibration training. Further studies on vibration training in the sitting position should focus on that. Our second hypothesis was confirmed, as there was a significant, but low cardiovascular activation in HRV, that was lower during training than at baseline (H2). Although HRV significantly decreased, it maintained in a low-load range<sup>[41]</sup>. In line with findings from SR-WBV<sup>[10,16]</sup>, cardiovascular activation was low. The method seems suitable for older individuals and patients with mild cardiovascular problems. As expected, balance (H3) and flexibility (H4) significantly increased.

Looking at separate analyses for training effectiveness in sinusoidal and stochastic vibration conditions, the stochastic vibration condition seemed to contribute more to overall changes than the sinusoidal vibration condition. Balance and flexibility increased significantly after one training session of STOCH, but not after SIN. This indicates that positive effects from previous studies about stochastic vibration in standing position would also appear in sitting position<sup>[12,15,42]</sup>. Group differences can not be explained by differences in muscular activity of the ES.

To assess cardiac activity, we measured HRV during SIN and STOCH. HRV is also known as a stress index<sup>[43,44]</sup>. As this study was conducted on a prototype of a vibration platform, participants would possibly be somewhat anxious about the experiment. As expected, HRV was significantly lower during STOCH than SIN but the RMSSD-value was within the range of  $27 \pm 12$  at all time as is recommended by Task Force of the European Society of Cardiology<sup>[41]</sup>. This implies that cardiac activation and/or stress level during SIN and STOCH was still low.

SR-WBV training seems to be a safe training intervention. Very few side effects of whole-body vibration were reported in a review of 112 studies. 104 studies that used sinusoidal whole-body vibration, reported 0.00120% side effects, whereas eight studies used SR-WBV and reported 0.00069% side effects. Additionally, side effects from sinusoidal whole-body vibration were

more serious compared to those from SR-WBV<sup>[45]</sup>. As mentioned by Eichelberger, Fankhauser<sup>[14]</sup> STOCH might be advantageous in deconditioned persons, who suffer from frailty, musculoskeletal complaints, Parkinson's disease, multiple sclerosis or after a stroke. Because the training was on a prototype of a vibration platform, which effects were only tested in a single case study before<sup>[14]</sup>, it was important that our participants were healthy.

In longitudinal studies SR-WBV showed promising results to increase musculoskeletal well-being<sup>[11-13]</sup>. As SR-WBV is practiced in standing position, these results are limited to the standing position. Therefore, further longitudinal studies should focus on SIN and STOCH in sitting position to make these benefits available to people who are unable to do SR-WBV (*e.g.*, people who are temporarily wheelchair-bound).

With this study we were able to make the first step in this direction. We found an immediate improvement of balance and flexibility after one training session of STOCH while cardiac-activation was low, but could not find a higher muscle activity of the ES in the lower back during the training session. This study had an experimental design, and many potential confounders were controlled by randomization. The participants were blinded with respect to their training condition. However, a blinding of the primary investigator was not feasible. As only one superficial back muscle was measured, there might have been an increase of muscle activity in other back muscles which were not measured.

## ARTICLE HIGHLIGHTS

### Research background

Stochastic resonance whole-body vibration (SR-WBV) is a promising health-intervention at the worksite. In previous works including 4 or even 8 weeks of training, SR-WBV was found to improve musculoskeletal pain and balance, measured as self-report and as recorded body sway on a balance platform. Improved 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.

### Research motivation

SR-WBV is practiced in standing position. However, some older individuals and individuals in a wheel-chair may not be able to stand. Therefore, this experimental study investigates partial-body vibration in sitting position and its related acute effects.

### Research objectives

The objective of this study was to investigate and quantify the acute effects of partial-body vibration in sitting position on muscle activity, heart-rate variability, balance and flexibility.

### Research methods

The vibration platform used in this study is a functional prototype, constructed specifically for vibration training in sitting position. Every participant attended a baseline and a training condition. For baseline assessment participants sat on the vibration platform without vibration. The training condition was either a sinusoidal partial-body vibration (SIN, 8 Hz) or a stochastic resonance partial-body vibration (STOCH,  $8 \pm 2$  Hz). Surface electromyography (EMG) of the

erector spinae (ES), one of the back muscles, and heart rate variability (HRV) were measured at baseline and during training. Balance and flexibility were assessed at baseline and immediately after training. Balance was measured with the modified star excursion balance test (mSEBT) and flexibility was assessed through the modified fingertip-to-floor method (mFTF).

### Research results

Paired sample *t*-test showed a significant increase in balance (STOCH:  $t = -2.22$ ,  $P = 0.018$ ; SIN:  $t = -0.09$ ,  $P = 0.466$ ) as well as in flexibility (STOCH:  $t = 2.65$ ,  $P = 0.007$ ; SIN:  $t = 1.41$ ,  $P = 0.086$ ) only after stochastic vibration in sitting position. There was no significant change of muscle activity in the ES-EMG in both training conditions. Also, HRV decreased significantly in both training conditions, but remained in a low-load range (STOCH:  $t = 2.89$ ,  $P = 0.004$ ; SIN:  $t = 2.55$ ,  $P = 0.009$ ).

### Research conclusions

This experimental study showed benefits in balance and flexibility only for stochastic but not for sinusoidal vibration. Stochastic vibration in sitting position could be a promising complement to stochastic resonance whole-body vibration in standing position, especially for individuals who are unable for the standing position (e.g., people who are temporarily wheelchair-bound).

### Research perspectives

As immediate effects of stochastic vibration in sitting position have not been tested before, especially on this prototype device, we needed to make sure that stochastic vibration in sitting position did have the expected effect and that no negative side-effects emerge from one single vibration training in this study. If side-effects would have appeared in healthy people, the device would not be used on an unhealthy sample in the future. As we observed the intended effects, and side effects did not appear in healthy people in this study, this device could possibly be used with patients in future research. Also, further studies should focus on long-term effects of partial-body vibration in sitting position.

## REFERENCES

- 1 **GBD 2016 Disease and Injury Incidence and Prevalence Collaborators.** Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; **390**: 1211-1259 [PMID: 28919117 DOI: 10.1016/S0140-6736(17)32154-2]
- 2 **Wieser S, Tomonaga Y, Riguzzi M, Fischer B, Telser H, Pletscher M, Eichler K, Trost M, Schwenkglens M.** Die Kosten der nichtübertragbaren Krankheiten in der Schweiz (Costs of non-communicable diseases in Switzerland). Bundesamt für Gesundheit BAG, Bern, 2014. Available from: URL: <https://www.bag.admin.ch/dam/bag/de/dokumente/npp/forschungsberichte/forschungsberichte-ncd/kosten-ncd-in-der-schweiz.pdf.download.pdf/Schlussbericht%20COI%20NCDs%20in%20CH%202014%2007%2021.pdf>
- 3 **Elfering A, Mannion AF.** Epidemiology and risk factors of spinal disorders, in *Spinal disorders*. Springer, 2008: 153-173 [DOI: 10.1007/978-3-540-69091-7\_6]
- 4 **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]
- 5 **Herren K, Hotz Hangartner 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]
- 6 **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]
- 7 **Cardinale M, Wakeling J.** Whole body vibration exercise: are vibrations good for you? *Br J Sports Med* 2005; **39**: 585-589; discussion 589 [PMID: 16118292 DOI: 10.1136/bjism.2005.016857]
- 8 **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]
- 9 **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]
- 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 **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]
- 12 **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]
- 13 **Elfering A, Schade V, Burger C, Stöcklin L, Bauer 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, 2014: 305-314. Available from: URL: <http://boris.unibe.ch/65745/>
- 14 **Eichelberger P, Fankhauser R, Geering R, Rogan S.** Trunk muscle activity and acceleration of the spine during partial-body vibration in a sitting position-a single case study. *Physiotherapy* 2015; **101**: e347 [DOI: 10.1016/j.physio.2015.03.556]
- 15 **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]
- 16 **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]
- 17 **SUVA.** Unfallstatistik UVG 2017, Koordinationsgruppe für die Statistik der Unfallversicherung, K.f.d.S.d. Unfallversicherung, Editor. 2017. Available from: URL: <https://www.unfallstatistik.ch/d/publik/unfstat/pdf/Ts17.pdf>
- 18 **EKAS.** Arbeitssicherheit und Gesundheitsschutz in Bürobetrieben. 2017. Available from: URL: <http://www.ekas.admin.ch/redirect.php?cat=f%2BR3rLeQL4g%3Did=94>
- 19 **Okubo Y, Schoene D, Lord SR.** Step training improves reaction time, gait and balance and reduces falls in older people: a systematic review and meta-analysis. *Br J Sports Med* 2017; **51**: 586-593 [PMID: 26746905 DOI: 10.1136/bjsports-2015-095452]
- 20 **Kawanabe K, Kawashima A, Sashimoto I, Takeda T, Sato Y, Iwamoto J.** Effect of whole-body vibration exercise and muscle strengthening, balance, and walking exercises on walking ability in the elderly. *Keio J Med* 2007; **56**: 28-33 [PMID: 17392595 DOI: 10.2302/kjm.56.28]
- 21 **Issurin VB, Liebermann DG, Tenenbaum G.** Effect of vibratory stimulation training on maximal force and flexibility. *J Sports Sci* 1994; **12**: 561-566 [PMID: 7853452 DOI: 10.1080/02640419408732206]
- 22 **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]
- 23 **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]
- 24 **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]
- 25 **Schollhorn WI, Beckmann H, Michelbrink M, Sechelmann M, Trockel M.** Does noise provide a basis for the unification of motor

- learning theories? *Int J Sport Psychol* 2006; **37**: 1-22
- 26 Seniam project. Cited 17 May 2018. Available from: URL: <http://www.seniam.org/>
- 27 **Farlex P.** R-R interval, in Medical Dictionary. 2012. Available from: URL: <https://medical-dictionary.thefreedictionary.com/R-R+interval>
- 28 **Giles D,** Draper N, Neil W. Validity of the Polar V800 heart rate monitor to measure RR intervals at rest. *Eur J Appl Physiol* 2016; **116**: 563-571 [PMID: 26708360 DOI: 10.1007/s00421-015-3303-9]
- 29 **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]
- 30 **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]
- 31 **Hertel J,** Miller SJ, Denegar CR. Intratester and Intertester Reliability during the Star Excursion Balance Tests. *J Sport Rehabil* 2000; **9**: 104-116 [DOI: 10.1123/jsr.9.2.104]
- 32 **Gribble PA,** Hertel J. Considerations for normalizing measures of the Star Excursion Balance Test. *MPEES* 2003; **7**: 89-100 [DOI: 10.1207/S15327841MPEE0702\_3]
- 33 **Gauvin MG,** Riddle DL, Rothstein JM. Reliability of clinical measurements of forward bending using the modified fingertip-to-floor method. *Phys Ther* 1990; **70**: 443-447 [PMID: 2141425 DOI: 10.1093/ptj/70.7.443]
- 34 **Buckup K.** Klinische Tests an Knochen, Muskeln und Gelenken. 5<sup>th</sup> ed. Thieme, Stuttgart, 2009
- 35 **Gifford LS.** Circadian variation in human flexibility and grip strength. *Aust J Physiother* 1987; **33**: 3-9 [PMID: 25025455 DOI: 10.1016/S0004-9514(14)60579-1]
- 36 **Wieben K,** Falkenberg B. Muskelfunktion: Prüfung und klinische Bedeutung. 6<sup>th</sup> ed. Georg Thieme Verlag, 2012
- 37 **Blasimann A.** Veränderungen des Finger-Boden-Abstands bei jungen Frauen im Tagesverlauf. *Manuelletherapie* 2013; **17**: 233-238 [DOI: 10.1055/s-0033-1363153]
- 38 **Toigo M,** Boutellier U. New fundamental resistance exercise determinants of molecular and cellular muscle adaptations. *Eur J Appl Physiol* 2006; **97**: 643-663 [PMID: 16845551 DOI: 10.1007/s00421-006-0238-1]
- 39 **Field A.** Discovering statistics using SPSS. 3<sup>rd</sup> ed. Sage publications, 2009
- 40 **Cohen J.** A power primer. *Psychol Bull* 1992; **112**: 155-159 [PMID: 19565683 DOI: 10.1037/0033-2909.112.1.155]
- 41 Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation* 1996; **93**: 1043-1065 [PMID: 8598068 DOI: 10.1161/01.CIR.93.5.1043]
- 42 **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]
- 43 **Thayer JF,** Ahs F, Fredrikson M, Sollers JJ 3rd, Wager TD. A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health. *Neurosci Biobehav Rev* 2012; **36**: 747-756 [PMID: 22178086 DOI: 10.1016/j.neubiorev.2011.11.009]
- 44 **Vrijkotte TG,** van Doornen LJ, de Geus EJ. Effects of work stress on ambulatory blood pressure, heart rate, and heart rate variability. *Hypertension* 2000; **35**: 880-886 [PMID: 10775555 DOI: 10.1161/01.HYP.35.4.880]
- 45 **Herren K,** Radlinger L. Risks and side-effects of whole body vibration training. WCPT Congress 2011 Amsterdam Holland. *Physiotherapy* 2011; **97**: Supplement S1. Available from: URL: [https://www.researchgate.net/publication/296456229\\_RISKS\\_AND\\_SIDE\\_EFFECTS\\_OF\\_WHOLE\\_BODY\\_VIBRATION\\_TRAINING](https://www.researchgate.net/publication/296456229_RISKS_AND_SIDE_EFFECTS_OF_WHOLE_BODY_VIBRATION_TRAINING)

**P- Reviewer:** Cheung WH, Dye DC **S- Editor:** Ji FF  
**L- Editor:** A **E- Editor:** Song H



## Randomized Clinical Trial

**Corticosteroid injection alone *vs* additional physiotherapy treatment in early stage frozen shoulders**

Tim Kraal, Inger Sierevelt, Derek van Deurzen, Michel PJ van den Bekerom, Lijkele Beimers

Tim Kraal, Inger Sierevelt, Lijkele Beimers, Department of Orthopedic Surgery, Slotervaart Center of Orthopedic Research and Education, Amsterdam 1066 EC, The Netherlands

Derek van Deurzen, Michel PJ van den Bekerom, Department of Orthopedic Surgery, Shoulder and Elbow Unit, OLVG Hospital, Amsterdam 1091 AC, The Netherlands

ORCID number: Tim Kraal (0000-0003-4377-6901); Inger Sierevelt (0000-0003-0924-9358); Derek van Deurzen (0000-0002-6948-183X); Michel PJ van den Bekerom (0000-0002-1184-0529); Lijkele Beimers (0000-0001-8856-1061).

**Author contributions:** Kraal T is the initiator of this study and wrote the study protocol and a large part of this manuscript; Sierevelt I is involved as a clinical epidemiologist and research coordinator; Sierevelt I is responsible for the statistical analysis and correct presentation of the results; van Deurzen D and van den Bekerom MPJ both included patients at their center, and were both responsible for follow up at this location; Beimers L is responsible for inclusions at the other center and responsible as supervisor for the protocol and progress of the study; all authors were involved in the writing and revising of this manuscript.

**Institutional review board statement:** Approval for a prospective randomized clinical trial (D-FROST; Dutch frozen shoulder study) was obtained by the MC Slotervaart Hospital Medical Ethics Committee (NL47325.048.13).

**Clinical trial registration statement:** The trial was registered in the Dutch Trial Register (NTR4587).

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

**CONSORT 2010 statement:** The authors have read the CONSORT 2010 Statement, and the manuscript was prepared and revised according to the CONSORT 2010 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/>

Manuscript source: Unsolicited manuscript

Correspondence to: Lijkele Beimers, MD, PhD, Staff Physician, Orthopedic Surgeon, Department of Orthopedic Surgery, Slotervaart Center of Orthopedic Research and Education, MC Slotervaart, Louwesweg 6, Amsterdam 1066 EC, The Netherlands. [lijkele.beimers@slz.nl](mailto:lijkele.beimers@slz.nl)  
Telephone: +31-20-5125116

Received: April 7, 2018

Peer-review started: April 7, 2018

First decision: June 14, 2018

Revised: July 1, 2018

Accepted: August 2, 2018

Article in press: August 3, 2018

Published online: September 18, 2018

**Abstract****AIM**

To investigate the additional value of physiotherapy after a corticosteroid injection in stage one or two idiopathic frozen shoulders (FSs).

**METHODS**

A two center, randomized controlled trial was done. Patients with a painful early stage idiopathic FS were eligible for inclusion. After written consent, patients were randomly allocated into two groups. All patients received an ultrasound-guided intra-articular corticosteroid injection. One group underwent additional physiotherapy treatment (PT) and the other group did not (non-PT). The primary outcome measure was the Shoulder Pain

and Disability Index (SPADI). Secondary outcomes were pain (numeric pain rating scale), range of motion (ROM), quality of life (RAND-36 score), and patient satisfaction. Follow-up was scheduled after 6, 12 and 26 wk.

## RESULTS

Twenty-one patients were included, 11 patients in the non-PT and ten in the PT group, with a mean age of 52 years. Both treatment groups showed a significant improvement at 26 wk for SPADI score (non-PT:  $P = 0.05$ , PT:  $P = 0.03$ ). At the 6 wk follow-up, median SPADI score was significantly decreased in the PT group (14 IQR: 6-38) *vs* the non-PT group (63 IQR: 45-76) ( $P = 0.01$ ). Pain decreased significantly in both groups but no differences were observed between both treatment groups at any time point, except for night pain at 6 wk in favor of the PT group ( $P = 0.02$ ). Significant differences in all three ROM directions were observed after 6 wk in favor of the PT group ( $P \leq 0.02$  for all directions). A significantly greater improvement in abduction ( $P = 0.03$ ) and external rotation ( $P = 0.04$ ) was also present in favor of the PT group after 12 wk. RAND-36 scores showed no significant differences in health-related quality of life at all follow-up moments. At 26 wk, both groups did not differ significantly with respect to any of the outcome parameters. No complications were reported in both groups.

## CONCLUSION

Additional physiotherapy after corticosteroid injection improves ROM and functional limitations in early-stage FSs up to the first three months.

**Key words:** Corticosteroid; Frozen shoulder; Adhesive capsulitis; Physiotherapy

© The Author(s) 2018. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Corticosteroids and physiotherapy are the most widely used treatment modalities in frozen shoulders (FSs). However, the role of physiotherapy, especially in early FSs, is controversial. Corticosteroid injection with additional physiotherapy leads to better Shoulder Pain and Disability Index scores and range of motion up to three months compared to corticosteroid injection alone. Although a trend was recognized in favor of the physiotherapy group, both groups did not differ significantly with respect to any of the outcome parameters at the final follow-up after 26 wk.

Kraal T, Sierevelt I, van Deurzen D, van den Bekerom MPJ, Beimers L. Corticosteroid injection alone *vs* additional physiotherapy treatment in early stage frozen shoulders. *World J Orthop* 2018; 9(9): 165-172 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/165.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.165>

## INTRODUCTION

Frozen shoulder (FS), a common cause of shoulder pain and disability, affects approximately 2% to 4% of the general population<sup>[1-3]</sup>. The peak incidence of FS is between the fifth and sixth decade of life, occurring slightly more frequently in women than in men. The pathophysiology of FS is poorly understood<sup>[4]</sup>. The generally accepted theory comprises an inflammatory cascade causing contracture of the anterosuperior capsule, the rotator interval and the coracohumeral ligaments of the shoulder joint. These events lead to the typical loss of the passive external rotation seen in FS<sup>[2]</sup>. Although there are histopathological similarities with Dupuytren's disease, FS follows a different natural course<sup>[5]</sup>. Historically, FS is considered to be self-limiting with three different stages; the freezing, frozen, and thawing stages<sup>[6,7]</sup>. However, clear distinction between separate stages is difficult without clear cut-off criteria, and a continuing spectrum is more appropriate. Functional recovery mainly takes place within one to three years<sup>[8,9]</sup>. However, the remaining pain and restriction in range of motion (ROM) of the shoulder joint can even persist long-term<sup>[10-12]</sup>.

There is no widely agreed consensus about the most optimal treatment regimen for FS. Systematic reviews point to a large gap in evidence for treatment strategies for FS<sup>[13-15]</sup>. Currently, there seems to be a trend towards more invasive treatments, like manipulation under anesthesia and particularly arthroscopic capsular release<sup>[16]</sup>. However, there is insufficient evidence to recommend these treatment modalities<sup>[13]</sup>. Less invasive treatment options are intra-articular corticosteroid injections and physiotherapy. These are the most widely used treatment modalities in FS in both primary and secondary healthcare settings<sup>[2,17,18]</sup>. Corticosteroid injections demonstrated a positive effect on shoulder pain and ROM, at least in the short-term<sup>[19,20]</sup>. However, the role of physiotherapy in the treatment of FS is more uncertain<sup>[14,21,22]</sup>. Supervised neglect, consisting of supportive therapy and exercises within pain limits, has been advocated as an appropriate treatment for FS<sup>[23]</sup>. In a systematic review, Blanchard *et al*<sup>[24]</sup> hypothesized a potential beneficial effect of combining corticosteroid injections with physiotherapy. Conclusive evidence to support this is lacking, which warrants further trials. The objective of this randomized controlled trial was therefore to investigate the additional value of physiotherapy treatment (PT) after an intra-articular corticosteroid injection in the management of early-stage idiopathic FSs. It is hypothesized that, with respect to ROM and shoulder function, additional physiotherapy is superior to corticosteroid injection alone.

## MATERIALS AND METHODS

Approval for a prospective randomized clinical trial (D-FROST; Dutch frozen shoulder study) was obtained

by the MC Slotervaart Hospital Medical Ethics Committee (NL47325.048.13). The trial was registered in the Dutch Trial Register (NTR4587). The study was undertaken in accordance with the declaration of Helsinki. Patients were recruited between February 2014 and December 2015 in two participating hospitals in Amsterdam. Patients were eligible for participation if they exhibited clinical signs of FS, including pain and stiffness of the involved shoulder without preliminary trauma persisting for more than three months. The required level of pain was a minimum score of six out of ten on a numeric pain scale. Restriction of the passive ROM of the shoulder joint of more than 30° in external rotation and a second direction (*i.e.*, abduction and/or forward flexion) when compared to the unaffected contralateral side was required for inclusion. Conventional radiographs of the shoulder joint and ultrasound studies were used to rule out osteoarthritis and rotator cuff ruptures. Exclusion criteria were: Corticosteroid injection in the shoulder joint region in the previous 6 wk, previous surgery to the shoulder, systemic inflammatory disease, neurological disorder with impairment of the upper limb, and the use of anti-coagulation therapy using a therapeutic dosage. These selection criteria are intended to select a clearly defined population of patients with early-stage (stage one or two) idiopathic FSs. Patients were informed both in word and with an information leaflet. Informed consent was obtained from all included patients.

### **Randomization and interventions**

Patients were randomly assigned into two groups. The intervention group undergoing a PT program (PT-group), or the control group without physiotherapy (non-PT). Patients were allocated to one of the study groups using an online website. Randomization was stratified by the participating hospital and performed in variable blocks using computer-generated randomization software. Participating orthopaedic surgeons who assessed patient eligibility had no access to the randomization software, hereby securing allocation concealment. Within two weeks after inclusion, patients in both study groups received an ultrasound-guided glenohumeral joint injection of 1 mL kenacort 40 mg in 4 mL lidocaine 1%, administered by an experienced radiologist. Both groups were informed about the possible self-limiting nature of FS, and received counseling about optional analgesics like acetaminophen, nonsteroidal anti-inflammatory drugs or tramadol, if needed. The non-PT group did not receive PT. Advice was given to try to use the affected arm in daily life activities within their pain limits. Patients in the PT group were referred to a participating physiotherapy clinic. All participating physiotherapists treated the referred study patients according to a standardized protocol, twice a week with a maximum duration of three months. This physiotherapy protocol was composed after a thorough literature review by the participating shoulder surgeons in accordance with two experienced shoulder-treating physiotherapists. The aim

of the PT was to increase ROM of the shoulder, decrease pain, and restore the function of the shoulder for daily activities. Tissue irritability of the shoulder joint was taken into account to guide the intensity of the treatment<sup>[25]</sup>. Passive mobilization techniques were used, except for Maitland grade five mobilizations<sup>[26]</sup>. Attention was paid to scapulothoracic movement, with the purpose to improve the scapulohumeral kinematics. Also, active and auto-assisted stretching techniques were part of the physiotherapy program. If there was an increase in pain lasting for more than four hours after the PT session, the next session had to be less intense. Hot packs, icing, and massage techniques were allowed to reduce pain. Transcutaneous electrical nerve stimulation, pulsed electromagnetic field, infrared, dry needling and medical taping were not allowed due to the lack of evidence of these treatment modalities in the treatment of FS<sup>[27]</sup>.

### **Outcome parameters and follow-up**

The main outcome parameter of this study was the Shoulder Pain and Disability Index (SPADI) at the 26 wk follow-up, consisting of 13 questions divided into two domains (pain and disability). Item responses were rated on a eleven-point scale (0-10) leading to a score between 0 (best) and 100 (worst)<sup>[28]</sup>. The SPADI has been translated and validated in Dutch<sup>[29,30]</sup>. Pain on average last week, and pain at night were scored on a ten-point numeric pain-rating scale (NPRS). Health-related quality of life was assessed using the RAND-36<sup>[31,32]</sup>. Passive ROM was measured in the standing position with the use of a goniometer. External rotation was measured in the horizontal plane, with the elbow at the side. Abduction was measured in the frontal plane and anteflexion in the sagittal plane. Patient satisfaction about their change in pain and function was assessed on a five-point Likert scale ("worse", "unchanged", "unsatisfactory improved", "satisfactory improved" and "good to very good improved")<sup>[33]</sup>. Repeated corticosteroid injections were allowed after 6 wk if the level of pain had not dropped by at least 50%. Follow-up was scheduled after 6, 12 and 26 wk.

### **Statistical analysis**

Statistical analysis was performed by use of the SPSS statistical package software (version 22.0; Armonk, NY: IBM Corp) according to the intention to treat principle. Statistical review was performed by a clinical epidemiologist. Due to the small sample sizes and skewed distributions, analyses were performed non-parametrically. Patient demographics and baseline characteristics were described and compared between groups according to their distributions. Continuous and ordinal data are presented as medians with interquartile ranges (IQR) and differences between the treatment groups were assessed by use of Mann Whitney *U* tests. Wilcoxon Signed Ranks tests were performed to assess changes from baseline at 26 wk.  $\chi^2$  tests were performed in case of categorical variables. A *P*-value < 0.05 was

**Table 1 Demographics and patient characteristics**

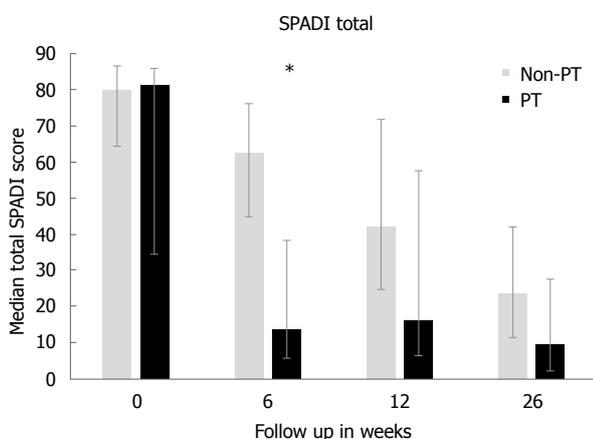
Characteristic	Total	Non-PT	PT	P-value
No. of patients	21	11	10	
Age (yr)	51.9 (SD 5.1)	50.4 (SD 6.1)	53.3 (SD 3.8)	0.17
Gender				
Male	9 (43)	4 (36)	5 (50)	
Female	12 (57)	7 (64)	5 (50)	0.67
Stage of frozen shoulder				
Freezing (stage I)	8 (38)	6 (55)	2 (20)	
Frozen (stage II)	13 (62)	5 (45)	8 (80)	0.18
Duration of symptoms prior to intervention				
< 6 mo	13 (62)	9 (82)	4 (40)	
> 6 mo	8 (38)	2 (18)	6 (60)	0.08
Previous injection around the shoulder	11 (52)	5 (45)	6 (60)	0.67
Previous PT	15 (71)	7 (64)	8 (80)	0.64
Disabled to work related to shoulder	4 (19)	2 (18)	2 (20)	1.00
Diabetes mellitus	2 (10)	2 (18)	0 (0)	

PT: Physiotherapy treatment.

**Table 2 Shoulder Pain and Disability Index scores for pain, disability and total Shoulder Pain and Disability Index scores (medians with interquartile range)**

	Non-PT	PT	P-value
SPADI pain			
Baseline (wk)	82 (70-90)	86 (46-92)	0.68
6	71 (24-79)	18 (9-43)	0.09
12	48 (22-68)	20 (9-57)	0.17
26	14 (8-30)	13 (4-32)	0.94
SPADI limitations			
Baseline (wk)	81 (58-88)	74 (28-84)	0.42
6	69 (47-76)	11 (4-36)	0.01
12	38 (25-72)	14 (5-58)	0.15
26	10 (9-50)	8 (1-25)	0.35
SPADI total			
Baseline (wk)	80 (65-87)	82 (35-86)	0.54
6	63 (45-76)	14 (6-38)	0.01
12	42 (25-72)	16 (7-58)	0.17
26	14 (11-39)	10 (2-28)	0.44

SPADI: Shoulder Pain and Disability Index; PT: Physiotherapy treatment.



**Figure 1 Median total SPADI score compared between both groups (non-physiotherapy treatment and physiotherapy treatment).** Error bars represent inter quartile range. The asterisk marks statistical significance between both groups. SPADI: Shoulder Pain and Disability Index; PT: Physiotherapy treatment.

considered statistically significant.

## RESULTS

### Patient population

A total of 21 patients were included, with 11 patients in the non-PT and ten in the PT group (Table 1). All patients had conventional radiographs of the shoulder without abnormalities. At baseline, external rotation was limited in both patient groups with a median external rotation measuring five degrees for all patients (IQR: 0-20). Median NPRS on average last week was eight (IQR: 7-8.5). In both groups, two patients were too disabled to work due to their FS symptoms. Two patients in both groups had received a previous corticosteroid injection more than three months prior to inclusion. After 26 wk, ROM measurements were available for 81% of the patients. Questionnaires were completed by 15 out of 21 patients (71%). An intra-articular corticosteroid injection was repeated after 12 wk in two patients in both groups. No complications or adverse events were reported in both groups.

### Clinical and functional outcome

The median total SPADI scores for all patients at baseline was 81 (IQR: 58-87), which confirmed the severe pain and disabilities of FS in the early stages. Both treatment groups showed a significant improvement at the primary endpoint of 26 wk for SPADI scores (non-PT:  $P = 0.05$ , PT:  $P = 0.03$ ). At the 6 wk follow-up, median SPADI scores had decreased to 63 (IQR: 45-76) in the non-PT group and 14 (IQR: 6-38) in the PT group. This difference was significant ( $P = 0.01$ ) and exceeded the minimal clinical important difference (range 8-13) of the SPADI<sup>[34]</sup>, but this difference had disappeared after 26 wk ( $P = 0.23$ ). At the final follow-up, median SPADI scores were 24 (IQR: 12-19) in the non-PT and ten (IQR: 2-28) in the PT group (Figure 1 and Table 2). Passive ROM increased significantly

**Table 3** Range of motion measurements, medians (with interquartile range)

	Non-PT	PT	P-value
Abduction			
Baseline (wk)	50 (40-60)	50 (41-102)	0.39
6	70 (43-90)	100 (80-140)	0.01
12	80 (65-98)	100 (90-165)	0.03
26	85 (80-149)	130 (85-170)	0.33
Anteflexion			
Baseline (wk)	70 (70-80)	95 (48-120)	0.25
6	90 (75-111)	140 (105-165)	0.02
12	90 (80-146)	130 (115-155)	0.06
26	100 (90-160)	155 (110-170)	0.17
External rotation			
Baseline (wk)	0 (0-5)	8 (0-24)	0.14
6	13 (5-26)	40 (30-43)	0.01
12	18 (8-29)	40 (25-65)	0.04
26	30 (13-44)	50 (35-60)	0.07

PT: Physiotherapy treatment.

**Table 4** Pain (numeric pain rating scale) scores, RAND-36 physical component scale and mental component scale

	Non-PT	PT	P-value
NPRS average last week			
Baseline (wk)	8 (7-9)	8 (5-8)	0.37
6	4 (2-8)	2 (1-4)	0.19
12	4 (2-7)	1 (0.5-5)	0.17
26	3 (1-4)	2 (0-3)	0.41
NPRS night			
Baseline (wk)	8 (8-9)	9 (7-9)	0.94
6	4 (3-7)	2 (0-3)	0.02
12	5 (2-7)	1 (0-6)	0.11
26	2 (1-3)	2 (0-3)	0.48
RAND-36 PCS			
Baseline (wk)	33 (31-40)	39 (34-46)	0.11
6	43 (35-46)	47 (44-52)	0.10
12	45 (43-50)	47 (43-55)	0.63
26	43 (35-56)	40 (46-56)	0.56
RAND-36 MCS			
Baseline (wk)	47 (36-54)	44 (35-54)	0.94
6	49 (35-52)	50 (42-56)	0.33
12	43 (29-51)	52 (40-55)	0.20
26	52 (50-57)	52 (35-57)	0.56
Satisfaction (wk)			
6	3 (2-3)	4 (3-4)	0.02
12	2 (0-4)	3 (2-4)	0.22
26	3 (3-4)	3.5 (3-4)	1.00

Satisfaction scores ("worse", "unchanged", "unsatisfactory improved", "satisfactory improved" and "good to very good improved"). Results reported as medians (with interquartile range). NPRS: Numeric pain rating scale; PT: Physiotherapy treatment.

compared to baseline in both groups ( $P < 0.03$  for all comparisons). Significant differences in all three ROM directions were observed after 6 wk in favor of the PT group ( $P \leq 0.02$  for all comparisons). At the final follow-up, all ROM measurements were still in favor of the PT group, but were not significant (Table 3).

Both of the NPRS items "night pain" and "average pain last week" showed significant decreases at the 26 wk follow-up for both groups ( $P < 0.03$  for all

comparisons). However, significant differences between both treatment groups were not observed at any time point, except for night pain at 6 wk in favor of the PT group ( $P = 0.02$ , Table 4). The results of the RAND-36 showed no significant differences between both groups regarding health-related quality of life at all follow-up moments. A slightly higher satisfaction score was reported by the PT group compared to the non-PT group at the 6 wk follow-up ( $P = 0.02$ ). At all other follow-up moments, the degree of satisfaction was comparable between the two treatment groups (Table 4).

## DISCUSSION

The aim of this trial was to investigate whether physiotherapy is of additional value after an intra-articular corticosteroid injection into the shoulder joint in the treatment of patients with FS in stage one or two. At the final follow-up after 26 wk, no clinical or functional differences were observed between both groups, with or without additional PT. However, total SPADI scores, ROM measurements and NPRS for pain at night were significantly superior in the physiotherapy group at 6 wk. The most considerable differences between the groups were observed for the ROM, in favor of the PT group until 12 wk of follow-up. This could imply that PT after an intra-articular corticosteroid injection is of additional clinical value in the treatment of FS. The result of physiotherapy is improved shoulder function, with less limitation in the rehabilitation process of patients with FS up to the first three months after a corticosteroid injection in the shoulder joint.

An initial good improvement is frequently reported in studies using corticosteroid injection for FS<sup>[22,35]</sup>. The beneficial value of additional physiotherapy was also reported by Carrette *et al.*<sup>[21]</sup>. In his clinical trial, corticosteroid injection followed by physiotherapy provided a faster recovery of shoulder function compared to injection alone, or placebo injection combined with physiotherapy. Ryans *et al.*<sup>[22]</sup> conducted a RCT comparing four treatment strategies for FS. The authors concluded that corticosteroids were effective for pain relief and shoulder disability in the short-term, and physiotherapy was effective in restoring external rotation. In both studies, the differences were most distinct at the early follow-up and at 6 and 12 wk, but not significant after more than three months. This is quite similar to our findings. A reason for this might be the self-limiting natural course of the disease. Nevertheless, the beneficial effect of physiotherapy in the short-term can be of clinically-relevant value in case the duration of both symptoms and disabilities is shortened with this strategy.

On the contrary, other studies do not support the use of physiotherapy in the treatment of FS<sup>[23,24]</sup>. In a systematic review, Blanchard *et al.*<sup>[24]</sup> found inferior results of PT compared to corticosteroid injection. Some even consider physiotherapy to be inappropriate during

early (painful) stage of FS<sup>[2,36]</sup>. A possible explanation for inferior results from physiotherapy in the treatment of FS is inadequacy to take in to account the tissue irritability level. Irritability is a term to reflect the tissue's ability to handle physical stress, presumably related to the extent of inflammatory activity. Tissue irritability can be categorized into three levels based on: patient reported pain, pain at end ROM, and the difference between active and passive ROM<sup>[25]</sup>. PT intensity can vary in the length of treatment, frequency of sessions, intensity of mobilization techniques, and types of exercises. Intensive physiotherapy at an early stage of FS without taking into account the tissue irritability level, can potentially worsen the symptoms of FS. For example, Diercks *et al.*<sup>[23]</sup> reported a negative effect of PT, including passive stretching and manual mobilization, compared to supportive therapy within pain limits. However, no corticosteroid injections were used in the trial of Diercks *et al.*<sup>[23]</sup>. Intra-articular corticosteroids have an anti-inflammatory effect, which is likely to attenuate tissue irritability<sup>[37]</sup>. We believe that in order to optimize treatment of early-stage FS, PT intensity should be guided by tissue irritability level. Moreover, PT is preferably started after an intra-articular corticosteroid injection.

In this prospective RCT, the study population was clearly defined according to strict criteria to include patients with idiopathic FS in stage one or two with symptoms lasting at least three months. The corticosteroid injections were administered under ultrasound guidance by experienced radiologists. Rehabilitation was performed according to a uniform physiotherapy protocol and carried out by specialized shoulder physiotherapists. The ROM measurements were assessed by the treating orthopedic surgeon. Although not blinded for the allocated intervention, these measurements were done consistently and by an experienced surgeon.

The major limitation of this study is the relatively small number of included patients. The results of this trial should therefore be interpreted with caution. A sample size of 41 subjects per group with a power of 90%, alpha 0.05 and a 10% drop-out rate was calculated at the beginning of the study. This was based on the primary outcome parameter SPADI, with a minimal clinically important difference of 13 and a standard deviation of 17. Unfortunately, it was impossible to include this number of patients within a reasonable period of time. This was attributable to two factors. Firstly, the costs for physiotherapy were supported by the Slotervaart Center of Orthopedic Research and Education, however this was only available for a limited number of patients. Three separate research grant applications for funding of the trial were declined. Secondly, there was an unexpected amount of unwillingness to participate among eligible patients. We tried to increase the number of inclusions by attracting attention for the trial in several ways. Printed posters were exposed in the waiting rooms of the Orthopaedic Department, an article about the trial was

published in the local hospital journal, and an information letter was sent to more than 200 general practitioners in the catchment area. However, even with these small numbers, a positive effect of physiotherapy was observed up to three months of follow-up. It is possible that more significant differences between both treatment groups would have been found with a larger number of included patients.

A control group without corticosteroid injection was not made available in the study design to monitor the true natural course of the condition. This was because of our assumption that this could raise more difficulties persuading patients to participate in the trial. Study patient compliance to physiotherapy sessions was not recorded. However, a high compliance rate was expected, as the provided PT was free of charge. We are not aware of any patient cross-over, *i.e.*, starting physiotherapy on their own once assigned to the non-PT group. A possible explanation for inferior SPADI scores and ROM measurements at 6 wk in the non-PT group could be the confounding role of diabetes in two patients in this group. A prolonged refractory course of FS can be expected with diabetes<sup>[38,39]</sup>. However, the results from additional analysis that excluded these two diabetic patients did not change the conclusions.

Nevertheless, it is important to note that there is no clear understanding of the exact mechanism responsible for the natural course of FS as well as its improvement over time for most patients. We do agree that an important aspect of treatment is expert advice and the education of patients, with attention paid to the patients' perspectives regarding their expectations and experiences with FS.

With the results of this trial and the current literature, we suggest to offer patients additional PT after an intra-articular corticosteroid injection in the treatment of early-stage FS. The SPADI scores, ROM and pain at night scores are significantly better in the PT group vs the non-PT group at 6 wk. With time, the positive effect of PT had faded out. There were no significant differences between patients in both groups at the final follow-up at 26 wk. Additional PT can improve shoulder function and shorten the duration of functional limitations during recovery for early-stage FS patients up to the first three months.

## ARTICLE HIGHLIGHTS

### Research background

Frozen shoulder (FS) is a common cause of shoulder pain and disability. A contracted capsule with a decreased capsular volume leads to a typical loss of passive external rotation seen in FS. Physiotherapy and corticosteroid injections are the most widely used treatment modalities in FS, in both primary and secondary healthcare settings.

### Research motivation

Corticosteroid injections demonstrated a positive effect on shoulder pain and range of motion (ROM), at least in the short term. However, the role of physiotherapy in the treatment of FS is more uncertain. For example,

supervised neglect, consisting of supportive therapy and exercises within pain limits, has also been advocated as an appropriate treatment for FS.

### Research objectives

The objective of this randomized controlled trial was therefore to investigate the additional value of physiotherapy treatment (PT) after an intra-articular corticosteroid injection in the management of early stage idiopathic FSs. It is hypothesized that additional physiotherapy is superior to corticosteroid injection alone with respect to ROM and shoulder function.

### Research methods

A two center prospective randomized controlled trial was undertaken. Patients with painful early-stage idiopathic FS were eligible for inclusion. After written consent, patients were randomly allocated into two groups. All patients received an ultrasound-guided intra-articular corticosteroid injection. One group underwent additional PT and the other group did not (non-PT). The primary outcome measure was the SPADI. Secondary outcomes were pain (NPRS), ROM, quality of life (RAND-36 score), and patient satisfaction. Follow-up was scheduled after 6, 12 and 26 wk.

### Research results

Twenty-one patients were included, 11 patients in the non-PT and ten in the PT group. Both treatment groups showed a significant improvement at 26 wk for SPADI score. At the 6 wk follow-up, median SPADI score was significantly decreased in the PT group (14 IQR: 6-38) vs the non-PT group (63 IQR: 45-76) ( $P = 0.01$ ). Significant differences in all three ROM directions were observed after 6 wk in favor of the PT group ( $P \leq 0.02$  for all directions). At 26 wk, both groups did not differ significantly with respect to any of the outcome parameters. No complications were reported in both groups.

### Research conclusions

Intra-articular corticosteroid infiltration is effective in the treatment of FS. Additional PT can improve shoulder function and shorten the duration of functional limitations during the recovery of early-stage FS patients up to the first three months. The physiotherapy intensity should be guided on tissue irritability. Future research should focus on the different populations other than idiopathic FSs, like post-operative or post-traumatic FSs. Furthermore, a small subset of patients is not satisfactorily treated with conservative treatment as an injection and physiotherapy. It would be very interesting to investigate if these patients with a prolonged and refractory course of disease could be identified at an early time point.

### Research perspectives

It would be very interesting to investigate if these patients with a prolonged and refractory course of disease could be identified at an early time point.

## REFERENCES

- 1 **Tasto JP**, Elias DW. Adhesive capsulitis. *Sports Med Arthrosc Rev* 2007; **15**: 216-221 [PMID: 18004221 DOI: 10.1097/JSA.0b013e3181595c22]
- 2 **Robinson CM**, Seah KT, Chee YH, Hindle P, Murray IR. Frozen shoulder. *J Bone Joint Surg Br* 2012; **94**: 1-9 [PMID: 22219239 DOI: 10.1302/0301-620X.94B1.27093]
- 3 **van der Windt DA**, Koes BW, de Jong BA, Bouter LM. Shoulder disorders in general practice: incidence, patient characteristics, and management. *Ann Rheum Dis* 1995; **54**: 959-964 [PMID: 8546527 DOI: 10.1136/ard.54.12.959]
- 4 **Pietrzak M**. Adhesive capsulitis: An age related symptom of metabolic syndrome and chronic low-grade inflammation? *Med Hypotheses* 2016; **88**: 12-17 [PMID: 26880627 DOI: 10.1016/j.mehy.2016.01.002]
- 5 **Bunker TD**, Anthony PP. The pathology of frozen shoulder. A Dupuytren-like disease. *J Bone Joint Surg Br* 1995; **77**: 677-683 [PMID: 7559688 DOI: 10.1302/0301-620X.77B5.7559688]
- 6 **Reeves B**. The natural history of the frozen shoulder syndrome. *Scand J Rheumatol* 1975; **4**: 193-196 [PMID: 1198072 DOI: 10.3109/03009747509165255]
- 7 **Jayson MI**. Frozen shoulder: adhesive capsulitis. *Br Med J (Clin Res Ed)* 1981; **283**: 1005-1006 [PMID: 6794738 DOI: 10.1136/bmj.283.6298.1005]
- 8 **Griggs SM**, Ahn A, Green A. Idiopathic adhesive capsulitis. A prospective functional outcome study of nonoperative treatment. *J Bone Joint Surg Am* 2000; **82-A**: 1398-1407 [PMID: 11057467 DOI: 10.2106/00004623-200010000-00005]
- 9 **Guyver PM**, Bruce DJ, Rees JL. Frozen shoulder - A stiff problem that requires a flexible approach. *Maturitas* 2014; **78**: 11-16 [PMID: 24636964 DOI: 10.1016/j.maturitas.2014.02.009]
- 10 **Binder AI**, Bulgen DY, Hazleman BL, Roberts S. Frozen shoulder: a long-term prospective study. *Ann Rheum Dis* 1984; **43**: 361-364 [PMID: 6742896 DOI: 10.1136/ard.43.3.361]
- 11 **Shaffer B**, Tibone JE, Kerlan RK. Frozen shoulder. A long-term follow-up. *J Bone Joint Surg Am* 1992; **74**: 738-746 [PMID: 1624489 DOI: 10.2106/00004623-199274050-00013]
- 12 **Hand C**, Clipsham K, Rees JL, Carr AJ. Long-term outcome of frozen shoulder. *J Shoulder Elbow Surg* 2008; **17**: 231-236 [PMID: 17993282 DOI: 10.1016/j.jse.2007.05.009]
- 13 **Rangan A**, Hanchard N, McDaid C. What is the most effective treatment for frozen shoulder? *BMJ* 2016; **354**: i4162 [PMID: 27554676 DOI: 10.1136/bmj.i4162]
- 14 **Maund E**, Craig D, Suekarran S, Neilson A, Wright K, Brealey S, Dennis L, Goodchild L, Hanchard N, Rangan A, Richardson G, Robertson J, McDaid C. Management of frozen shoulder: a systematic review and cost-effectiveness analysis. *Health Technol Assess* 2012; **16**: 1-264 [PMID: 22405512 DOI: 10.3310/hta16110]
- 15 **Lewis J**. Frozen shoulder contracture syndrome - Aetiology, diagnosis and management. *Man Ther* 2015; **20**: 2-9 [PMID: 25107826 DOI: 10.1016/j.math.2014.07.006]
- 16 **Mun SW**, Baek CH. Clinical efficacy of hydrodistention with joint manipulation under interscalene block compared with intra-articular corticosteroid injection for frozen shoulder: a prospective randomized controlled study. *J Shoulder Elbow Surg* 2016; **25**: 1937-1943 [PMID: 27771263 DOI: 10.1016/j.jse.2016.09.021]
- 17 **van der Windt DA**, Koes BW, Devillé W, Boeke AJ, de Jong BA, Bouter LM. Effectiveness of corticosteroid injections versus physiotherapy for treatment of painful stiff shoulder in primary care: randomised trial. *BMJ* 1998; **317**: 1292-1296 [PMID: 9804720 DOI: 10.1136/bmj.317.7168.1292]
- 18 **Winters JC**, Sobel JS, Groenier KH, Arendzen HJ, Meyboom-de Jong B. Comparison of physiotherapy, manipulation, and corticosteroid injection for treating shoulder complaints in general practice: randomised, single blind study. *BMJ* 1997; **314**: 1320-1325 [PMID: 9158469 DOI: 10.1136/bmj.314.7090.1320]
- 19 **Shah N**, Lewis M. Shoulder adhesive capsulitis: systematic review of randomised trials using multiple corticosteroid injections. *Br J Gen Pract* 2007; **57**: 662-667 [PMID: 17688763]
- 20 **Song A**, Higgins LD, Newman J, Jain NB. Glenohumeral corticosteroid injections in adhesive capsulitis: a systematic search and review. *PM R* 2014; **6**: 1143-1156 [PMID: 24998406 DOI: 10.1016/j.pmrj.2014.06.015]
- 21 **Carette S**, Moffet H, Tardif J, Bessette L, Morin F, Frémont P, Bykerk V, Thorne C, Bell M, Bensen W, Blanchette C. Intraarticular corticosteroids, supervised physiotherapy, or a combination of the two in the treatment of adhesive capsulitis of the shoulder: a placebo-controlled trial. *Arthritis Rheum* 2003; **48**: 829-838 [PMID: 12632439 DOI: 10.1002/art.10954]
- 22 **Ryans I**, Montgomery A, Galway R, Kernohan WG, McKane R. A randomized controlled trial of intra-articular triamcinolone and/or physiotherapy in shoulder capsulitis. *Rheumatology (Oxford)* 2005; **44**: 529-535 [PMID: 15657070 DOI: 10.1093/rheumatology/keh535]
- 23 **Diercks RL**, Stevens M. Gentle thawing of the frozen shoulder: a prospective study of supervised neglect versus intensive physical therapy in seventy-seven patients with frozen shoulder syndrome followed up for two years. *J Shoulder Elbow Surg* 2004; **13**: 499-502 [PMID: 15383804 DOI: 10.1016/j.jse.2004.03.002]
- 24 **Blanchard V**, Barr S, Cerisola FL. The effectiveness of cortico-

- steroid injections compared with physiotherapeutic interventions for adhesive capsulitis: a systematic review. *Physiotherapy* 2010; **96**: 95-107 [PMID: 20420956 DOI: 10.1016/j.physio.2009.09.003]
- 25 **Kelley MJ**, Shaffer MA, Kuhn JE, Michener LA, Seitz AL, Uhl TL, Godges JJ, McClure PW. Shoulder pain and mobility deficits: adhesive capsulitis. *J Orthop Sports Phys Ther* 2013; **43**: A1-31 [PMID: 23636125 DOI: 10.2519/jospt.2013.0302]
- 26 **Vermeulen HM**, Rozing PM, Obermann WR, le Cessie S, Vliet Vlieland TP. Comparison of high-grade and low-grade mobilization techniques in the management of adhesive capsulitis of the shoulder: randomized controlled trial. *Phys Ther* 2006; **86**: 355-368 [PMID: 16506872]
- 27 **Green S**, Buchbinder R, Hetrick S. Physiotherapy interventions for shoulder pain. *Cochrane Database Syst Rev* 2003; (2): CD004258 [PMID: 12804509 DOI: 10.1002/14651858.CD004258]
- 28 **Roach KE**, Budiman-Mak E, Songsiridej N, Lertratanakul Y. Development of a shoulder pain and disability index. *Arthritis Care Res* 1991; **4**: 143-149 [PMID: 11188601 DOI: 10.1002/art.1790040403]
- 29 **Elvers JWH**, Oostendorp RAB, Siervelt IN, van der Heijden KWAP. De Nederlandstalige Shoulder pain and Disability Index (SPADI-Dutch Version) bij patiënten na een subacromiale decompressie volgens Neer. *Ned Tijdschr voor Fysiother* 2003; **113**: 126-131
- 30 **Thoomes-de Graaf M**, Scholten-Peeters GG, Duijn E, Karel Y, Koes BW, Verhagen AP. The Dutch Shoulder Pain and Disability Index (SPADI): a reliability and validation study. *Qual Life Res* 2015; **24**: 1515-1519 [PMID: 25471288 DOI: 10.1007/s11136-014-0879-1]
- 31 **VanderZee KL**, Sanderman R, Heyink JW, de Haes H. Psychometric qualities of the RAND 36-Item Health Survey 1.0: a multidimensional measure of general health status. *Int J Behav Med* 1996; **3**: 104-122 [PMID: 16250758 DOI: 10.1207/s15327558ijbm0302\_2]
- 32 **Ware JE Jr**, 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]
- 33 **ten Klooster PM**, Drossaers-Bakker KW, Taal E, van de Laar MA. Patient-perceived satisfactory improvement (PPSI): interpreting meaningful change in pain from the patient's perspective. *Pain* 2006; **121**: 151-157 [PMID: 16472915 DOI: 10.1016/j.pain.2005.12.021]
- 34 **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]
- 35 **Griesser MJ**, Harris JD, Campbell JE, Jones GL. Adhesive capsulitis of the shoulder: a systematic review of the effectiveness of intra-articular corticosteroid injections. *J Bone Joint Surg Am* 2011; **93**: 1727-1733 [PMID: 21938377 DOI: 10.2106/JBJS.J.01275]
- 36 **Harris G**, Bou-Haidar P, Harris C. Adhesive capsulitis: review of imaging and treatment. *J Med Imaging Radiat Oncol* 2013; **57**: 633-643 [PMID: 24283550 DOI: 10.1111/1754-9485.12111]
- 37 **Roh YH**, Yi SR, Noh JH, Lee SY, Oh JH, Gong HS, Baek GH. Intra-articular corticosteroid injection in diabetic patients with adhesive capsulitis: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 1947-1952 [PMID: 22113218 DOI: 10.1007/s00167-011-1776-6]
- 38 **White D**, Choi H, Peloquin C, Zhu Y, Zhang Y. Secular trend of adhesive capsulitis. *Arthritis Care Res (Hoboken)* 2011; **63**: 1571-1575 [PMID: 22034118 DOI: 10.1002/acr.20590]
- 39 **Wang K**, Ho V, Hunter-Smith DJ, Beh PS, Smith KM, Weber AB. Risk factors in idiopathic adhesive capsulitis: a case control study. *J Shoulder Elbow Surg* 2013; **22**: e24-e29 [PMID: 23352186 DOI: 10.1016/j.jse.2012.10.049]

**P- Reviewer:** Hernandez-Sanchez S, Mittal R, Peng B, Scibek J

**S- Editor:** Ji FF **L- Editor:** Filipodia **E- Editor:** Song H



## Is there consensus regarding surgical treatment of bone sarcomas?

Thomas Baad-Hansen, Sarah Stammose Freund, Bodil Hammer Bech, Johnny Keller

Thomas Baad-Hansen, Sarah Stammose Freund, Johnny Keller, Department of Orthopaedic Oncology, Aarhus University Hospital, Aarhus C8000, Denmark

Bodil Hammer Bech, Department of Public Health, Aarhus University, Aarhus C8000, Denmark

ORCID number: Thomas Baad-Hansen (0000-0003-4826-8412); Sarah Stammose Freund (0000-0002-9471-296X); Bodil Hammer Bech (0000-0002-0287-3687); Johnny Keller (0000-0003-2092-5425).

**Author contributions:** Baad-Hansen T and Keller J designed the study; Baad-Hansen T, Bech BH performed data analysis; Baad-Hansen T, Keller J, Bech BH and Freund SS wrote the paper.

**Conflict-of-interest statement:** The 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/>

**Manuscript source:** Unsolicited manuscript

**Correspondence to:** Thomas Baad-Hansen, PhD, Chief Doctor, Consultant, Department of Orthopaedic Oncology, Aarhus University Hospital, Nørrebrogade 44, Aarhus C8000, Denmark. [baadhansen@dadlnet.dk](mailto:baadhansen@dadlnet.dk)  
Telephone: +45-28603490

Received: April 10, 2018

Peer-review started: April 10, 2018

First decision: May 15, 2018

Revised: May 20, 2018

Accepted: June 27, 2018

Article in press: June 27, 2018

Published online: September 18, 2018

### Abstract

#### AIM

To perform an Internet based survey on the surgical management of bone sarcomas in the lower extremity amongst sarcoma surgeons.

#### METHODS

All orthopedic surgical members of the Scandinavian Sarcoma Group were invited to participate in an online questionnaire. The questionnaire consisted of a clinical case involving resection of a malignant bone tumor. Several questions were asked, subdivided into categories. Among these, surgical/technical considerations, *e.g.*, choice of implant; choice of antibiotics, dosage, and duration of treatment, choice of antithrombotic drug, initial start-up, dosage, and duration were included.

#### RESULTS

In terms of choice of implant fixation, the majority of surgeons preferred an uncemented prosthesis in younger patients until the age of 50. All participants administer intravenous prophylactic antibiotics for endoprosthetic reconstructive surgery. First choice of antibiotics was cephalosporin. Less common used was glycopeptide, penicillin, or a combination. Duration of prophylactic antibiotics ranged from less than one day to more than four days. All participants used low molecular weight heparins as antithrombotic prophylaxis and 55% of the participants answered that initial treatment was started preoperatively, 3% perioperatively and 42% postoperatively. Duration of the antithrombotic treatment ranged from five days to more than twenty-eight days.

#### CONCLUSION

The use of resection prosthesis in the treatment of bone sarcomas is a well-established procedure. However, there is a significant discrepancy in the surgical treatment algorithm between the sarcoma centers. Still the treatment is mainly based on best clinical practice,

due to the lack of evidence-based medicine in the surgical management of bone sarcomas.

**Key words:** Sarcoma; Reconstruction; Megaprosthesis; Antibiotics; Antithrombotic prophylaxis

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Today the majority of patients diagnosed with bone sarcomas located in the lower extremities are offered reconstruction with a megaprosthesis. However, no clear golden standard is available in the international surgical oncology community with regard to choice of implant, choice of antibiotics, dosage, and duration of treatment, or choice of antithrombotic drug, initial start-up, dosage, and duration. The current study reveals a clear lack of consensus.

Baad-Hansen T, Freund SS, Bech BH, Keller J. Is there consensus regarding surgical treatment of bone sarcomas? *World J Orthop* 2018; 9(9): 173-179 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/173.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.173>

## INTRODUCTION

Evidence-based surgical treatment of bone sarcomas is challenged by a limited number of patients and a considerable variation in anatomical location of the bone tumors. This is in contrast to the non-surgical treatment of bone sarcomas, where standard protocols are available to test new treatment regimes because the location of the sarcoma is of less importance in this context<sup>[1,2]</sup>. Guidelines for surgical management of hip and knee replacement due to more prevalent disorders such as osteoarthritis are available from most national hip and knee societies based on randomized clinical trials and large-scale database studies<sup>[3,4]</sup>. This level of evidence is difficult to achieve dealing with endoprosthetic reconstructive surgery in osteosarcoma patients<sup>[5]</sup>.

Since 2013 a randomized multicenter study, PARITY, has been ongoing with the aim to determine whether a five-day regimen of post-operative antibiotics, in comparison to a single day regimen, will change the risk of postoperative infection in patients receiving mega prosthesis<sup>[6,7]</sup>. The trial still lacks the inclusion of more than 600 patients and seven countries with a total of 35 different sarcoma centers are including patients. Such a multicenter study is time consuming, and it can be questioned if the results can be generalized to the rest of the world due to different antibiotic national policies.

The aim of the present study was to identify differences in surgical treatment strategies for patients with bone sarcomas in the lower extremities between



Figure 1 Radiograph of a reconstruction with a proximal tibia tumor prosthesis.

the Scandinavian countries based on best clinical practice. The study focuses on three main areas: (1) Surgical-technical considerations; (2) use of antibiotics; and (3) antithrombotic treatment.

## MATERIALS AND METHODS

All orthopedic surgical members of the Scandinavian sarcoma group (SSG) were invited to participate in an online questionnaire. The questionnaire consisted of a clinical case involving resection of a malignant bone tumor located in the proximal tibia, reconstruction with a megaprosthesis and a gastrocnemius myocutaneous flap coverage (Figure 1). Several questions were asked, subdivided into categories, among these, surgical/technical considerations, *e.g.*, choice of implant, choice of antibiotics, dosage, and duration of treatment, and choice of antithrombotic drug, initial start-up, dosage, and duration. A complete list of the questions can be seen in supplemental Appendix 1.

The participants could add supplementary comments to certain questions. No participants were financially compensated for completion of the survey.

## RESULTS

A total of 42 surgeons were asked to participate. Five did not return the questionnaire; two declined to answer due to inadequate clinical experience. A total of 35 participants returned a complete survey resulting in a response rate of 83%, eight from Denmark (23%), six from Finland (17%), one from Iceland (3%), seven from Norway (20%), and thirteen from Sweden (37%). The following hospitals were represented: Aarhus University Hospital, Rigshospitalet, Copenhagen, Karolinska University Hospital, Linköping University Hospital, Sahlgrenska University Hospital, University Hospital of Umeå, Skåne University Hospital, Oslo University Hospital, Radiumhospitalet, Haukeland University Hospital, Tampere University Hospital, Helsinki University Hospital and University Hospital of Iceland.

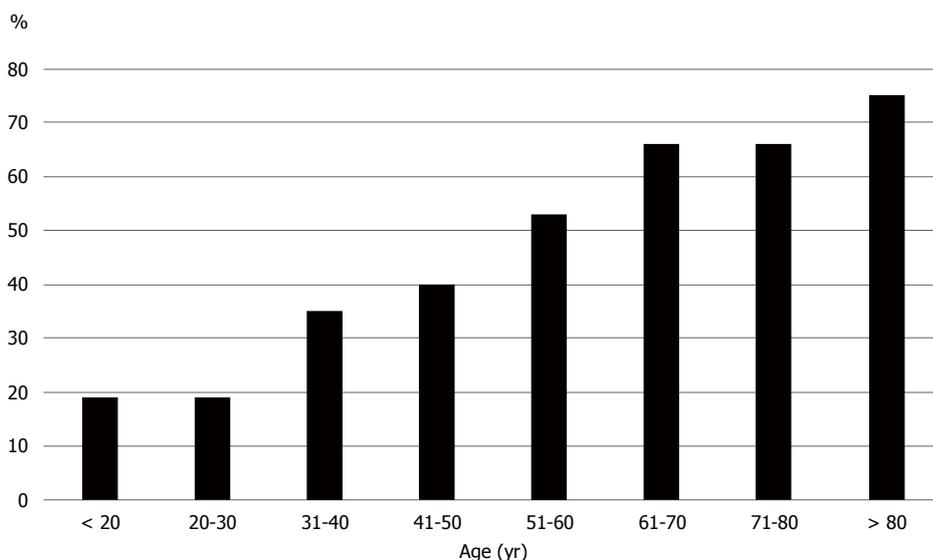


Figure 2 Proportion of patients in each age group that the study participants would treat with a cemented implant.

About 50% of the participants had worked as orthopedic oncologists for more than ten years. Female: male ratio was 1:7.

### **Surgical/technical considerations**

With regard to preoperative planning, 47% of the participants indicated that they would always perform a preoperative templating in order to determine prosthesis size and anatomical position whereas 25% answered sometimes and 28% answered that they would never perform templating. No differences between centers or countries were observed with regards to templating.

In case a needle biopsy was done prior to the surgical procedure, 66% indicated that they would excise the biopsy tract. However, in case an open biopsy was performed there was full consensus amongst all sarcoma centers to excise the open biopsy tract if surgically feasible.

In terms of choice of implant fixation, the majority of surgeons preferred an uncemented prosthesis in the younger patients until the age of 50, whereas a cemented prosthesis was the preferred implant from age 51 and up (Figure 2).

There was an overall agreement between countries to select uncemented fixation for the younger patients, however the Danish and Swedish sarcoma centers tended to consider a cemented prosthesis also to the youngest patients below 20 years old. Several reservations were noted with regard to the implant choice. The following comments were obtained. "It depends on the individual bone stock, length of resection," "routinely we will use uncemented prosthesis in the absence of osteoporosis and if postoperative radiotherapy is not considered," and "We do not use uncemented prosthesis".

### **Postoperative treatment**

In patients receiving a proximal tibia prosthesis, 72%

of the participants would apply a drain. Removal of the drain was dependent on two factors: time or drain production, or a combination of the two. The majority of the participants (67%) said that they would remove the drain after 3-4 d, whereas 33% of the participants would remove the drain 1-2 d postoperatively. Looking at drain production as a parameter, 82% of the participants would remove the drain when production was less than 25-50 mL/d. With regard to drain usage, no clear pattern could be observed between countries or within individual institutions. Several comments on this topic were made: "Less than 50 mL/d or before the fifth day," "Especially if a drain is needed in the area of the calf where the gastrocnemius muscle is rotated I will leave it for a longer time until drain production is less than 10 mL/d," and "Max time for drain is 7 d, even if the output is > 50 mL/d".

### **Use of prophylactic antibiotics**

All participants confirmed that they administer intravenous prophylactic antibiotics for endoprosthetic reconstructive surgery. First choice of antibiotics was cephalosporin, second was penicillin followed by glycopeptide or a combination of the above mentioned. According to the answers, the antibiotic prophylaxis was initiated preoperatively by 71% of the participating surgeons and was initiated perioperatively by 29% of participants. In contrast to the sarcoma centers in Finland, Norway and Sweden, who used cephalosporin, the predominantly used prophylactic antibiotic in Denmark and Iceland was penicillin. Duration of prophylactic antibiotics ranged from less than one day to more than four days. Thirty-nine percent of the participants stated that antibiotics were used for 1-2 d. Lastly, 32% of the participants answered that they used antibiotics until drain removal. Comments were added: "Until the surgical wound is completely dry and drain has been removed,"

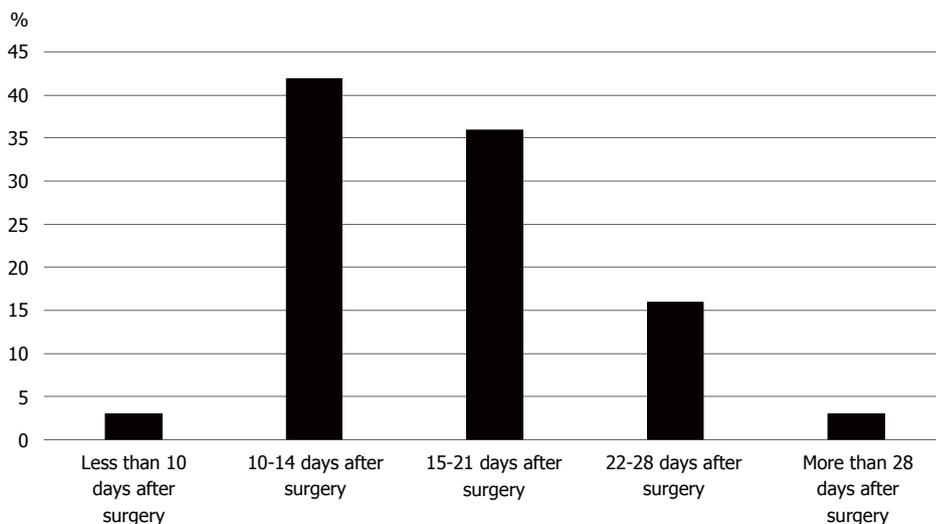


Figure 3 The distribution of the timing of initiation of postoperative chemotherapy.

“Only one dose if there has been limited bleeding during surgery, and an extra dose if the bleeding has been substantial,” “3 types of antibiotics. If surgery is prolonged the regime is altered and may be given for 2-3 d,” “ If drainage is used, antibiotics will be prolonged,” and “1-2 d sometimes longer, depending on if splitskin-graft is needed”.

**Pain management**

The majority of the participants (58%) would use some kind of nerve block. Of these, the most common pain management strategy was an epidural catheter (45% of participants). Less commonly, a peripheral catheter was used by 22%, and a combination of the above was indicated by 33%. All answers revealed duration of epidural and/or peripheral catheters of 2-4 d.

**Antithrombotic prophylaxis**

All participants presented a united front for the use of antithrombotic treatment. All participants preferred low molecular weight heparins. Antithrombotic treatment was initiated preoperatively by 55%, perioperatively by 3%, and postoperatively by 42%. Duration of the antithrombotic treatment ranged from 5-7 d (13% of the participants) to more than 28 d (6% of the participants). Most of the participants answered 8-14 d (58%) and 23% answered 15-28 d. It was stated several times that duration of the antithrombotic therapy also depended on the degree of mobilization.

**Weight bearing**

The participants were asked to indicate at which time full weight bearing was allowed in the case of insertion of an uncemented prosthesis. Exclusively looking at the fixation method, 32% answered within a week postoperatively, 10% answered one to six weeks after surgery, 48% answered seven to twelve weeks after surgery, and finally 10% answered more than twelve

weeks after surgery. In contrast, 52% of the participants allowed full weight bearing of a cemented prosthesis within the first week after surgery. This pattern was observed in all sarcoma centers. Some participants raised concerns due to postoperative chemotherapy and the re-insertion of the patella tendon leading to delayed full weight bearing.

**Postoperative chemotherapy**

In terms of initiation of postoperative chemotherapy, a clear difference between sarcoma centers was seen. The majority of surgeons in the Swedish and Norwegian centers allowed commencement of chemotherapy 10-14 d after surgery, whereas centers in Denmark and Finland waited up to 28 d postoperatively. Figure 3 shows the results from all participants with regard to delay of postoperative chemotherapy.

**DISCUSSION**

The European Society for Medical Oncology (ESMO) provides Clinical Practice Guidelines for diagnosis, treatment and follow-up of bone sarcomas. However, the surgical procedures are only briefly discussed<sup>[8]</sup>. The lack of surgical recommendations is displayed in the results from the present survey revealing great heterogeneity in the surgical treatment strategy of bone sarcomas located in the proximal tibia. However, there is also some agreement between surgeons (*e.g.*, in choice of implant fixation, use of antibiotics, and antithrombotic treatment). The individual surgeon’s preferences may be influenced by knowledge based on clinical trials almost similar to reconstruction with tumor-prostheses (*e.g.*, primary or revision knee surgery and national recommendations for endoprosthetic joint replacement)<sup>[9,10]</sup>. Furthermore, based on the participant’s statements in the results paragraph, previous personal experiences and clinical tradition may also influence the

clinical decision-making.

Some surgical procedures are widely accepted as reference standards. For decades, there has been consensus regarding removal of the biopsy tract during surgery, grounded in the theory that the biopsy tract is potentially contaminated by tumor cells<sup>[11]</sup>. According to Mankin *et al*<sup>[11]</sup>, 15 out of 329 patients experienced what might be unnecessary amputation due to unfavorable location of the biopsy, compromising definitive reconstruction procedures. This assumption is based more on empirical knowledge than on scientific data<sup>[12]</sup>. The above-mentioned standard is in accordance with the ESMO guideline for Clinical Practice Guidelines for diagnosis, treatment and follow-up of bone sarcomas stating that the biopsy tract from an open biopsy must be considered to be contaminated with tumor cells and must be removed together with the resection specimen to avoid local recurrences. However, no randomized studies have been published to support this widely accepted procedure.

A recent systematic review by Oliveira *et al*<sup>[13]</sup> reports that tumor contamination along the biopsy tract in musculoskeletal cancer can cause local recurrence and lead to an unfavorable prognosis. However, it was not possible for the authors to conclude whether a needle biopsy is associated with a lower risk of contamination than an open biopsy. Nevertheless, only 66% of the asked participants in the actual survey would excise the needle biopsy tract in contrast to an open biopsy, whereas all participants would remove the open biopsy tract.

The risk of developing a deep postoperative infection in sarcoma patients undergoing large endoprosthetic reconstructions is high compared with conventional total joint replacement<sup>[14]</sup>. The reason for this is multifactorial. Immune compromised patients undergoing complex and protracted procedures increase the risk of complications<sup>[15]</sup>.

The absence of a standard practice for antibiotic treatment has led to an attempt to launch an international multi-center RCT study including patients with lower extremity bone tumors undergoing endoprosthetic reconstruction, randomized to receive either cefazolin a single day post-operatively or five days post-operatively. Due to the low incidence of primary bone tumors, the study requires a sample size of approximately 600 patients, demanding inclusion of multiple sarcoma centers. Local variations in factors such as bacterial or fungal prevalence, *e.g.*, Methicillin-resistant *Staphylococcus aureus*, *Mycobacteria* or *Candida*. Lack of consensus with regard to choice of implant (some manufactures provide silver or gentamycin coating) complicates the study<sup>[16]</sup>. Furthermore, cefazolin is not standard practice or available in all countries leading to a reduced number of potential participating centers. Finally, patient-related and technical concerns must be taken into account when addressing type and duration of antibiotic treatment, which also is supported by the statements of the participants of the

present survey. The fact that a nearly equal percentage of orthopedic surgeons participating in our study chose the duration of prophylactic antibiotics to be from less than one day to more than four days (39%) emphasizes the need for supporting new RCTs.

According to a study by Husted *et al*<sup>[17]</sup>, a high degree of agreement in the clinical setup of patients undergoing fast track primary knee endoprosthetic surgery in four large orthopedic institutions has been described. With regard to deep venous thrombosis prophylaxis in this patient group, the treatment was initiated 6-8 h postoperatively and continued until discharge or up to seven days postoperatively. The clinical setup in primary total knee arthroplasty (TKA) surgery, however, differs significantly from patients undergoing tumor resection and reconstruction with a megaprosthesis and a direct comparison cannot be done. Patients receiving a primary TKA are most likely to be mobilized on the same day as the index surgery or at least on the first postoperative day. In contrast, patients treated with a resection prosthesis of the proximal tibia will need soft tissue reconstruction and demands complete immobilization to achieve soft tissue healing. Furthermore, cancer patients have an increased risk of a venous thromboembolism event with a hazard ratio of 4.7 compared to the background population<sup>[18]</sup>. The current study demonstrates a clear consensus amongst the participating surgeons regarding the need for venous thrombosis prophylaxis in the treatment of bone sarcomas. In contrast, absolutely no agreement was seen with regard to time for initiating treatment or duration of venous thrombosis prophylaxis. Approximately half of the participants started initial thrombosis prophylaxis preoperatively, and duration of the treatment ranged from 5-28 d.

The current study has some limitations. National legislations may influence clinical practices (*e.g.*, choice of antibiotics). A restrictive antibiotic policy will cause utilization of small spectrum antibiotics, leading to problematic direct comparison between countries. Furthermore, geographic variation in the prevalent bacterial/fungal species will require the surgeons to address a potential infection based on the local microbiological species. In the current study the choice of antibiotics is based on Scandinavian preferences, which potentially can lead to a reduced external validity.

In conclusion, the use of resection prosthesis in the treatment of bone sarcomas is a well-established procedure providing good functional outcomes and acceptable complication rates. However, the clinical considerations that follow management of bone sarcomas patients are predominantly based on best clinical practice and to a lower extent on evidence-based knowledge, which leads to a substantial variation in treatment protocols. In order to gain evidence-based knowledge, international multicenter studies have been initiated but are challenged by national heterogeneity with possible consequences for the generalizability of

their conclusions.

## ARTICLE HIGHLIGHTS

### Research background

Reconstructive surgery using megaprosthesis is widely applied as a treatment for bone sarcomas of the lower extremities. Even though reconstructive surgery has been used for several decades it seems that there is no clear consensus in surgical treatment strategies for this group of patients.

### Research motivation

The low number of bone sarcomas limits the possibility to run randomized clinical trials. This is in contrast to non-surgical treatment of bone sarcomas, where standard protocols are available to test new treatment regimes since the sites of the sarcoma are of less significance. Only a few international randomized studies have been initiated to gain new evidence on the surgical treatment of bone sarcoma patients. This is due to the difficulty in achieving sufficient sample sizes due to the rarity of the disease.

### Research objectives

The goal of this study was to identify common strategies in the surgical treatment of patients with bone sarcomas of the lower extremities in terms of surgical/technical considerations, choice of antibiotics, dosage, and duration of treatment, and choice of antithrombotic drug, initial start-up, dosage, and duration.

### Research methods

The study was based on an internet-based survey on the surgical management of bone sarcomas in the lower extremity amongst sarcoma surgeons in the Scandinavian countries.

### Research results

This study demonstrates a large variation in the treatment of patients with bone sarcomas located in the lower extremities. With regard of implant fixation, the Danish and Swedish sarcoma centers tended to consider a cemented prosthesis not only for the older patients but also for the youngest patients below 20 years old, contrary to the rest of the Scandinavian centers. All participants would administer intravenous prophylactic antibiotics regarding endoprosthetic reconstructive surgery. First choice of antibiotics was cephalosporin. Less commonly used were glycopeptide, penicillin, or a combination. The duration of prophylactic antibiotic treatment ranged from less than one day to more than four days. All participants would administer heparins as antithrombotic prophylaxis. Fifty-five percent of the participants answered that initial treatment was started preoperatively, 3% perioperatively and 42% postoperatively. Range of antithrombotic treatment went from 5-28 d.

### Research conclusions

Today, patients diagnosed with bone sarcomas of the lower extremity are to a great extent offered treatment with a resection prosthesis. The treatment is well established, however, there is a significant inconsistency in the surgical treatment algorithm between sarcoma centers. Still the treatment is primarily based on best clinical practice, due to the absence of evidence-based medicine in the surgical management of bone sarcomas.

### Research perspectives

The current study elucidates, that the surgical sarcoma community needs to support the ongoing randomized control trials and encourage the initiation of new randomized studies to gain knowledge of the surgical treatment of bone sarcoma patients based on evidence-based medicine.

## REFERENCES

- 1 **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/psc.20820]
- 2 **Schuetze SM**, Wathen JK, Lucas DR, Choy E, Samuels BL, Staddon AP, Ganjoo KN, von Mehren M, Chow WA, Loeb DM, Tawbi HA, Rushing DA, Patel SR, Thomas DG, Chugh R, Reinke DK, Baker LH. SARC009: Phase 2 study of dasatinib in patients with previously treated, high-grade, advanced sarcoma. *Cancer* 2016; **122**: 868-874 [PMID: 26710211 DOI: 10.1002/cncr.29858]
- 3 **Tjørnild M**, Søballe K, Hansen PM, Holm C, Stilling M. Mobile-vs. fixed-bearing total knee replacement. *Acta Orthop* 2015; **86**: 208-214 [PMID: 25280132 DOI: 10.3109/17453674.2014.968476]
- 4 **Gundtoft PH**, Pedersen AB, Varnum C, Overgaard S. Increased Mortality After Prosthetic Joint Infection in Primary THA. *Clin Orthop Relat Res* 2017; **475**: 2623-2631 [PMID: 28236084 DOI: 10.1007/s11999-017-5289-6]
- 5 **Evaniew N**, Nuttall J, Farrokhyar F, Bhandari M, Ghert M. What are the levels of evidence on which we base decisions for surgical management of lower extremity bone tumors? *Clin Orthop Relat Res* 2014; **472**: 8-15 [PMID: 24081669 DOI: 10.1007/s11999-013-3311-1]
- 6 **Ghert M**, Dehesi B, Holt G, Randall RL, Ferguson P, Wunder J, Turcotte R, Werier J, Clarkson P, Damron T, Benevenia J, Anderson M, Gebhardt M, Isler M, Mottard S, Healey J, Evaniew N, Racano A, Sprague S, Swinton M, Bryant D, Thabane L, Guyatt G, Bhandari M; PARITY Investigators. Prophylactic antibiotic regimens in tumour surgery (PARITY): protocol for a multicentre randomised controlled study. *BMJ Open* 2012; **2** [PMID: 23194956 DOI: 10.1136/bmjopen-2012-002197]
- 7 **Hasan K**, Racano A, Dehesi B, Farrokhyar F, Wunder J, Ferguson P, Holt G, Schwartz H, Petrisor B, Bhandari M, Ghert M. Prophylactic antibiotic regimens in tumor surgery (PARITY) survey. *BMC Musculoskelet Disord* 2012; **13**: 91 [PMID: 22676321 DOI: 10.1186/1471-2474-13-91]
- 8 **ESMO/European Sarcoma Network Working Group**. Bone sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2014; **25** Suppl 3: iii113-iii123 [PMID: 25210081 DOI: 10.1093/annonc/mdu256]
- 9 **Kishida Y**, Sugano N, Sakai T, Nishii T, Haraguchi K, Ohzono K, Yoshikawa H. Full weight-bearing after cementless total hip arthroplasty. *Int Orthop* 2001; **25**: 25-28 [PMID: 11374263 DOI: 10.1007/s002640000221]
- 10 **Strange S**, Whitehouse MR, Beswick AD, Board T, Burston A, Burston B, Carroll FE, Dieppe P, Garfield K, Gooberman-Hill R, Jones S, Kunutsor S, Lane A, Lenguerrand E, MacGowan A, Moore A, Noble S, Simon J, Stockley I, Taylor AH, Toms A, Webb J, Whittaker JP, Wilson M, Wylde V, Blom AW. One-stage or two-stage revision surgery for prosthetic hip joint infection--the INFORM trial: a study protocol for a randomised controlled trial. *Trials* 2016; **17**: 90 [PMID: 26883420 DOI: 10.1186/s13063-016-1213-8]
- 11 **Mankin HJ**, Lange TA, Spanier SS. The hazards of biopsy in patients with malignant primary bone and soft-tissue tumors. *J Bone Joint Surg Am* 1982; **64**: 1121-1127 [PMID: 7130225 DOI: 10.2106/00004623-198264080-00002]
- 12 **Moore TM**, Meyers MH, Patzakis MJ, Terry R, Harvey JP Jr. Closed biopsy of musculoskeletal lesions. *J Bone Joint Surg Am* 1979; **61**: 375-380 [PMID: 429406 DOI: 10.2106/00004623-197961030-00010]
- 13 **Oliveira MP**, Lima PM, da Silva HJ, de Mello RJ. Neoplasm seeding in biopsy tract of the musculoskeletal system. A systematic review. *Acta Ortop Bras* 2014; **22**: 106-110 [PMID: 24899866 DOI: 10.1590/1413-78522014220200422]
- 14 **Lee DK**, Kim HJ, Cho IY, Lee DH. Infection and revision rates following primary total knee arthroplasty in patients with rheumatoid arthritis versus osteoarthritis: a meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 3800-3807 [PMID: 27605127 DOI: 10.1007/s00167-016-4306-8]
- 15 **Racano A**, Pazonis T, Farrokhyar F, Dehesi B, Ghert M. High infection rate outcomes in long-bone tumor surgery with

- endoprosthetic reconstruction in adults: a systematic review. *Clin Orthop Relat Res* 2013; **471**: 2017-2027 [PMID: 23404421 DOI: 10.1007/s11999-013-2842-9]
- 16 **PARITY Investigators**. Prophylactic antibiotic regimens in tumour surgery (PARITY): a pilot multicentre randomised controlled trial. *Bone Joint Res* 2015; **4**: 154-162 [PMID: 26423584 DOI: 10.1302/2046-3758.49.2000482]
- 17 **Husted H**, Solgaard S, Hansen TB, Søballe K, Kehlet H. Care principles at four fast-track arthroplasty departments in Denmark. *Dan Med Bull* 2010; **57**: A4166 [PMID: 20591341]
- 18 **Cronin-Fenton DP**, Søndergaard F, Pedersen LA, Fryzek JP, Cetin K, Acquavella J, Baron JA, Sørensen HT. Hospitalisation for venous thromboembolism in cancer patients and the general population: a population-based cohort study in Denmark, 1997-2006. *Br J Cancer* 2010; **103**: 947-953 [PMID: 20842120 DOI: 10.1038/sj.bjc.6605883]

**P- Reviewer:** Elgafy H, Li JM **S- Editor:** Cui LJ  
**L- Editor:** Filipodia **E- Editor:** Song H



## Spontaneous and simultaneous complete bilateral rupture of the quadriceps tendon in a patient receiving hemodialysis: A case report and literature review

Wassim Zribi, Mohamed Zribi, Ahmed Racem Guidara, Mohamed Ben Jemaa, Ameer Abid, Nabil Krid, Abdessalem Naceur, Hassib Keskes

Wassim Zribi, Mohamed Zribi, Ahmed Racem Guidara, Mohamed Ben Jemaa, Ameer Abid, Abdessalem Naceur, Hassib Keskes, Department of Orthopaedic Surgery and Traumatology, Habib Bourguiba University Hospital, Sfax 3000, Tunisia

Nabil Krid, Department of Orthopaedic Surgery and Traumatology, Marechal Leclerc Argentan Hospital, Argentan 61200, France

ORCID number: Wassim Zribi (0000-0001-7210-9361); Mohamed Zribi (0000-0001-9328-3246); Ahmed Racem Guidara (0000-0002-1406-9872); Mohamed Ben Jemaa (0000-0001-6958-9878); Ameer Abid (0000-0003-2334-2057); Nabil Krid (0000-0002-2809-8850); Abdessalem Naceur (0000-0002-7829-5828); Hassib Keskes (0000-0003-2231-760X).

**Author contributions:** Zribi W and Zribi M performed the surgery; Guidara AR is the corresponding author, he wrote the great part of the manuscript; Ben Jemaa M, Krid N and Abid A contributed in gathering the data and writing the manuscript; Naceur A corrected some grammar mistakes and contributed in the improvement of English language; Keskes H corrected the hole manuscript and gave his permission for submitting.

**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 other conflicts of interest that may bias the current study.

**CARE Checklist (2013) statement:** The authors have read the CARE Checklist (2013), and the manuscript was prepared and revised according to the CARE Checklist (2013).

**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:** Ahmed Racem Guidara, MD, Doctor, Surgeon, Department of Orthopaedic Surgery and Traumatology, Habib Bourguiba University Hospital, El Ain Street, Sfax 3000, Tunisia. [rassimou@live.fr](mailto:rassimou@live.fr)  
**Telephone:** +216-22-650267

**Received:** May 8, 2018

**Peer-review started:** May 8, 2018

**First decision:** June 5, 2018

**Revised:** June 18, 2018

**Accepted:** June 28, 2018

**Article in press:** June 28, 2018

**Published online:** September 18, 2018

### Abstract

The spontaneous and simultaneous rupture of both quadriceps tendons is uncommon and has rarely been reported in the literature. The current case involves a 43-year-old man with end-stage renal disease requiring hemodialysis for the past 20 years. The patient experienced bilateral knee pain and swelling and was unable to bear weight. Physical examination revealed bilateral quadriceps tendon defect above the patella and loss of active extension. Although plain radiographs of both knees showed no fracture or widening of the joint space, an inferiorly positioned patella was observed. Ultrasonography of the knees revealed a quadriceps tendon defect at the upper edge of each patella, while MR imaging revealed a tear in each quadriceps tendon

from the superior poles of the patella. The patient then underwent surgical correction wherein the tendons were repaired using sutures passed through drill holes in the patella. The knees were immobilized with splints for 4 wk before starting physiotherapy. The patient subsequently regained full functional activity within 1 year.

**Key words:** Quadriceps tendon; Tear; Krackow sutures; Renal failure; Hyperparathyroidism

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Spontaneous bilateral quadriceps tendon rupture is uncommon, while the symmetry of physical findings may make the diagnosis even more difficult. Testing the extensor mechanism must be an essential part of every knee examination. Early diagnosis and surgical repair are associated with the best outcomes. The most likely etiology of tendon ruptures in patients receiving hemodialysis is the fragility of the junction between the tendon and the bone resulting from long-standing and poorly controlled hyperparathyroidism.

Zribi W, Zribi M, Guidara AR, Ben Jemaa M, Abid A, Krid N, Naceur A, Keskes H. Spontaneous and simultaneous complete bilateral rupture of the quadriceps tendon in a patient receiving hemodialysis: A case report and literature review. *World J Orthop* 2018; 9(9): 180-184 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i9/180.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i9.180>

## INTRODUCTION

Bilateral quadriceps rupture is a very rare disabling injury. Although traumatic in nature, it is often secondary to metabolic disorders and predisposing medical conditions, such as diabetes, gout, hyperparathyroidism<sup>[1]</sup>, systemic diseases, or chronic renal failure<sup>[2,3]</sup>. The spontaneous and simultaneous rupture of both quadriceps tendons has been rarely reported in the literature and is usually observed in patients aged over 40 years; a sex ratio of 6:1 has been recorded for this phenomenon<sup>[4,5]</sup>. The most commonly reported mechanism is the sudden reflexive eccentric contraction of the quadriceps, with the foot anchored to the ground and the knees flexed. We herein report a case involving spontaneous bilateral rupture of the quadriceps tendon in a patient with renal failure receiving hemodialysis. Accordingly, we present clinical particularities, imaging data, and the management employed.

## CASE REPORT

A 43-year-old male with renal failure (hemodialysis for 20 years) presented with bilateral pain and cutaneous



Figure 1 Palpation showing bilateral depression above the patella.

depression upon palpation above the patella (Figure 1). The patient exhibited good general conditions with no signs of malnutrition. Bone densitometry, which was previously performed, revealed osteopenia related to chronic kidney disease. There was no significant medical history, and no other co-morbidities were noted. Although no traumatic context had been reported, clinical examination noted incomplete active knee extension that was very painful. Radiographs of the knee showed a lowering of the patella with diffuse bone demineralization due to renal failure (Figure 2). The patient subsequently underwent ultrasonography and magnetic resonance imaging (MRI) to examine the appearance of the overlying tendon and muscle (Figure 3). Accordingly, simultaneous and spontaneous rupture of both quadriceps tendons at the patellar insertion was confirmed. Laboratory analyses revealed a white blood cell count of 8540/mm<sup>3</sup>, hemoglobin of 8 g/dL, platelet count of 352000/mm<sup>3</sup>. Blood testing revealed the following values: sodium, 137 mmol/L; potassium, 4.8 mmol/L; calcium, 2.2 mmol/L; phosphorus, 0.9 mmol/L; serum uric acid, 267 μmol/L; creatinine, 765 μmol/L; and serum parathyroid hormone, 45 pg/mL (normal, 9-65 pg/mL). Hemostasis assessment was within normal limits. The treatment consisted of tendon reinsertion through tendon-to-bone repair (Figure 4). The patient was immobilized for 4 wk with a splint before undergoing regular rehabilitation. He was allowed to fully bear weight 6 wk after his surgery. The operative follow-up was simple. A year later, the patient showed excellent results and regained his former autonomy (Figure 5).

## DISCUSSION

Bilateral rupture of the quadriceps tendon is a rare injury. Accordingly, the first reported case of simultaneous bilateral rupture of quadriceps tendons had been by Steiner and Palmer in 1949. Patients usually complain of severe knee pain and complete functional disability



Figure 2 Knee radiographs showing patellar lowering and diffuse bone demineralization. A: Antero-posterior X-rays; B: Lateral X-rays.

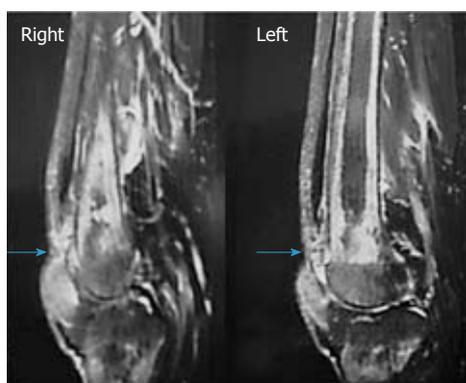


Figure 3 Magnetic resonance imaging of the knee (sagittal view) showing a complete bilateral rupture of the tendon.



Figure 4 Surgical management of the injury through bilateral reinsertion of the tendon. A: Exposing the bilateral rupture of the quadriceps tendon; B: Quadriceps tendon reinserted through tendon-to-bone repair.



Figure 5 Complete active extensions of the knees.

of the lower limbs. In younger patients, however, major trauma by direct shock or laceration by a blunt object has been more common. In the absence of a traumatic context, assessment should be focused on identifying systemic diseases wherein tendons become weakened. Hence, tendon ruptures could be caused by the diminution of local circulation, abnormalities in collagen metabolism, repeated microtrauma, weakening, and calcifications, which consequently reduce the elasticity of the tendon. Most authors agree that bone resorption at the tendon insertion sites due to secondary hyperparathyroidism contributes to the pathogenesis of tendon ruptures. In addition, weakening of the tendon may be observed when collagen is replaced by elastin during chronic metabolic acidosis due to chronic renal failure. Such patients are therefore at risk for bilateral ruptures. Many cases of bilateral ruptures in athletes consuming anabolic agents have been also reported in the literature<sup>[6]</sup>. Moreover, direct corticosteroid injections and fluoroquinolone use have all been associated with increased risk of tendon rupture<sup>[6]</sup>. Though fluoroquinolone use has most commonly affected the Achilles tendon, cases involving the rotator cuff, biceps, wrist extensors, and quadriceps tendons among others, have also been described<sup>[7,8]</sup>. The diagnosis of quadriceps tendon rupture has been based primarily on anamnesis and clinical examination.

Accordingly, Siwek and Rao<sup>[4]</sup> in 1981 showed that 28% of ruptures had not been initially diagnosed. Therefore, clinical examination is crucial and allows for rapid diagnosis, which is critical for optimal therapeutic management. Clinically, patients are no longer able to perform full active extension of the knee<sup>[9]</sup>. In a supine position, patients cannot elevate the lower limb while keeping it extended or maintain this position against gravity. In a seated position with the knees flexed at 90°, patients are unable to completely extend the knee when both the quadriceps tendon and retinaculum (aponeurosis of the vastus medialis and vastus lateralis, which are inserted on the patella) are torn. On the other hand, when the quadriceps tendon is torn while the retinaculum is intact, patients are able to achieve partial active extension without reaching full extension. During palpation of the quadriceps tendon, a "hole" and an interruption of tendon continuity are felt. However, the swelling and hematoma that subsequently develop may obscure the palpability of this "hole"<sup>[5]</sup>. Quadriceps tendon tears generally occur 2 cm above the upper pole of the patella. However, tearing occasionally occurs higher at the myotendinous junction, particularly in patients with reduced mobility and muscle atrophy. A differential diagnosis for patients unable to perform full active knee extension may include femoral nerve palsy, which might be traumatic or iatrogenic<sup>[10]</sup>. Accordingly, radiological examinations may help establish a more accurate diagnosis. Radiographic views of the knee may show soft tissue swelling above the kneecap. Calcifications at the superior pole of the patella may indirectly indicate quadriceps tendinopathy, which is a predisposition to

rupture<sup>[11]</sup>. Considering that the patella is no longer subject to quadriceps traction, it may be located lower compared to the uninjured side in unilateral conditions (patella baja or patella infera).

Although ultrasonography is a non-invasive, rapid, and effective diagnostic tool for confirming a partial or complete quadriceps tendon rupture, interpretation of its results is examiner-dependent and must be performed by a trained specialist. MRI is another very sensitive diagnostic tool that can precisely locate the tear, determine which four layers of the quadriceps tendon are affected or whether the rupture is partial, and determine whether the retinaculum is torn<sup>[5]</sup>. As such, our patient underwent MRI to identify quadriceps tendon ruptures prior to surgery. Surgery based on reintegration for fresh lesions and tendinous plasty for old ones has always been the standard treatment for ruptures, with early surgical repair providing the best results<sup>[5]</sup>. Nonetheless, various surgical techniques have been described. In the case of tendon body tearing, an end-to-end suture allows for an excellent repair. For ruptures close to the patellar insertion, Krackow points<sup>[12]</sup> can be made in the tendon stump, which is then passed through the patella using longitudinal bony tunnels, ensuring good holding. A torn retinaculum must also be sutured. Lighthart *et al.*<sup>[13]</sup> studied quadriceps tendon strength after transosseous suturing and tendon anchoring. Accordingly, their results showed no difference between the two techniques.

After the operation, walking was permitted albeit with a splint keeping the knee extended for 4 to 6 wk, which helps protect the reconstruction<sup>[14]</sup>. A mobilization of 0°-30° can be allowed to prevent adhesions. Most authors have reported good functional results, always with complete motion recovery and return to previous activities<sup>[13,14]</sup>. Though quadriceps amyotrophy is quite common, it carries no functional repercussions in everyday life. Moreover, recovery is difficult despite physiotherapy. In fact, only 4 to 6 wk of actual physiotherapy is provided postoperatively. Furthermore, a secondary rupture may occur but remains rare<sup>[7]</sup>.

A missed diagnosis may lead to delayed repair, which could be problematic due to significant quadriceps retraction. As a result, end-to-end tendon suturing becomes difficult, and more complex surgical techniques are often necessary to fix the consequent defect and restore the extensor system of the knee. Several techniques have been described<sup>[5]</sup>, including tendon grafting (auto- or allograft) and tendon flap advancement. Nonetheless, delayed repairs have worse results and higher complication rates. Early diagnosis and treatment are therefore essential for good healing and functional recovery.

Spontaneous ruptures of the knee extensor system are rare, and bilateral forms, which result in functional disability of both lower limbs, are exceptionally rare. Given that early diagnosis allows for rapid surgical management and thus optimal functional recovery, careful investigation of such ruptures through clinical examination, plain radiographs, and MRI is therefore

necessary for better tear analysis.

## ARTICLE HIGHLIGHTS

### Case characteristics

This case involves spontaneous bilateral rupture of the quadriceps tendon in a patient with renal failure receiving hemodialysis. Accordingly, we present clinical particularities, imaging data, and the management employed.

### Clinical diagnosis

Bilateral rupture of the quadriceps tendon.

### Differential diagnosis

Femoral nerve palsy.

### Laboratory diagnosis

Blood testing revealed renal failure and anemia without other abnormalities.

### Imaging diagnosis

Knee radiographs revealed lowering of the patella with diffuse bone demineralization caused by renal failure. Magnetic resonance imaging confirmed the diagnosis of bilateral rupture of the quadriceps tendon.

### Treatment

Tendon reinsertion through tendon-to-bone repair.

### Related reports

Only few cases of spontaneous bilateral rupture of the quadriceps tendon have been to date reported in the literature.

### Experiences and lessons

This case will help improve the understanding of the management of bilateral rupture of the quadriceps tendon, which is a rare injury. The main lesson learned was that early diagnosis and surgical repair are essential for achieving the best outcomes.

## ACKNOWLEDGEMENTS

We thank the patient described for allowing us to share his details and thank Dr. Wassim Zribi and Dr. Mohamed Zribi for advice and performing the surgery.

## REFERENCES

1 Mokoko-Louckou AE, Chaibou B, Abdouli I, Bouhelo-Pam

- KPB, Idrissi ME, Shimi M, Ibrahim AE, Mrini AE. [Spontaneous simultaneous bilateral rupture of the quadriceps tendon in patients with parathyroid adenoma: case report and literature review]. *Pan Afr Med J* 2018; **29**: 14 [PMID: 29662599 DOI: 10.11604/pamj.2018.29.14.13540]
- 2 Arumilli B, Adeyemo F, Samarji R. Bilateral simultaneous complete quadriceps rupture following chronic symptomatic tendinopathy: a case report. *J Med Case Rep* 2009; **3**: 9031 [PMID: 19918285 DOI: 10.4076/1752-1947-3-9031]
- 3 Neubauer T, Wagner M, Potschka T, Riedl M. Bilateral, simultaneous rupture of the quadriceps tendon: a diagnostic pitfall? Report of three cases and meta-analysis of the literature. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 43-53 [PMID: 16951978 DOI: 10.1007/s00167-006-0133-7]
- 4 Siwek CW, Rao JP. Ruptures of the extensor mechanism of the knee joint. *J Bone Joint Surg Am* 1981; **63**: 932-937 [PMID: 6985557 DOI: 10.2106/00004623-198163060-00010]
- 5 Ilan DI, Tejwani N, Keschner M, Leibman M. Quadriceps tendon rupture. *J Am Acad Orthop Surg* 2003; **11**: 192-200 [PMID: 12828449 DOI: 10.5435/00124635-200305000-00006]
- 6 Lewis AC, Purushotham B, Power DM. Bilateral simultaneous quadriceps tendon rupture in a bodybuilder. *Orthopedics* 2005; **28**: 701-702 [PMID: 16119286]
- 7 Stinner DJ, Orr JD, Hsu JR. Fluoroquinolone-associated bilateral patellar tendon rupture: a case report and review of the literature. *Mil Med* 2010; **175**: 457-459 [PMID: 20572481 DOI: 10.7205/MILMED-D-09-00142]
- 8 Casparian JM, Luchi M, Moffat RE, Hinthorn D. Quinolones and tendon ruptures. *South Med J* 2000; **93**: 488-491 [PMID: 10832946 DOI: 10.1097/00007611-200005000-00008]
- 9 Ramsey RH, Muller GE. Quadriceps tendon rupture: a diagnostic trap. *Clin Orthop Relat Res* 1970; **70**: 161-164 [PMID: 5445722 DOI: 10.1097/00003086-197005000-00019]
- 10 Thoms RJ, Kondrashov D, Silber J. Iatrogenic femoral nerve palsy masquerading as knee extensor mechanism rupture. *Am J Orthop (Belle Mead NJ)* 2009; **38**: 142-144 [PMID: 19377648]
- 11 Hardy JR, Chimutengwende-Gordon M, Bakar I. Rupture of the quadriceps tendon: an association with a patellar spur. *J Bone Joint Surg Br* 2005; **87**: 1361-1363 [PMID: 16189308 DOI: 10.1302/0301-620X.87B10.16624]
- 12 Krackow KA, Thomas SC, Jones LC. A new stitch for ligament-tendon fixation. Brief note. *J Bone Joint Surg Am* 1986; **68**: 764-766 [PMID: 3522596 DOI: 10.2106/00004623-198668050-00020]
- 13 Lighthart WA, Cohen DA, Levine RG, Parks BG, Boucher HR. Suture anchor versus suture through tunnel fixation for quadriceps tendon rupture: a biomechanical study. *Orthopedics* 2008; **31**: 441 [PMID: 19292325 DOI: 10.3928/01477447-20080501-18]
- 14 Ennaciri B, Montbarbon E, Beaudouin E. Surgical management of acute quadriceps tendon rupture (a case report with literature review). *Pan Afr Med J* 2015; **22**: 243 [PMID: 26958106 DOI: 10.11604/pamj.2015.22.243.7533]

P- Reviewer: Kocazeybek B, Kute VB, Zaky A S- Editor: Ji FF  
L- Editor: A E- Editor: Song H





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 October 18; 9(10): 185-234



**MINIREVIEWS**

- 185 Intra-operative computed tomography guided navigation for pediatric pelvic instrumentation: A technique guide  
*Anari JB, Cahill PJ, Flynn JM, Spiegel DA, Baldwin KD*

**ORIGINAL ARTICLE****Basic Study**

- 190 Dose of alendronate directly increases trabeculae expansivity without altering bone volume in rat femurs  
*Weiss SG, Kuchar GO, Gerber JT, Tiboni F, Storrer CLM, Casagrande TC, Giovanini AF, Scariot R*

**Retrospective Study**

- 198 Reducing costly falls after total knee arthroplasty  
*Bolarinwa SA, Novicoff W, Cui Q*
- 203 Screw placement is everything: Risk factors for loss of reduction with volar locking distal radius plates  
*Drobtz H, Black A, Davies J, Buttner P, Heal C*

**Observational Study**

- 210 Long-term results of an anatomically implanted hip arthroplasty with a short stem prosthesis (MiniHip™)  
*von Engelhardt LV, Breil-Wirth A, Kothny C, Seeger JB, Grasselli C, Jerosch J*
- 220 Does ethnicity and education influence preoperative disability and expectations in patients undergoing total knee arthroplasty?  
*Kudibal MT, Kallemose T, Troelsen A, Husted H, Gromov K*

**SYSTEMATIC REVIEW**

- 229 Total knee arthroplasty in patients with Paget's disease of bone: A systematic review  
*Popat R, Tsitskaris K, Millington S, Dawson-Bowling S, Hanna SA*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Antonios Angoules, MD, PhD, Surgeon, Orthopaedic Department, Athens Medical Center, 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 abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), China National Knowledge Infrastructure (CNKI), and Superstar Journals Database.

**EDITORS FOR THIS ISSUE**

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

**Responsible Science Editor:** *Ying Dou*  
**Proofing Editorial Office Director:** *Jin-Lei Wang*

**NAME OF JOURNAL**  
*World Journal of Orthopedics*

**ISSN**  
 ISSN 2218-5836 (online)

**LAUNCH DATE**  
 November 18, 2010

**FREQUENCY**  
 Monthly

**EDITOR-IN-CHIEF**  
**Bao-Gan Peng, MD, PhD, Professor**, Department of Spinal Surgery, General Hospital of Armed Police Force, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com/2218-5836/editorialboard.htm>

**EDITORIAL OFFICE**  
 Jin-Lei Wang, Director

*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f0publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f0publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 October 18, 2018

**COPYRIGHT**  
 © 2018 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.f0publishing.com>

## Intra-operative computed tomography guided navigation for pediatric pelvic instrumentation: A technique guide

Jason B Anari, Patrick J Cahill, John M Flynn, David A Spiegel, Keith D Baldwin

Jason B Anari, Patrick J Cahill, John M Flynn, David A Spiegel, Keith D Baldwin, Department of Orthopaedic Surgery, Children's Hospital of Philadelphia, Philadelphia, PA 19104, United States

ORCID number: Jason B Anari (0000-0002-2190-6333); Patrick J Cahill (000-0002-7129-1007); John M Flynn (0000-0003-0643-0506); David A Spiegel (0000-0001-6417-7735); Keith D Baldwin (0000-0002-2333-9061).

Author contributions: Anari JB contributed to primary manuscript preparation; Cahill PJ, Flynn JM and Spiegel DA contributed to manuscript review, contributed patients; Baldwin KD contributed to secondary manuscript preparation, contributed patients.

Conflict-of-interest statement: The authors have no conflicts-of-interest to disclose that are pertinent to 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: Keith D Baldwin, MD, Assistant Professor, Department of Orthopaedic Surgery, Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Philadelphia, PA 19104, United States. [baldwink@email.chop.edu](mailto:baldwink@email.chop.edu)  
Telephone: +1-856-4040635  
Fax: +1-215-5907861

Received: July 2, 2018

Peer-review started: July 2, 2018

First decision: July 19, 2018

Revised: July 29, 2018

Accepted: August 4, 2018

Article in press: August 5, 2018

Published online: October 18, 2018

### Abstract

Pelvic instrumentation for neuromuscular scoliosis has been part of neuromuscular scoliosis surgery since the era of the Luque Galveston construct. Unit Rod (Medtronic Sofamor-Danek, Nashville, TN) instrumentation brought with it the concept of cantilever correction by placing the implants in the pelvis and then gradually bringing the rod to the spine by sequentially tightening the sublaminar wires, with the goal of creating a level pelvis over a straight spine. More recently surgeons have utilized pedicle screw constructs in which the corrective strategies have varied. Challenges with pelvic fixation using iliac screws linked to the spinal rod have led to the development of the S2-alar-iliac technique (S2AI) in which the spinal rod connects to the pelvic screw. The screw is placed in the S2 ala, crosses the sacro-iliac joint and into the ilium through a large column of supra-acetabular bone. This column is the same area used for anterior inferior iliac spine external fixation frames used in trauma surgery. S2AI screw placement can be technically difficult and can require experienced radiology technologists to provide the appropriate views. Additionally, although the technique was originally described being placed *via* freehand technique with intra-operative fluoroscopy, the freehand technique suffers from the anatomic anomalies present in the pelvis in neuromuscular scoliosis. As such, we prefer to place them using intra-operative navigation for all pediatric spinal deformity cases. Below in detail we report our intra-operative technique and an illustrative case example.

**Key words:** Posterior instrumentation; Pediatric; Spinal deformity; Image guidance; Technique

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** S2-alar-iliac technique (S2AI) screws are used commonly in 2018 in posterior spinal fusion surgery

when a fusion to the pelvis is indicated. The benefits of this instrumentation choice are well known; and now with 3D technology surgeons can safely place S2AI screws reproducibly even in aberrant pediatric anatomy.

Anari JB, Cahill PJ, Flynn JM, Spiegel DA, Baldwin KD. Intra-operative computed tomography guided navigation for pediatric pelvic instrumentation: A technique guide. *World J Orthop* 2018; 9(10): 185-189 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i10/185.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i10.185>

## INTRODUCTION

Neuromuscular scoliosis is a common cause of spinal deformity, and nonambulatory patients commonly have a thoracolumbar or lumbar curve associated with pelvic obliquity (Figure 1). While corrective strategies have varied, the initial approach using the Luque-Galveston technique involved extension of the spinal rod into the posterior ilium/pelvis. The corrective strategy in the unit rod occurred by first placing the pelvic limbs of the fixation in the pelvis, and then gradually bringing the rod to the spine by applying cantilever forces and sequentially tightening sublaminar wires to bring the spine to the rod<sup>[1]</sup>. Problems include prominence of the implants, loosening of the pelvic limbs within the pelvis ("windshield wiper"), and rod fracture. The unit rod is a pre-contoured rod which was developed to avert the need for intraoperative rod contouring, and the technique for correction was the same. Subsequent variations in lumbo-pelvic fixation have included iliac screws, which are placed into the posterior iliac crest and attached to the spinal rod *via* connectors. Some authors have placed dual screws into the ilium, while others have advocated for screws in both the first sacral vertebra and the ilium. Challenges with this fixation include implant prominence and failure of the implant at the junction between either the screw and the connector or the connector and the rod.

In 2007, Sponseller introduced the S2-alar-iliac technique (S2AI) in which the pelvic screw is placed from the sacrum into the pelvis. The screw head is low profile and connects directly with the spinal rod<sup>[2]</sup>. While initial reports documented safety and placement in both pediatric and adult spinal deformity patients, much of the recent literature regarding safety of placement using the S2AI technique has been published in adults<sup>[3-6]</sup>. Shillingford *et al*<sup>[3]</sup> report a free hand technique without intra-operative imaging that has a cortical breach rate of 7% posteriorly and 1% anteriorly. Anterior perforation into the pelvis or inferior perforation into the sciatic notch can have catastrophic result given the neurovascular and visceral structures found in such locations<sup>[3]</sup>. There may also be variations in anatomy, for example the relationship between the iliac wings and the pelvis. In the setting of considerable pelvic obliquity, the patient may bear weight on the downside iliac wing, and one may observe asymmetry in the relationship between



Figure 1 Posteroanterior of a sweeping thoracolumbar curve with pelvic obliquity typical of neuromuscular scoliosis.



Figure 2 Navigation probe.

the iliac wings and the pelvis such as adduction of one iliac wing with abduction of the other.

We have utilized computed tomography (CT) image navigation for placement of pedicle screws at our institution for more than 10 years, and we have extended this practice to the placement of S2AI screws<sup>[7]</sup>. Here we describe our technique for CT guided pediatric pelvic fixation using the S2AI technique.

## TECHNIQUE

The patient is placed in the prone position on an open Jackson table and a subperiosteal exposure from the upper instrumented vertebrae to S2 is performed. Adequate exposure on the sacrum includes visualization of both the S1 and S2 neural foramina. An anchor point is picked proximally in the lumbar or thoracic spine that is sturdy enough to hold a reference array (4 tines at a minimum) and simultaneously remain out of the surgeon's working space while placing instrumentation. Our preferred location is the lower thoracic spine (T11/12) as this is usually far enough away to be out of the working field but not too far from the insertion point to alter the information acquired by the CT scan. Patient lordosis must be taken into account as significant differences in trajectory may lead to interference of the guidance probe with the sensor array.

Once the exposure is complete and the array in a stable location a low dose CT scan (2.25 mSv) is performed from the top of the femoral heads to the lower lumbar spine region (O-Arm Medtronic Sofamor-Danek, Nashville, TN). Following completion of the CT scan the navigation probe (Figure 2) is connected to the



Figure 3 Starting point for the S2-alar-iliac technique screw. A: On pelvis; B: Navigation probe identifying the appropriate location.

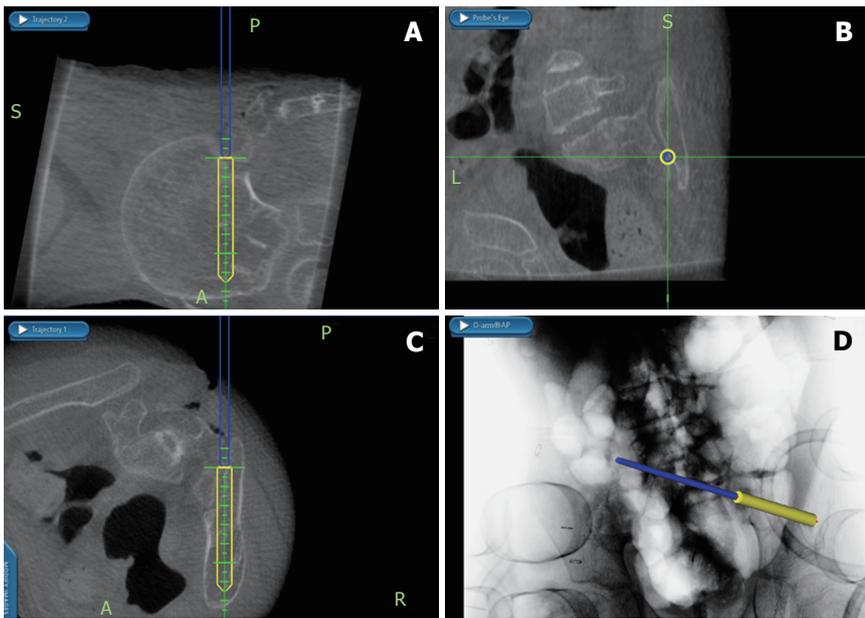


Figure 4 Intra-operative navigation screen depicting safe starting point and projected placement of an S2-alar-iliac technique screw. A: Sagittal; B: Coronal; C: Axial; D: Current position of navigation probe.

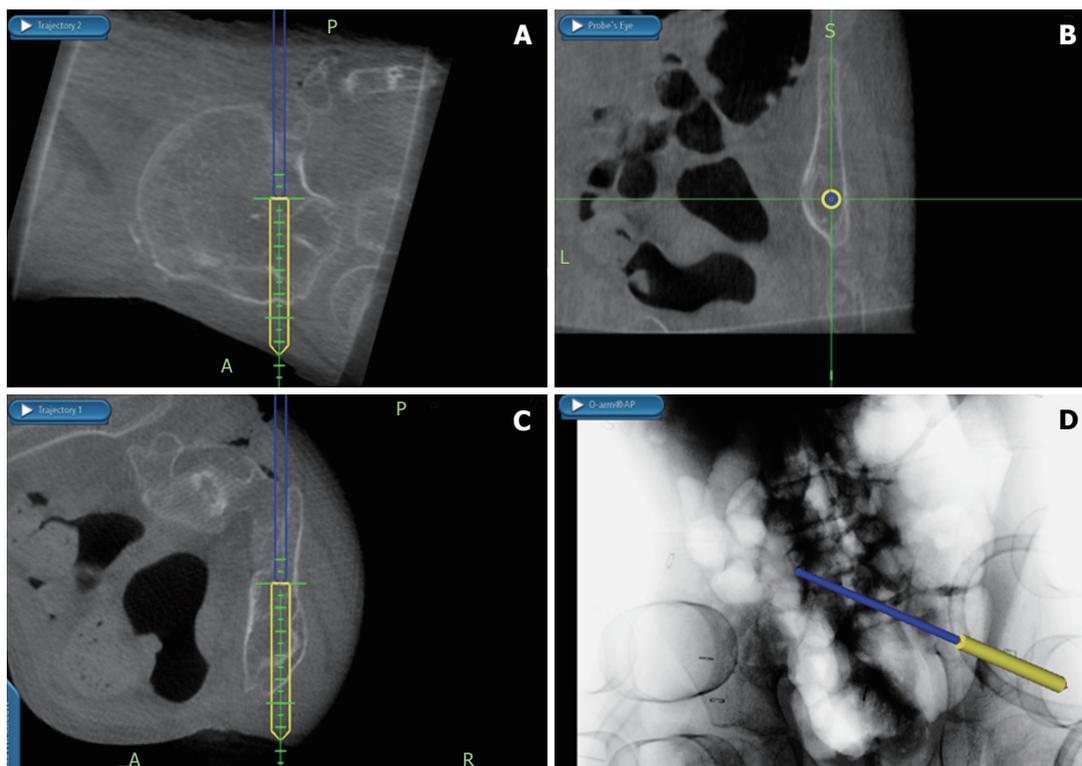


Figure 5 Intraoperative clinical photo depicting the navigation probe placed down the dilated path for the S2-alar-iliac technique screw with a guidewire in place.

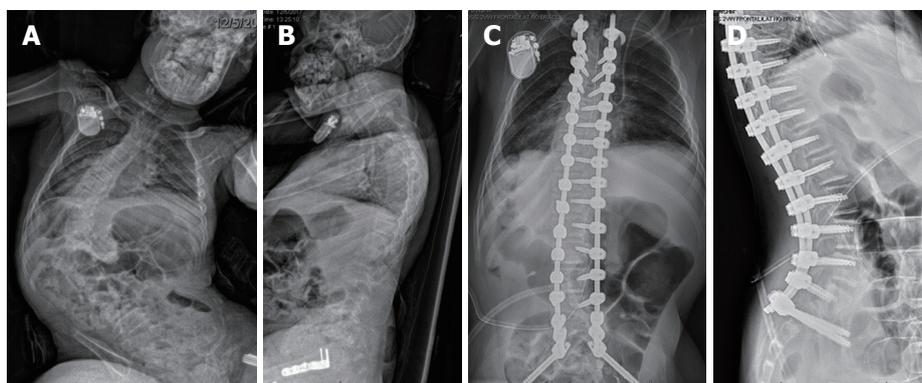
array by docking the probe in the array's recess. Once confirmation of coupling occurs 3D anatomy from the CT scan is confirmed by placing the probe over a lumbar spinous process correlating the imaging seen on the screen with the patient. The surgeon, who stands on the patient's left places the right sided S2AI screw and switches sides for the left sided screw. The typical entry point insertion for the S2AI screws are just lateral to

the lateral edge of the S1 and S2 foramina midway between the two (Figure 3), although minor variations may be required depending on the local anatomy. Once this point is identified using the probe a 4 mm acorn burr is used to create a pilot hole for the pedicle probe approximately 3 mm in depth. The navigation probe is replaced in the pilot hole to confirm trajectory in both the axial and sagittal planes. Normal anatomy puts the S2AI trajectory at approximately 40° lateral in the axial plane and 20°-40° caudal in the sagittal plane<sup>[2,8]</sup>. Once surgeon has trajectory memorized the straight gearshift is passed through the sacrum into the sacroiliac joint and into the ilium (Figure 4). In rare cases the proper trajectory may require that the screw be placed directly into the ilium and not through the sacrum.

On the navigation screen depth and trajectory can be checked anytime with gearshift removal and placement of navigation probe. The authors prefer to place gearshift to the desired screw depth, dilate the tract, and then place the navigation probe down the tract to ensure circumferential bone and a floor alongside a guide wire (Figure 5). A ball tip probe then palpates the walls of the tract, and the channel is tapped to a



**Figure 6** Intra-operative navigation screens depicting a safe trajectory for the S2-alar-iliac technique pelvic screw. A: Sagittal; B: Coronal; C: Axial; D: Anterior-posterior radiograph showing current position of navigation probe.



**Figure 7** Pre-operative and post-operative radiographs in a patient with neuromuscular scoliosis who underwent T3 to pelvis instrumented posterior spinal fusion using navigation to place pedicle screw and S2-alar-iliac technique instrumentation. A: Posteroanterior; B: Lateral; C: Anteroposterior; D: Lateral.

diameter 0.5 mm less than the desired screw diameter, over the guide wire. The walls of the tract are palpated one last time before the cannulated screw is placed over the guide wire. Lastly the navigation probe is placed down the cannulated screw to palpate a floor as well as ensure the trajectory taken by the screw (Figure 6). Final position of the S2AI screws align with the cephalad instrumentation facilitating rod insertion. Figure 7 depicts a patient with neuromuscular scoliosis and pelvic obliquity who had S2AI instrumentation placed during an instrumented posterior fusion.

## DISCUSSION

The extension of spinal instrumentation and fusion across

the lumbosacral junction and into the pelvis is required in a number of clinical scenarios in both children and adults. In the pediatric population this is most commonly to address pelvic obliquity in the neuromuscular population, while in adults a common indication is to achieve rigid distal anchors for correcting sagittal imbalance in the setting of osteoporotic bone and to enhance the chances of arthrodesis across the lumbosacral junction<sup>[9-12]</sup>. Each situation offers varying complexity with regard to the insertion of implants, for example in pediatric patients in which there may be variations in the relationship between the iliac wings and the sacrum. We have also observed that the isthmus may be quite narrow in some pediatric patients, and the navigation allows us to identify this and choose the optimal sized screw, which is important given

the literature suggestion screw diameter < 8 mm are at an increased risk of implant complications<sup>[13]</sup>.

We have utilized a CT guided approach for more than 10 years and have been satisfied with our ability to safely place the implants, and this approach also serves as a valuable training tool for our residents and fellows who are being exposed to the challenge of lumbo-pelvic fixation. Reports concerning both free hand instrumentation and navigation assisted instrumentation are available<sup>[14-16]</sup>. The discussions include a comparison of cost, radiation safety for patient/surgeon/staff, reliance on technology, and associated risks with the learning curve<sup>[17-19]</sup>. At our institution the intra-operative CT dose is extremely low and all faculty are prepared to place without image guidance if the technology fails intra-operatively<sup>[20]</sup>.

## REFERENCES

- 1 **Herkowitz HN**, Garfin SR, Eismont FJ, Bell GR, Balderson RA. Rothman-Simeone the Spine. 6<sup>th</sup> edition. Philadelphia: Elsevier Saunders, 2011
- 2 **Chang TL**, Sponseller PD, Kebaish KM, Fishman EK. Low profile pelvic fixation: anatomic parameters for sacral alar-iliac fixation versus traditional iliac fixation. *Spine (Phila Pa 1976)* 2009; **34**: 436-440 [PMID: 19247163 DOI: 10.1097/BRS.0b013e318194128c]
- 3 **Shillingford JN**, Laratta JL, Tan LA, Sarpong NO, Lin JD, Fischer CR, Lehman RA Jr, Kim YJ, Lenke LG. The Free-Hand Technique for S2-Alar-Iliac Screw Placement: A Safe and Effective Method for Sacropelvic Fixation in Adult Spinal Deformity. *J Bone Joint Surg Am* 2018; **100**: 334-342 [PMID: 29462037 DOI: 10.2106/JBJS.17.00052]
- 4 **Hu X**, Lieberman IH. Robotic-guided sacro-pelvic fixation using S2 alar-iliac screws: feasibility and accuracy. *Eur Spine J* 2017; **26**: 720-725 [PMID: 27272491 DOI: 10.1007/s00586-016-4639-5]
- 5 **Shillingford JN**, Laratta JL, Park PJ, Lombardi JM, Tuchman A, Saifi CS, Lehman RA, Lenke LG. Human versus Robot: A Propensity-Matched Analysis of the Accuracy of Free Hand versus Robotic Guidance for Placement of S2 Alar-Iliac (S2AI) Screws. *Spine (Phila Pa 1976)* 2018 [PMID: 29672421 DOI: 10.1097/BRS.0000000000002694]
- 6 **Laratta JL**, Shillingford JN, Lombardi JM, Alrabaa RG, Benkli B, Fischer C, Lenke LG, Lehman RA. Accuracy of S2 Alar-Iliac Screw Placement Under Robotic Guidance. *Spine Deform* 2018; **6**: 130-136 [PMID: 29413734 DOI: 10.1016/j.jspd.2017.08.009]
- 7 **Ughwanogho E**, Patel NM, Baldwin KD, Sampson NR, Flynn JM. Computed tomography-guided navigation of thoracic pedicle screws for adolescent idiopathic scoliosis results in more accurate placement and less screw removal. *Spine (Phila Pa 1976)* 2012; **37**: E473-E478 [PMID: 22020579 DOI: 10.1097/BRS.0b013e318238bbd9]
- 8 **Zhu F**, Bao HD, Yuan S, Wang B, Qiao J, Zhu ZZ, Liu Z, Ding YT, Qiu Y. Posterior second sacral alar iliac screw insertion: anatomic study in a Chinese population. *Eur Spine J* 2013; **22**: 1683-1689 [PMID: 23508334 DOI: 10.1007/s00586-013-2734-4]
- 9 **O'Brien JP**, Dwyer AP, Hodgson AR. Paralytic pelvic obliquity. Its prognosis and management and the development of a technique for full correction of the deformity. *J Bone Joint Surg Am* 1975; **57**: 626-631 [PMID: 1150703 DOI: 10.2106/00004623-197557050-00007]
- 10 **Hayer SD**, Rabago DP, Amaza IP, Kille T, Coe CL, Zgierska A, Zakletskaia L, Mundt MP, Krahn D, Obasi CN, Molander RC. Effectiveness of nasal irrigation for chronic rhinosinusitis and fatigue in patients with Gulf War illness: protocol for a randomized controlled trial. *Contemp Clin Trials* 2015; **41**: 219-226 [PMID: 25625809 DOI: 10.1016/j.cct.2015.01.008]
- 11 **Lee MC**, Jarvis C, Solomito MJ, Thomson JD. Comparison of S2-Alar and traditional iliac screw pelvic fixation for pediatric neuromuscular deformity. *Spine J* 2018; **18**: 648-654 [PMID: 28870838 DOI: 10.1016/j.spinee.2017.08.253]
- 12 **Sponseller PD**, Zimmerman RM, Ko PS, Pull Ter Gunne AF, Mohamed AS, Chang TL, Kebaish KM. Low profile pelvic fixation with the sacral alar iliac technique in the pediatric population improves results at two-year minimum follow-up. *Spine (Phila Pa 1976)* 2010; **35**: 1887-1892 [PMID: 20802390 DOI: 10.1097/BRS.0b013e3181e03881]
- 13 **Jain A**, Kebaish KM, Sponseller PD. Sacral-Alar-Iliac Fixation in Pediatric Deformity: Radiographic Outcomes and Complications. *Spine Deform* 2016; **4**: 225-229 [PMID: 27927507 DOI: 10.1016/j.jspd.2015.11.005]
- 14 **Kim YJ**, Lenke LG, Bridwell KH, Cho YS, Riew KD. Free hand pedicle screw placement in the thoracic spine: is it safe? *Spine (Phila Pa 1976)* 2004; **29**: 333-42; discussion 342 [PMID: 14752359 DOI: 10.1097/01.BRS.0000109983.12113.9B]
- 15 **Du JP**, Fan Y, Wu QN, Wang DH, Zhang J, Hao DJ. Accuracy of Pedicle Screw Insertion Among 3 Image-Guided Navigation Systems: Systematic Review and Meta-Analysis. *World Neurosurg* 2018; **109**: 24-30 [PMID: 28917704 DOI: 10.1016/j.wneu.2017.07.154]
- 16 **Mason A**, Paulsen R, Babuska JM, Rajpal S, Burneikiene S, Nelson EL, Villavicencio AT. The accuracy of pedicle screw placement using intraoperative image guidance systems. *J Neurosurg Spine* 2014; **20**: 196-203 [PMID: 24358998 DOI: 10.3171/2013.11.SPINE13413]
- 17 **Hu X**, Lieberman IH. What is the learning curve for robotic-assisted pedicle screw placement in spine surgery? *Clin Orthop Relat Res* 2014; **472**: 1839-1844 [PMID: 24048889 DOI: 10.1007/s11999-013-3291-1]
- 18 **Yoshihara H**, Paulino CB. Radiation Exposure to the Surgeons and Patients in Fluoroscopic-guided Segmental Pedicle Screw Placement for Pediatric Scoliosis. *Spine (Phila Pa 1976)* 2018 [PMID: 29762341 DOI: 10.1097/BRS.0000000000002718]
- 19 **Ghasem A**, Sharma A, Greif DN, Alam M, Maaieh MA. The Arrival of Robotics in Spine Surgery: A Review of the Literature. *Spine (Phila Pa 1976)* 2018 [PMID: 29672420 DOI: 10.1097/BRS.0000000000002695]
- 20 **Sarwahi V**, Payares M, Wendolowski S, Maguire K, Thornhill B, Lo Y, Amaral TD. Low-Dose Radiation 3D Intraoperative Imaging: How Low Can We Go? An O-Arm, CT Scan, Cadaveric Study. *Spine (Phila Pa 1976)* 2017; **42**: E1311-E1317 [PMID: 28296816 DOI: 10.1097/BRS.0000000000002154]

**P- Reviewer:** Kung WM, Pavone V **S- Editor:** Ji FF  
**L- Editor:** A **E- Editor:** Song H



## Basic Study

**Dose of alendronate directly increases trabeculae expansivity without altering bone volume in rat femurs**

Suyany G Weiss, Gabrielle O Kuchar, Jennifer T Gerber, Fernanda Tiboni, Carmen Lucia M Storrer, Thaís C Casagrande, Allan F Giovanini, Rafaela Scariot

Suyany G Weiss, Gabrielle O Kuchar, Jennifer T Gerber, Fernanda Tiboni, Carmen Lucia M Storrer, Allan F Giovanini, Rafaela Scariot, School of Health Science, Department of Dentistry, Positivo University, Curitiba, Paraná 81280-330, Brazil

Thaís C Casagrande, School of Health Science, Department of Biotechnology, Positivo University, Curitiba, Paraná 81280-330, Brazil

ORCID number: Suyany G Weiss (0000-0002-5778-3144), Gabrielle O Kuchar (0000-0003-3785-6817), Jennifer T Gerber (0000-0003-3881-1434), Fernanda Tiboni (0000-0002-2511-8019), Carmen Lucia M Storrer (0000-0002-1188-8848), Thaís C Casagrande (0000-0001-9437-4043), Allan F Giovanini (0000-0002-1637-2955), Rafaela Scariot (0000-0002-4911-6413).

**Author contributions:** Weiss SG performed the majority of the experiments and analyzed the data; Kuchar GO, Gerber JT and Tiboni F participated in treatment of animals; Casagrande TC was involved in surgical procedures; Storrer CLM and Giovanini AF contributed to the writing of the paper; Scariot R designed the study, performed some surgical procedures and coordinated the research.

**Institutional animal care and use committee statement:** The Ethics Committee on the Use of Animals (ECUA 320) approved this research.

**Conflict-of-interest statement:** All authors have no conflicts of interest to report.

**ARRIVE guidelines statement:** The authors have read the ARRIVE guidelines, and the manuscript was prepared and revised according to the ARRIVE guidelines.

**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: Rafaela Scariot, PhD, Associate Professor, School of Health Science, Department of Dentistry, Positivo University, 5300 Professor Pedro Viriato Parigot de Souza Street, Campo Comprido, Curitiba, Paraná 81280-330, Brazil. [rafaela.moraes@up.edu.br](mailto:rafaela.moraes@up.edu.br)  
Telephone: +55-41-33173454  
Fax: +55-41-33173454

Received: May 7, 2018

Peer-review started: May 7, 2018

First decision: June 14, 2018

Revised: June 20, 2018

Accepted: June 28, 2018

Article in press: June 28, 2018

Published online: October 18, 2018

**Abstract****AIM**

To evaluate the effects of sodium alendronate on bone repair in fractures created in appendicular bones.

**METHODS**

Wistar rats ( $n = 36$ ) were allocated into three distinct groups: group C (control), group B1 (received 1 mg/kg of alendronate), and group B2 (received 3 mg/kg of alendronate). The rats underwent femoral transversal linear fracture surgery using stable internal fixation with a 2.0 mm plate and screw system. Each animal randomly received intraperitoneal applications of sodium alendronate at a dose corresponding to group B1 or B2 three times a week, while the control group received a 0.9% saline solution. Drug administration was performed until euthanasia at 45 d. The femurs were removed and each surgical piece was sent for radiographic, tomographic and microtomographic analysis. Data were submitted to descriptive and inferential statistical analysis (95% confidence interval).

## RESULTS

Quantitative evaluations of bone neoformation did not show differences among the groups in the radiographic ( $P = 0.341$ ), microtomographic ( $P = 0.581$ ) and tomographic evaluations ( $P = 0.171$ ). In the qualitative microtomographic analysis, a smaller distance was observed between the internal bone trabeculae in the groups that used alendronate ( $P = 0.05$ ). On the other hand, group B2 had a higher amount of bone trabeculae per unit length when compared to the other groups ( $P = 0.04$ ).

## CONCLUSION

It is likely that the use of alendronate did not have a direct influence on the amount of bone neoformation, however it did influence the bone quality in a dose-dependent manner, ultimately affecting the distance and quantity of the trabeculae.

**Key words:** Alendronate; Bone regeneration; Fracture; Femur; Bisphosphonates

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Several studies have been carried out to determine both the influence of alendronate in bone repair and the appropriate dose of this drug to promote bone regeneration. In this research, 36 Wistar rats were allocated into three distinct groups that received applications of either alendronate at different doses or saline solution three times a week for 45 d. The rats underwent femoral fracture surgery with stable internal fixation. The imaginologic results suggested that the use of alendronate did not have a direct influence on the amount of bone neoformation, however it did influence bone quality in a dose-dependent manner.

Weiss SG, Kuchar GO, Gerber JT, Tiboni F, Storrer CLM, Casagrande TC, Giovanini AF, Scariot R. Dose of alendronate directly increases trabeculae expansivity without altering bone volume in rat femurs. *World J Orthop* 2018; 9(10): 190-197 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i10/190.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i10.190>

## INTRODUCTION

The repair of transversal appendicular bones requires a complex process that involves several biological stages, including cell recruitment, proliferation and differentiation<sup>[1]</sup>. The literature has described both direct and indirect types of bone repair for these fractures. Direct bone healing is uncommon and is characterized by a healing area that lacks periosteal or endosteal callus formation. This effect occurs when the fracture area is rigidly fixed, causing direct remodeling of the lamellar bone, angiogenesis, and the formation of Haversian channels<sup>[2]</sup>. Indirect bone repair, the most common form of fracture healing, consists of endochondral and intra-

membranous bone healing and is characterized by the formation of a bone callus<sup>[3]</sup>.

The establishment of a fracture pattern in an animal model requires both surgical and technical abilities, as well as accurate positioning and adequate bone fixation. The majority of these studies on rats are conducted with intramedullary pins, external fixators, pin-clips, *etc*<sup>[4]</sup>. The use of plates and screws for stable fixation in animal models is known to both favor and accelerate the repair process when compared to dispositive techniques that lack stable methods<sup>[5]</sup>. This is even the case when the bone repair is not considered direct. In this pilot study, we determined that the 2.0 system containing 4 hole plates presents better results for the bone repair of femur fractures when compared to other fixation systems.

Pharmacological agents that may modulate bone formation and bone remodeling are widely used and developed for the treatment of osteoporosis and other disorders involving bone fragility<sup>[6]</sup>. Bisphosphonates are a class of drugs that may act on bone remodeling by reducing bone resorption in a dose-dependent manner, mainly by inhibiting recruitment and promoting apoptosis of osteoclasts, while also stimulating osteoblastic activity. Bisphosphonates are available both orally (alendronate, ibandronate and risedronate) and intravenously (ibandronate and zoledronate). Among these, sodium alendronate (part of the second generation Bisphosphonate class) causes fewer side effects than the first generation class and is the most widely used antiresorptive drug<sup>[7]</sup>.

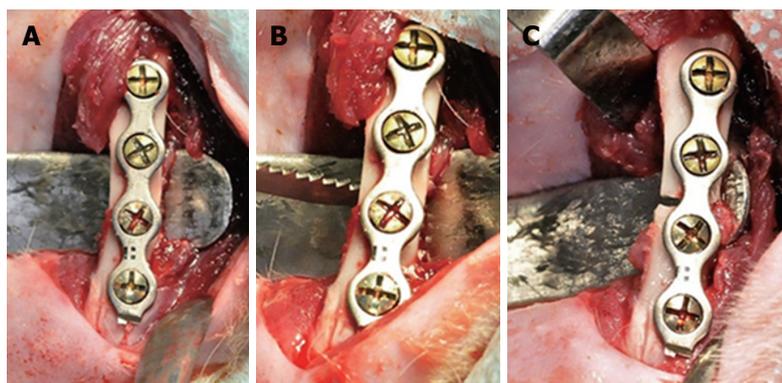
There are some studies that have investigated the positive effects of sodium alendronate in bone repair<sup>[8-10]</sup>. Based on the mechanism of action of this drug, it is hypothesized that alendronate, when applied at the appropriate dose following fracture fixation, accelerates the bone repair process and thus makes prognoses more favorable.

## MATERIALS AND METHODS

The animal protocol was designed to minimize pain and discomfort to the animals. The experiments were carried out in the Vivarium, in the Imaging Laboratory at Positivo University, and in the Laboratory of Analysis of Minerals and Rocks at Federal University Paraná following approval by the Ethics Committee on the Use of Animals (ECUA 320). This study followed the guidelines of ARRIVE (Animal Research: Reporting *in Vivo* Experiment). Throughout the experiment, the ambient light, temperature and humidity of each room were controlled by a digital panel in order to maintain a photoperiod of 12 h, a temperature range of 18 °C - 22 °C, and 65% humidity. The animals were euthanized on the 45th day.

### Experimental design

Thirty-six 4 - 5 mo old Wistar rats weighing approximately 500 g were randomly divided equally into three groups: Group C (control), group B1 (received 1 mg/kg of alendronate) and group B2 (received 3 mg/



**Figure 1** Fracture made with a reciprocating saw. A: First, the bone is fixated with a plate and screws; B: Second, a fracture is induced with a reciprocating saw; C: Finally, the fractured femur is fixed.

kg). Following fracture, the intraperitoneal application of sodium alendronate was administered three times per week, and the control group concomitantly received applications of 0.9% saline solution until the time of euthanasia. Intraperitoneal applications were performed on the opposite side of the fracture.

#### **Fracture preparation and stabilization**

During all surgical procedures, aseptic criteria were maintained. The rats were sedated for one minute *via* inhalation with isoflurane (Cristália, Itapira, SP, Brazil) and anesthetized with 10% ketamine hydrochloride (Vetbrands, Paulínia, SP, Brazil) and 2% xylasin hydrochloride (Vetbrands, Paulínia, SP, Brazil) by intraperitoneal injection. After anesthesia, the rats were placed in the left lateral decubitus position, and a right femur trichotomy was then performed with vigorous antiseptics using iodopovidone. A straight incision was made approximately 5 cm along the long axis of the femur with blade number 15C, with the aid of blunt scissors, and the tissue was divided into muscular planes. After incision and detachment of the periosteum with a scalpel, the surface of the femur could be accessed.

Before proceeding with the osteotomy, it was necessary to complete the positioning, drilling and adaptation of the 2.0 mm 4 hole titanium plate system with 4 mm-long screws (Orthoface, Curitiba-PR, Brazil) in order to avoid poor positioning of the bone segments. The fracture was then made using a reciprocating saw (Figure 1). Abundant lavage of the wound was done using saline solution. The suture was performed in planes with isolated stitches, using Vicryl-0® thread (Ethicon, Johnson and Johnson, São José dos Campos, SP, Brazil) for the muscular plane, and nylon 4-0 (Ethicon, Johnson and Johnson, São José dos Campos, SP, Brazil) for the skin. Analgesia, inflammation and infection were controlled throughout the postoperative period.

#### **Applications**

Immediately following the surgeries, intraperitoneal applications were initiated, which lasted until euthanasia. Three weekly applications were carried out. The control group (C) received 0.9% physiological saline solutions,

while the animals in groups B1 and B2 received a 1 mg/kg and 3 mg/kg dose of alendronate, respectively.

#### **Euthanasia**

At 45 d, the animals were euthanized, and then the right femurs, plates and screws were removed. The specimens were stored separately in pots containing 10% formaldehyde. For euthanasia, the rats were exposed to overdoses of isoflurane for about 10 min. The specimens were then sent for analysis. The statistical methods used in this study were reviewed by Rafaela Scariot, Professor of Biostatistics in the Masters Program in Dentistry at Positivo University.

#### **Radiographic analysis**

In order to evaluate the postoperative recovery as well as the positioning of the bone segments, the animals were submitted to digital radiography at days 7 and 45. The time-point of 7 d served only as a radiographic follow-up to observe the control and evaluate the plaque adaptation, while the time-point of 45 d was used to evaluate bone repair. The animals were sedated within 7 d and their femurs were positioned on a digital sensor (Kodak RVG 5100, Carestream Dental, Rochester, NY, United States) for radiographic imaging with an exposure time of 1.0 sec. The images were then processed and evaluated using Dental Imaging software (version 6.12.17.0 - A, Carestream Dental, Rochester, NY, United States). By the time that radiographic evaluation was taken at day 45, the animals had already been euthanized.

For evaluation of bone neoformation using the Image J program (version 1.49t National Institute of Health-NIH Bethesda, MD, United States), the examiner had previously been trained. The fracture's region of interest was then established. To define the region of interest, a 10 mm line was drawn, 5 mm before the fracture line and 5 mm posterior to it. From this line, a rectangle was then created using the Selection Brush tool to delineate the edges surrounding the bone callus and therein obtain the total area value. Outside of the fracture region, a rectangle was also constructed to obtain the total bone area so that bone formation could later be compared with individual femur thickness. The area value in the

fracture region was subtracted from the total bone area without the fracture. From this value, the excess bone value was calculated.

### Tomographic analysis

The 36 specimens were sent to a dental tomography center, which used the same tomography device calibrated at 120 kVp and 36.12 mAs (i-CAT<sup>®</sup> CONE BEAM 3-D, Kavo Kerr, Joinville-SC, Brazil), to construct images using an exposure time of 40 s with 0.25 Voxel. From this scan, 216 tomographic sections with a 250  $\mu\text{m}$  pixel size were obtained for each set of five samples. In order to decrease the number of intakes, the femurs to be evaluated by tomography were grouped into an acrylic base that accommodated up to five femurs. These were placed vertically and, with the help of utility wax, attached to the base. After acquisition of the tomographic sections, the images were analyzed using I-CAT Vision software.

The longitudinal distance of the defect, in which the amount of bone was generated laterally in the sample, was evaluated. The distance between the contact points of the femurs and the femoral diameter were also measured without considering the effects of formation and the formed bone callus. The I-CAT Vision software helped facilitate the analysis of distances by allowing the examiner to view samples in two distinct ways: through the Implant Screen, which provides an analysis of multiple tomographic sections within a selected region of interest, or the MPR Screen, which displays three views of the obtained femurs. In the MPR Screen, it was possible to analyze distances by using the axial, coronal and sagittal views of the samples, and also by using regions of interest that delineated the femurs individually. This screen was therefore used for analysis. In addition to the advantage of easily performing distance analysis, the brightness and contrast scales could also be altered so that only the femur, which is more radiopaque, is detected. This makes it possible to identify the diameter of the femur. Despite using the diameter for analysis, the femur is not exactly cylindrical, so the distance acquired corresponds to the greater distance of the femur and the longitudinal dimension of the defect. This sample movement was possible with the "Explore" function in the software. Once the region of interest, which corresponded to a single femur, was selected by using the rulers shown on the sides of each image of the figure, the "Explore" function of the software was performed. In the coronal image, the formation of a circle indicating the presence of a diameter was observed. Using the cursor, we could rotate the inscribed sample in any direction within the plane. The distance measurements were done by selecting the "Distance" software tool and dragging the cursor.

### Micro-CT analysis

The computerized microtomography analysis was performed using a Skyscan computed micro-CT model 1172 (Bruker Skyscan, Luxembourg, Belgium), with power

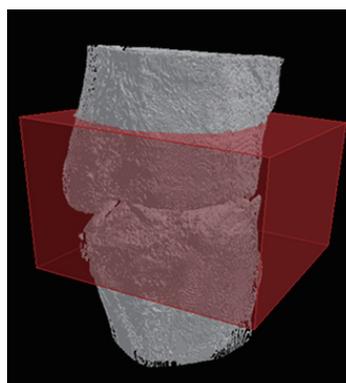
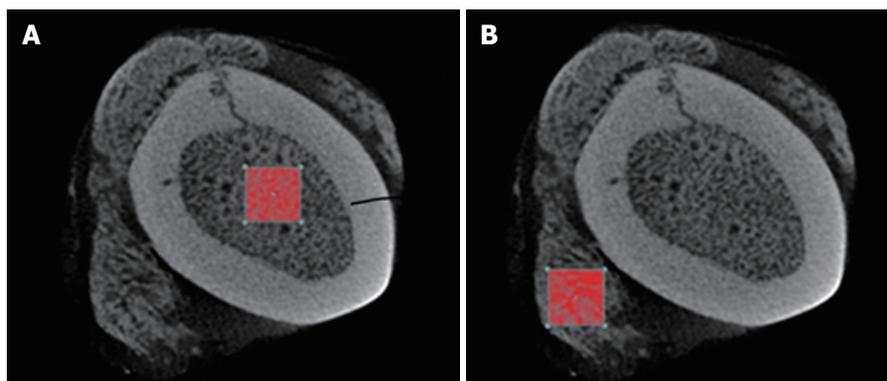


Figure 2 Delimitation of the defect for analysis.

and current adjusted to 90 kV and 112  $\mu\text{A}$ , respectively. The pixel size was 12.8  $\mu\text{m}$ , and a multichannel acquisition camera with a resolution of 2000 x 1336 pixels was used to detect signal. No filters were used to correct the energy of the X-ray beam. The portion was rotated 180° with a rotation step of 0.4°. A projection image of the part was obtained for each rotation step. The exposure time of the sample within the X-ray beam was 1.1 s per rotation step, and the total acquisition time of the projection images was 30 min. After acquisition, projection images were processed using NRecon software (Bruker, Luxembourg, Belgium). The software reconstructed the projection images into tomographic sections using the Feldkamp algorithm. After obtaining the tomographic sections, the measurements of the three-dimensional space, trabecular formation and bone volume were evaluated by the software, which included the CT Analyzer (v.1.16.1.0 +; Bruker Skyscan, Kontich, Belgium) and the Dataviewer (v.1.5.2.4; Bruker Skyscan, Kontich, Belgium). In the CT Analyzer software, it is possible to separate different mineral densities from the contrast difference shown in the tomographic section slices. The contrast in the tomographic section image comes from the different radiopacities of the materials in the sample, according to the interaction of these phases with the X-ray beam. This makes it possible to separate the neoformed bone from both the autogenous bone and cartilaginous material, each of which have different radiopacities.

### Quantitative analysis

Quantitative analysis begins with the binarization process of the sample's different phases. This binarization process corresponds to a range of gray tones to which each radiopaque material fits. The range of gray tones used to determine neoformed bone volume corresponds to 50 - 105 on a total dimensionless scale from 0 - 255. The determination of this volume occurs through the delimitation of a region of interest into a prismatic format (12 mm x 11 mm x 6.3 mm). This involves the whole region of the defect and bone callus, which is in the center of the defect (Figure 2). Thus, bone formation was investigated both in the defect region and in the volume of bone callus formed. This created region was used for



**Figure 3** Regions of interest. A: Region of internal interest; B: Followed by region of external interest.

all pieces. From this procedure, the analysis of initial bone, neoformed bone and total surface area of bone formation, including the bone callus (lateral available area of the femoral bone), were obtained. The measurements of the relationship between the new bone formation and the femoral surface area were obtained by determining the difference in thickness between samples.

#### **Qualitative analysis**

To analyze the trabeculae that was internally generated in both the bone and external region, a region of interest was made both inside and outside of the femur bone (Figure 3) by selection an area that had the maximum density of trabecular bone within the bone callus. Calculations using CTAn software were made of the following: the mean trabecular thickness (Tb.Th) of the internal and external regions, the trabecular linear density (Tb.N), which measures the average number of trabeculae per unit length, and the average distance between the internal and external trabeculae (Tb.Sp)<sup>[11,12]</sup>.

#### **Statistical analysis**

The results were subjected to descriptive and statistical analysis. Statistical evaluation was performed using a frequency data specific test called the Statistical Package for Social Science program (SPSS, version 24.0; SPSS Inc., Chicago, IL – United States) using a 95% confidence interval. The values obtained were subjected to a normality test (Shapiro-Wilk), and parametric variables were described using mean and standard deviation. Nonparametric variables were described as minimum, median and maximum. For comparison between groups, the ANOVA and Kruskal-Wallis tests were used, according to the normality of the variable. When there was a statistical difference detected between the groups, a Tukey test was performed for parametric samples. For nonparametric samples, comparisons were performed in two groups using the Mann-Whitney test.

## **RESULTS**

#### **Radiographic analysis**

Bone formation, which was evaluated by radiographic

analysis, was higher in group B2 ( $91.683 \pm 35.657 \text{ mm}^2$ ), followed by the control group ( $65.57 \pm 32.642 \text{ mm}^2$ ) and group B1 ( $62.670 \pm 45.578 \text{ mm}^2$ ). The measurements obtained (bone surplus) showed no difference between the groups ( $P = 0.341$ ).

#### **Tomographic analysis**

Tomographic evaluation of the samples did not show quantitative differences in bone neoformation among the groups (One-way ANOVA test;  $P = 0.171$ ). In Group C, the measurement between the defect and femur ratio ( $\text{mm}^3/\text{mm}^2$ ) was  $1.76 \pm 0.56$ . The measurements in group B1 and B2 were  $1.59 \pm 0.31$  and  $1.44 \pm 0.21$ , respectively.

#### **Micro-CT analysis**

Considering the relationship between the new bone formation and the femur surface area, the B2 group [ $5.87 (2.10 - 14.60) \text{ mm}^3/\text{mm}^2$ ] presented greater bone formation when compared with the B1 group [ $4.88 (2.30-16.02) \text{ mm}^3/\text{mm}^2$ ] and C group [ $5.65 (3.64 - 12.40) \text{ mm}^3/\text{mm}^2$ ]; however, there was no difference among the groups (Kruskall-wallis test/ $P = 0.581$ ).

#### **Qualitative analysis**

In qualitative microtomographic analysis, it was possible to observe that there was a difference in the number of trabeculae per unit length (Tb.N) between groups ( $P = 0.05$ ). Group B2, when compared with both groups, had higher linear density.

There was also a significant difference between groups in the spacing of the internal bone trabeculae, showing that the Tb.Sp is lower in the control group vs. the B2 group ( $P = 0.04$ , Figures 4 and 5). The data for Tb.N, Tb.Th and Tb.Sp can be found in Table 1.

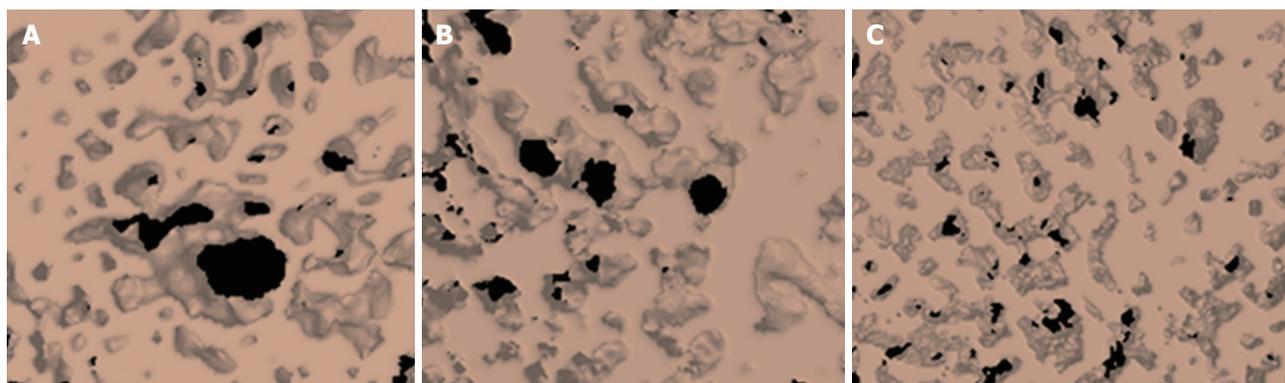
## **DISCUSSION**

The aim of this study was to use image analysis to evaluate the evolution of appendicular femur repair when fixed with plates and treated with varying alendronate concentrations. It is known that during the early stages of bone healing, a less rigid mechanical environment

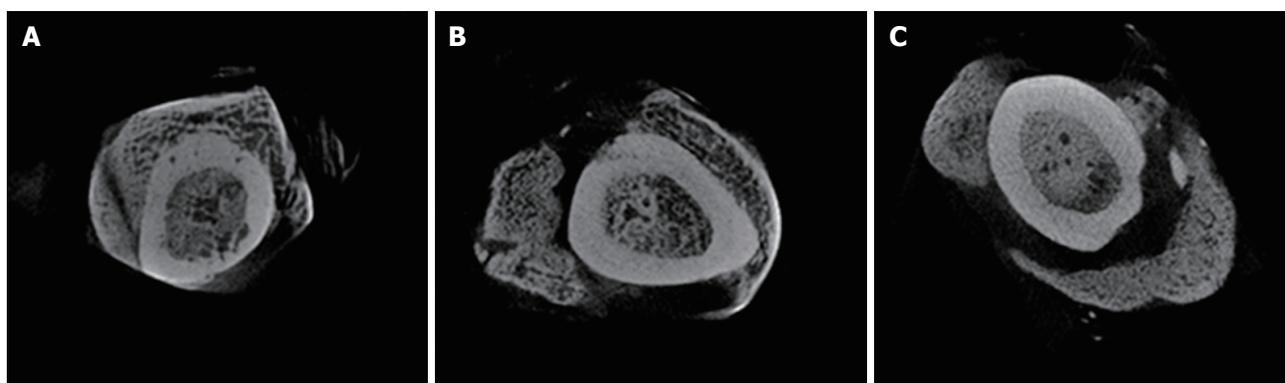
**Table 1 Results of qualitative analysis by micro-computed tomography [median (min-max)]**

	Group C	Group B1	Group B2	P
Tb.Th	0.11 (0.09-0.14)	0.09 (0.07-0.16)	0.14 (0.09-0.16)	0.07
Tb.N	5.26 (3.39-6.24) <sup>1</sup>	5.45 (1.42-5.87) <sup>2</sup>	5.94 (2.49-6.40) <sup>1,2</sup>	0.05
Tb.Sp	0.10 (0.06-0.16)	0.09 (0.05-0.35)	0.06 (0.05-0.21)	0.07
Tb.Th	0.09 (0.07-0.13)	0.10 (0.06-0.23)	0.12 (0.06-0.15)	0.06
Tb.N	4.60 (0.13-6.15)	4.78 (0.15-6.90)	6.15 (0.22-7.22)	0.13
Tb.Sp	0.20 (0.08-0.50) <sup>3,4</sup>	0.09 (0.05-0.44) <sup>3</sup>	0.07 (0.05-0.42) <sup>4</sup>	0.04

<sup>1</sup>P = 0.049; <sup>2</sup>P = 0.028; <sup>3</sup>P = 0.032; <sup>4</sup>P = 0.03. Kruskal-Wallis/Mann-Whitney. Data from external and internal areas, respectively.



**Figure 4** Region of internal interest of the femur, showing different patterns of trabeculae among groups. A; Group C: Control; B; Group B1: Bisphosphonate 1 mg/kg; C: Group B2: Bisphosphonate 3 mg/kg.



**Figure 5** Region of internal interest of the femur, showing different patterns of trabeculae among groups. A: Group C: Control; B: Group B1: Bisphosphonate 1 mg/kg; C: Group B2: Bisphosphonate 3 mg/kg.

results in a prolonged phase of chondral bone regeneration, whereas the intramembranous ossification process appears to be independent of mechanical stability<sup>[13]</sup>. In direct osseous repair, there is no formation of a bone callus. Therefore, it is possible to predict that when using fixation with plates and screws, direct healing occurs since there is no movement of the bone preserves. However, in animal models, this is not true; indirect healing occurs instead because the animal is not immobilized and the plates are not designed for animals, thus generating micro-movement in the region. During early fracture healing, mechanical stimulation appears to enhance callus formation, however the extent of callus formation does not correspond to rigidity<sup>[14]</sup>.

Sodium alendronate is a drug that prevents bone

resorption and may induce osteogenesis by inhibiting osteoclast activity. As a result, it is able to both maintain and promote callus formation in bone repair of fractures, as well as increase bone mineral density in the fracture region<sup>[15]</sup>. In the present study, we demonstrated that alendronate at concentrations of 1 mg/kg and 3 mg/kg did not alter the amount of bone neoformation according to imaging analysis. Remarkably, bone neoformation was equal among all treatment groups.

Under qualitative microtomographic analysis, we observed that bone repair was more effective in the groups that received sodium alendronate applications, especially in the group with the highest dosage. This was visualized through the greater number of trabeculae and smaller spacing between the trabeculae in the 3

mg/kg group. Since alendronate promotes osteoblasts and mesenchymal cell osteoblastogenesis, while also inhibiting osteoclastic activity<sup>[6,16]</sup>, this may suggest that the amount and arrangement of bone trabeculae is directly linked to the dosage and administration of alendronate. This study suggests that the higher the dose, the larger the expansion of mineral-like matrices, while spacing among these areas (chondroid or osteoid matrix) remains lower.

One hypothesis that should be considered and may explain the results found here is the likely action of TGF $\beta$ 1, which was previously shown to increase upon alendronate administration<sup>[17]</sup>. It is noteworthy that this cytokine is an important growth factor that may contribute to mineral expansion. In the endosteum area, bone matrix deposition is common and independent of the chondroid area. Thus, alendronate could be responsible for the increase of this cytokine that may, in turn, increase BMP2 expression. This was observed in a recent study where specimens receiving alendronate showed a significant increase of this protein, which improved bone deposition in rabbit calvarias<sup>[18]</sup>.

On the other hand, the same situation may be extrapolated for the periosteal area. Regarding this peculiar topography, chondrocyte expansion may be an effect that is strictly associated with functional endogenous TGF $\beta$  signaling. In addition to this effect, TGF $\beta$ 1 also induces the differentiation of hypertrophic cartilage, which is required for calcium deposition and ossification in this topography. To reach this conclusion, the authors of this study induced the inhibition of specific TGF $\beta$  receptors. They therein verified that TGF $\beta$  suppression culminated in the inhibition of cartilaginous growth and chondroid differentiation, while also inhibiting both the medullary area and hematopoiesis<sup>[19]</sup>.

Thus, all these hypotheses are possible explanations of our results. We observed an important growth in minerals through accurate imaging analysis, independent of whether the matrix was chondroid or osteoid.

Sodium alendronate at concentrations of 1 mg/kg and 3 mg/kg, when assessed by imaging tests, did not alter the amount of bone neoformation.

Sodium alendronate interferes with the quality of bone neoformation in the context of the quantity and disposition of bone trabeculae. The higher the dose of alendronate, the greater the number of trabeculae and the smaller the spaces among them.

## ARTICLE HIGHLIGHTS

### Research background

Bisphosphonates are potent inhibitors of bone resorption. Sodium alendronate is the most used drug of this class, and may act on bone remodeling by reducing bone resorption in a dose-dependent manner. Its mechanism of action works primarily by both inhibiting the recruitment and promoting the apoptosis of osteoclasts, while simultaneously stimulating osteoblastic activity.

### Research motivation

Despite what is currently known about alendronate-induced bone repair

alterations, the literature has not yet fully elucidated the appropriate dose required to achieve better bone regeneration, nor the effects of this drug when using fixation methods.

### Research objectives

To evaluate the dose-dependent effects of sodium alendronate on bone repair in treated femur fractures by using stable internal fixation and imaging tests (radiography, tomography and microtomography).

### Research methods

Wistar rats were separated into three distinct groups that received applications of either saline solution (control) or different doses of alendronate. The rats then underwent femoral transversal linear fracture surgery using stable internal fixation. Drug administration lasted 45 d. The femurs were sent for radiographic, tomographic and microtomographic analysis in order to evaluate bone quantity and quality.

### Research results

Results did not reveal differences in bone quantity by radiographic, tomographic and microtomography analysis. However, when analyzing bone quality, it was evident that alendronate affected the distance and quantity of trabeculae in a dose-dependent manner, thus promoting better bone regeneration.

### Research conclusions

Our research results reveal that sodium alendronate, at concentrations of 1 - 3 mg/kg when assessed by imaging tests, does not alter the amount of bone neoformation. Nevertheless, it does interfere with the quality of bone neoformation when considering the quantity and disposition of bone trabeculae. The higher the dose of alendronate, the greater the number of trabeculae and the smaller the spaces among them.

### Research perspectives

More research using this method of fixation and sodium alendronate are required and may relate, for example, to the mechanical force of the specimens. It is also important to compare the effects of alendronate with different markers. We suggest that follow-up studies use a dose of 1 mg/kg alendronate, since we have demonstrated here that it successfully promotes bone regeneration.

## REFERENCES

- 1 **Einhorn TA.** The science of fracture healing. *J Orthop Trauma* 2005; **19**: S4-S6 [PMID: 16479221 DOI: 10.1097/00005131-200511101-00002]
- 2 **Marsell R, Einhorn TA.** The biology of fracture healing. *Injury* 2011; **42**: 551-555 [PMID: 21489527 DOI: 10.1016/j.injury.2011.03.031]
- 3 **Green E, Lubahn JD, Evans J.** Risk factors, treatment, and outcomes associated with nonunion of the midshaft humerus fracture. *J Surg Orthop Adv* 2005; **14**: 64-72 [PMID: 16115430]
- 4 **Holstein JH, Garcia P, Histing T, Kristen A, Scheuer C, Menger MD, Pohlemann T.** Advances in the establishment of defined mouse models for the study of fracture healing and bone regeneration. *J Orthop Trauma* 2009; **23**: S31-S38 [PMID: 19390374 DOI: 10.1097/BOT.0b013e31819f27e5]
- 5 **Neagu TP, Țiglic M, Popp CG, Jecan CR.** Histological assessment of fracture healing after reduction of the rat femur using two different osteosynthesis methods. *Rom J Morphol Embryol* 2016; **57**: 1051-1056 [PMID: 28002523]
- 6 **Fu L, Tang T, Miao Y, Zhang S, Qu Z, Dai K.** Stimulation of osteogenic differentiation and inhibition of adipogenic differentiation in bone marrow stromal cells by alendronate via ERK and JNK activation. *Bone* 2008; **43**: 40-47 [PMID: 18486585 DOI: 10.1016/j.bone.2008.03.008]
- 7 **Maeda SS, Lazaretti-Castro M.** An overview on the treatment of postmenopausal osteoporosis. *Arq Bras Endocrinol Metabol* 2014; **58**: 162-171 [PMID: 24830593 DOI: 10.1590/0004-273000003039]
- 8 **Fu LJ, Tang TT, Hao YQ, Dai KR.** Long-term effects of alendro-

- nate on fracture healing and bone remodeling of femoral shaft in ovariectomized rats. *Acta Pharmacol Sin* 2013; **34**: 387-392 [PMID: 23459092 DOI: 10.1038/aps.2012.170]
- 9 **Oliveira D**, Hassumi JS, Gomes-Ferreira PH, Polo TO, Ferreira GR, Faverani LP, Okamoto R. Short term sodium alendronate administration improves the peri-implant bone quality in osteoporotic animals. *J Appl Oral Sci* 2017; **25**: 42-52 [PMID: 28198975 DOI: 10.1590/1678-77572016-0165]
  - 10 **Sandberg O**, Bernhardsson M, Aspenberg P. Earlier effect of alendronate in mouse metaphyseal versus diaphyseal bone healing. *J Orthop Res* 2017; **35**: 793-799 [PMID: 27233101 DOI: 10.1002/jor.23316]
  - 11 **Hildebrand T**, Rügsegger P. A new method for the model-independent assessment of thickness in three-dimensional images. *J Microsc* 1997; **185**: 67-75 [DOI: 10.1046/j.1365-2818.1997.1340694.x]
  - 12 **Bouxsein ML**, Boyd SK, Christiansen BA, Guldberg RE, Jepsen KJ, Müller R. Guidelines for assessment of bone microstructure in rodents using micro-computed tomography. *J Bone Miner Res* 2010; **25**: 1468-1486 [PMID: 20533309 DOI: 10.1002/jbmr.141]
  - 13 **Epari DR**, Schell H, Bail HJ, Duda GN. Instability prolongs the chondral phase during bone healing in sheep. *Bone* 2006; **38**: 864-870 [PMID: 16359937 DOI: 10.1016/j.bone.2005.10.023]
  - 14 **Jagodzinski M**, Krettek C. Effect of mechanical stability on fracture healing--an update. *Injury* 2007; **38** Suppl 1: S3-10 [PMID: 17383483 DOI: 10.1016/j.injury.2007.02.005]
  - 15 **Aonuma H**, Miyakoshi N, Kasukawa Y, Kamo K, Sasaki H, Tsuchie H, Segawa T, Shimada Y. Effects of combined therapy of alendronate and low-intensity pulsed ultrasound on metaphyseal bone repair after osteotomy in the proximal tibia of aged rats. *J Bone Miner Metab* 2014; **32**(3):232-239 [PMID: 23921832 DOI: 10.1007/s00774-013-0492-3]
  - 16 **Giuliani N**, Pedrazzoni M, Negri G, Passeri G, Impicciatore M, Girasole G. Bisphosphonates stimulate formation of osteoblast precursors and mineralized nodules in murine and human bone marrow cultures in vitro and promote early osteoblastogenesis in young and aged mice in vivo. *Bone* 1998; **22**: 455-461 [PMID: 9600778 DOI: 10.1016/S8756-3282(98)00033-7]
  - 17 **Giovanini AF**, Göhringer I, Tavella R, Linzmeyer MC, Priesnitz TF, Bonetto LM, Resende RG, Scariot R, Zielak JC. Intermittent administration of PTH induces the expression of osteocalcin and BMP-2 on choroid plexus cells associated with suppression of sclerostin, TGF- $\beta$ 1, and Na<sup>+</sup>-K<sup>+</sup>ATPase. *Endocrine* 2018; **59**: 685-689 [PMID: 29235067 DOI: 10.1007/s12020-017-1490-3]
  - 18 **Göhringer I**, Muller CLS, Cunha EJ, Passoni GNS, Vieira JS, Zielak JC, Scariot R, Deliberador TM, Giovanini AF. Would Be Prophylactic Administrations of Low Concentration of Alendronate an Alternative for Improving the Craniofacial Bone Repair? A Preliminary Study Focused in the Period of Cellular Differentiation and Tissue Organization. *J Craniofac Surg* 2017; **28**: 1869-1873 [PMID: 28692499 DOI: 10.1097/SCS.00000000000003617]
  - 19 **Tekari A**, Luginbuehl R, Hofstetter W, Egli RJ. Transforming growth factor beta signaling is essential for the autonomous formation of cartilage-like tissue by expanded chondrocytes. *PLoS One* 2015; **10**: e0120857 [PMID: 25775021 DOI: 10.1371/journal.pone.0120857]

**P- Reviewer:** Anand A, Elgafy H, Li JM **S- Editor:** Ma YJ

**L- Editor:** Filipodia **E- Editor:** Song H



## Retrospective Study

## Reducing costly falls after total knee arthroplasty

Surajudeen Adebola Bolarinwa, Wendy Novicoff, Qunjun Cui

Surajudeen Adebola Bolarinwa, Wendy Novicoff, Qunjun Cui, Department of Orthopaedic Surgery, University of Virginia Health System, Charlottesville, VA 22903, United States

ORCID number: Surajudeen Adebola Bolarinwa (0000-0002-6160-4153); Wendy Novicoff (0000-0002-5146-7706); Qunjun Cui (0000-0003-4285-4488).

**Author contributions:** Bolarinwa SA, Novicoff W and Cui Q contributed to the paper; all authors have approved this manuscript prior to submission and believe that this manuscript represents honest work.

**Institutional review board statement:** At our institution, this study meets criteria for exemption from IRB review.

**Informed consent statement:** Informed consent is not necessary, for this is a quality improvement study.

**Conflict-of-interest statement:** The authors declare that there is 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:** Unsolicited manuscript

**Correspondence to:** Surajudeen Adebola Bolarinwa, MD, Doctor, Resident Physician, Department of Orthopaedic Surgery, University of Virginia Health System, 400 Ray C Hunt Dr. #300, Charlottesville, VA 22903, United States. [sb3dv@hscmail.mcc.virginia.edu](mailto:sb3dv@hscmail.mcc.virginia.edu)  
Telephone: +1-919-3320966  
Fax: +1-434-2431673

Received: May 29, 2018

Peer-review started: May 29, 2018

First decision: June 6, 2018

Revised: July 6, 2018

Accepted: July 14, 2018

Article in press: July 15, 2018

Published online: October 18, 2018

## Abstract

### AIM

To investigate whether adductor canal nerve block (ACB) reduces patient falls when compared to femoral nerve block (FNB) after total knee arthroplasty (TKA).

### METHODS

We conducted an institutional review of all-cause falls after TKA from January 2013 to August 2016 using a quality improvement database. Our inclusion criteria were patients with diagnosis of primary knee osteoarthritis who underwent primary unilateral TKA with either a FNB or an ACB and sustained a fall during their hospitalization. We excluded patients who had revision TKA and extensor mechanism reconstruction. We also excluded patients with a history of post-traumatic arthritis, prior history of lower extremity fracture, history of neurological disease, or cerebrovascular disease.

### RESULTS

A total of 834 patients had TKA with femoral nerve block and knee immobilizer (FNB + KI). Of those patients, 11 (1.3%) experienced a fall during their hospital stay. In contrast, 791 patients had TKA with ACB. Of those patients, only one (0.13%) patient fall was recorded within this group. We used the Fisher's exact test to compare the differences between the two groups. The difference between the two groups achieves statistical significance ( $P = 0.006$ ). We also found that 11 out of the 12 patients that fell had a right TKA procedure while one patient had a left TKA procedure. Nine out of twelve patients that fell were female, while only three patients were male.

### CONCLUSION

Given the reduction in the number of falls with ACB, it

is recommended that ACB be considered the preferred analgesia for patients undergoing a TKA procedure.

**Key words:** Reducing falls; Adductor canal nerve block; Total knee arthroplasty; Femoral nerve block; Costly falls

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** When compared to femoral nerve block, adductor canal nerve block (ACB) contributed to fewer patient falls after total knee arthroplasty (TKA) at our institution from a rate of 1.3% to 0.13%. We also discovered a significant increase in fall rate after right TKA as compared to a left TKA. We recommend ACB as the preferred regional analgesia for the TKA procedure.

Bolarinwa SA, Novicoff W, Cui Q. Reducing costly falls after total knee arthroplasty. *World J Orthop* 2018; 9(10): 198-202 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i10/198.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i10.198>

## INTRODUCTION

Total knee arthroplasty (TKA) is one of the most replicable and effective orthopedic procedures available. It is used to treat end-stage knee osteoarthritis, post-traumatic arthritis and rheumatoid arthritis of the knee. TKA is an elective procedure performed to relieve pain and restore function to an arthritic knee. The goal of a knee replacement procedure is to relieve pain, improve quality of life, and maintain or improve knee function<sup>[1]</sup>. It is approximated that 700000 total knee replacement procedures are performed annually in the United States, and it is projected to increase to 3.48 million procedures per year by 2030<sup>[2]</sup>. With the increasing demand for TKA, recent TKA reimbursement changes and limited hospital beds, most hospitals are transitioning to outpatient TKA procedures. Major limitations to outpatient TKA include management of comorbidities, post-operative fall prevention and postoperative pain control<sup>[3]</sup>.

Inadequate pain control postoperatively can limit rehabilitation and slow down recovery<sup>[4]</sup>. Femoral nerve block (FNB) used to be the preferred regional analgesic modality for TKA due to adequate pain control and ease of application. It is administered around the femoral nerve at the level of the inguinal crease. At this level, the femoral nerve contains both motor and sensory distribution. Therefore, one of the complications of FNB is motor blockade, which is due to the anesthesia infiltrating the femoral motor nerve. This causes quadriceps weakness, which could lead to instability in the affected extremity, subsequently increasing the risk of falls. Several studies have shown that quadriceps weakness slows the rehabilitation process and limits ambulatory distance post-operatively<sup>[5]</sup>. To reduce post-operative falls at our institution, we started placing patients' operative

extremity in DeRoyal 24-in knee immobilizers (KI) to help improve knee stability. Previously, we performed a retrospective study comparing the fall rate between TKA patients who used KI post-operatively and patients that did not use KI. The study showed that the use of KI reduces the number of patient falls from 3.7% to 1.6%<sup>[4]</sup>. A fall rate of 1.6% was considered unacceptable given the high cost and morbidity associated with patient falls. During the study and after polling the floor staff, we discovered that the majority of patients were noncompliant with the use of the KI and a couple of patients fell while wearing the KI. Given the unsatisfactory compliance with the use of the KI and relatively high fall rate, the adult reconstruction team discontinued the use of KI and started considering better alternatives to help reduce fall rate. One of the alternatives proposed was switching the regional anesthesia from FNB to adductor canal block (ACB).

There have been multiple recent studies indicating that ACB, a relatively new sensory block technique that predominantly blocks sensory nerves by anesthetizing only the saphenous nerve in the adductor canal, might be a safer option when compared to FNB, as it preserves quadriceps function while still effectively alleviating post-operative pain<sup>[5,6]</sup>. Most studies, including a randomized control trial and a meta-analysis, have shown that patients who receive ACB have faster pain relief, greater quadriceps strength, earlier ambulation, greater average distance of ambulation during physical therapy, faster timed up and go test, and decreased hospital length of stay<sup>[5]</sup>. There have been several studies comparing the fall rate between the two regional block techniques (FNB vs ACB), and all findings thus far have been equivocal<sup>[7]</sup>. A great deal of knee replacement centers has adopted ACB as the analgesia of choice, even though the data comparing fall rates between the two nerve blocks are inconclusive. Our institution transitioned to using ACB as the preferred anesthesia over FNB for TKA in 2015 to reduce patient falls, however the effects of this change in practice has yet to be evaluated. Therefore, the purpose of this study was to perform an institutional review comparing the fall rate between ACB and FNB + KI after TKA to evaluate its effectiveness at our institution and compare our own fall rates to those reported in the literature.

## MATERIALS AND METHODS

We identified patients that fell during their hospitalization period after TKA using our institutional quality improvement reporting database, Be-Safe. The Be-Safe database is used by the floor staff at our Hospital to report in-house unexpected patient outcomes, including falls. All data obtained from the Be-Safe database is used for quality improvement and is exempt from Institutional Review Board approval. The fall data from January 2013 to September 2016 was evaluated. The data included documentation of the date of the fall, procedure performed, the patient's medical record number and a

**Table 1** The annual number of reported falls after total knee arthroplasty

Year	Total number of TKA	No. of falls
2013	402	9
2014	432	2
2015	434	0
2016	357	1

TKA: Total knee arthroplasty.

**Table 2** The total number of reported falls for each regional nerve block

Nerve block	No. of TKAs per block	No. of reported falls per block	P-value
ACB	791	1	0.006
FNB + KI	834	11	

TKA: Total knee arthroplasty; ACB: Adductor canal nerve block; FNB: Femoral nerve block; KI: Knee immobilizer.

brief description of the circumstances surrounding the incident. We then accessed the electronic medical records for each patient to confirm the procedure that was performed on the patient, the type of regional anesthesia received prior to the fall and the patient's past medical history. We also reviewed operative notes, fall event notes, injuries sustained secondary to the fall, treatments received and any deviation from a normal post-operative course as a result of the fall, including requirement for additional imaging studies. Inclusion criteria included patients with the diagnosis of primary knee osteoarthritis who underwent primary unilateral TKA with either a FNB or ACB regional block and sustained a fall during their hospitalization. Exclusion criteria were patients with history of post-traumatic arthritis, prior history of lower extremity fracture, history of neurological disease, cerebrovascular disease, psychiatric diagnosis, non-ambulatory patients, and patients with a history of chronic opioid use. We also excluded patients who had revision TKA, unicompartmental knee replacements, history of total hip arthroplasty and extensor mechanism reconstruction.

We reviewed anesthesia records on all the patients who fell to confirm the type of regional anesthesia they received. The standard protocol for FNB done for all the TKA patients at our institution consisted of a single shot of 20 mL of 0.5% Ropivacaine injection around the femoral nerve under ultrasound guidance with a continuous infusion of 0.2% Ropivacaine at a rate of 6 mL/h through a femoral catheter that was removed on post-operative day two. The protocol for the ACB consisted of a single shot of 30 mL of 0.5% Ropivacaine under ultrasound guidance around the saphenous nerve in the adductor canal. For both types of regional blocks, a resident performed or assisted with the procedure while a supervising attending was always present.

### Statistical analysis

A statistical review of the study was performed by a

biomedical statistician. We used the Fisher's exact test to evaluate differences between the two groups. A  $P$ -value  $< 0.05$  was considered statistically significant.

## RESULTS

Seven patients were excluded from the study. One patient was excluded from the ACB fall group due to prior history of falls and history of a neurological disease. Five patients were excluded from the FNB group because they had revision TKA. One patient was excluded from the FNB fall group because the patient had an extensor mechanism reconstruction procedure along with a revision TKA. There was a total of 834 patients that had TKA with FNB + KI between January 2013 and December 2014 (Table 1). Of those patients, 11 (1.3%) experienced a fall during their hospital stay (Table 2). One patient had an ankle fracture necessitating operative fixation. One patient sustained facial laceration, which required sutures. Three patients' injuries necessitated X-rays of their extremity after the fall, but no fractures were identified. Within the FNB group, four patients fell on post-operative day one and seven patients fell on post-operative day two. The age range of the patients that fell after FNB was between 49-92 years old with an average age of 65.5. Eight of the eleven patients in this group were females. The average body mass index (BMI) of the patients that fell after FNB was 33.3. In contrast, of the total 791 patients that had TKA with ACB between January 2015 and August of 2016, only one patient (0.13%) fall was recorded (Table 1). The patient who fell after ACB was a 59-year-old female with a BMI of 41.77, who fell on post-operative day two. The difference between the two groups reached statistical significance ( $P < 0.006$ ) (Table 2). It was noted that out of the total twelve patients that fell, 11 (92%) had right TKA compared to one patient fall after a left TKA. Also, nine out of twelve patients that fell were female, while only three patients were male. These last two findings warrant further investigation.

## DISCUSSION

Most large joint replacement institutions have switched to ACB as the preferred regional anesthesia for TKA. The reasoning in most cases revolves around reducing the fall rate after TKA. There is a considerable amount of literature to support the use of ACB over FNB due to faster pain relief, greater quadriceps strength, earlier ambulation, greater average distance of ambulation during physical therapy, faster timed up and go test, and decreased hospital stay<sup>[5]</sup>. However, there is no evidence to support reduction in fall rate when ACB is compared with FNB to date<sup>[7]</sup>. Our study showed a reduction in fall rate after institution-wide transition to ACB as the preferred analgesic method over FNB. Caution must be taken when interpreting and applying our study because this study is a retrospective, non-matched design without control groups for possible confounding variables or

differing patient group risk factors. Underreporting by staff members is an inherent limitation to using a quality assurance report like the one used in this present study. We also had a very low number of falls.

While gathering data for this study, we reviewed fall data exclusively from the dedicated orthopedic surgery post-operative acute inpatient ward. In very rare circumstances, patients were transferred to other floors if the orthopedic ward was at capacity or if the patient's comorbidities or intra-operative complications required admission to the intensive care unit or the intermediate care unit. It is possible that some of the TKA patients fell while on other floors.

A major confounding variable is the general institutional emphasis on reducing all cause falls during the same time period. Over the past five years, there has been a hospital wide initiative to reduce the number of falls at our institution. Our institution has invested in fall prevention awareness programs, which included frequent education of floor staff, replacing old hospital beds with new beds equipped with bed alarms and motion sensors that detect patients' movement out of bed and automatically notify floor staff. All patients with increased fall risk are now identified early in the pre-admission phase based on several factors including age, past medical history and medications being taken. These patients are provided bright yellow wristbands, yellow gowns, yellow slip resistant socks and are monitored more frequently. All patients having an arthroplasty procedure are now required to attend an arthroplasty course in which they are well educated on fall prevention. We believe that the new fall prevention initiative could possibly have contributed to the reduction in fall rate, but the effect of ACB is likely additive. Our analysis would be strengthened with more fall patients, which will allow us to have more data points to analyze and perform a multivariate analysis for potentially confounding variables (spinal vs general anesthesia, use of PCA vs oral analgesics, BMI and age).

An interesting result we found during this study was increased fall rate after right TKA compared with left TKA. A literature search showed no prior studies comparing the fall rate between right TKA vs left TKA. The increase in fall rate could be due to several factors, including extremity dominance, higher rate of right TKA procedures than left TKA at our institution, or it could be a stochastic anomaly. Nevertheless, the association of laterality with fall risk merits further investigation given our findings.

In conclusion, the present study found a significant relationship between ACB and fall reduction as compared with FNB + KI. This study is limited by the small numbers of falls and confounding variables that were not controlled for.

## ARTICLE HIGHLIGHTS

### Research background

There have been multiple recent studies indicating that adductor canal block

(ACB) might be a safer option for patients undergoing total knee arthroplasty (TKA) procedure when compared to femoral nerve block (FNB) because of its potential ability to reduce patient falls, as it preserves quadriceps function while still effectively alleviating postoperative pain. Most studies, including a randomized control trial and a couple meta-analysis studies, have shown that patients who ACB have faster pain relief, greater quadriceps strength, and decreased hospital length of stay. There have been several studies comparing the fall rate between the two regional block techniques (FNB vs ACB), and all findings thus far have been equivocal. A lot of institutions have switched to ACB as their preferred regional analgesia simply based on preservation of quadriceps strength and early mobilization. Our institution made the switch to ACB as the primary regional analgesia after the occurrence of several patient falls following a TKA procedure using FNB. This study is significant and was done to evaluate the effectiveness of ACB at preventing falls at our institution and compare our fall rates to those reported in the literature.

### Research motivation

The motivation behind this research is to evaluate and compare the fall rate after TKA procedure between ACB and FNB at our institution. This research is significant because it allows us to evaluate how effective ACB is at reducing patient falls after TKA when compared to FNB. Results from this study can be applied at various institutions to help decrease patient falls. Results from this study could also be a source of data points for future meta-analysis.

### Research objectives

The main objective of this study was to evaluate and compare the fall rate after TKA procedure between ACB and FNB at our institution. Our results indicated that there was significant reduction in patient falls after TKA procedure after switching to ACB. This is important because our institution will continue to use ACB as the preferred regional analgesia for TKA procedure.

### Research methods

In this study, we analyzed the fall data at our institution using our institutional quality improvement reporting database, Be-Safe from January 2013 to September 2016. We then accessed the electronic medical records for each patient that fell to confirm the procedure that was performed on the patient, the type of regional anesthesia received prior to the fall and the patient's past medical history. We only included patients with the diagnosis of primary knee osteoarthritis who underwent primary unilateral TKA with either a FNB or ACB regional block and sustained a fall during their hospitalization. We excluded patients who had revision TKA, unicompartmental knee replacements, history of total hip arthroplasty and extensor mechanism reconstruction. We then compared the fall rates in patients after receiving ACB vs FNB after a TKA procedure. We used the Fisher's exact test to compare differences between the two groups, and there was a statistical significant difference between the groups ( $P < 0.006$ ).

### Research results

A total of 11 (1.3%) experienced a fall during their hospital stay after receiving FNB for a TKA procedure while one patient (0.13%) fell after receiving ACB for a TKA procedure. Results from this study indicated a significant drop in the fall rate at our institution after switching from FNB to the ACB. Our data indicate that patient and staff education on fall prevention and the use of ACB for patients undergoing TKA is effective at reducing falls.

### Research conclusions

New findings in this study highlighted that there was an increased rate of patient falls after right TKA compared to left TKA. We also found that more female patients fell after TKA compared to male patients. We propose a new theory that due to extremity dominance, patients are more likely to fall after having a TKA procedure on their dominant lower extremity due to instability and weakness in their dominant/lead extremity. For unknown reasons, we also think that female patients are more likely to fall after TKA procedure when compared to male patients. We summarize that switching to ACB helped contribute to reducing the fall rate after TKA at our institution. We believe that the reduction in the fall rate is related to the preservation of the quadriceps strength with ACB as demonstrated by multiple prior studies<sup>[5]</sup>. We hypothesize that a systematic review or a case control study will help confirm our theory that female patients and patients that have TKA on their dominant extremity are more likely to fall

when compared to male patients and patients that have TKA on their non-dominant extremity. There were no new methods proposed by this study. Our hypothesis that ACB reduces patient falls was confirmed in this study. Based on this study, our institution will continue to use ACB as the regional anesthesia for a TKA procedure. We will also continue to educate and take special precautions with patients that are high fall risk.

### Research perspectives

This study helped highlight the importance of developing and maintaining patient safety initiatives in healthcare. It also helped in displaying the importance of patient and staff education and awareness to difficult safety issues in the hospital. The direction of future research will be to do a meta-analysis or retrospective study to further investigate if there is truly an increased risk in patient falls in females and after TKA on the dominant extremity. The best method for future research will be to perform a prospective study looking at the degree of quadriceps weakness, ambulatory distance, earlier or late ambulation, distance of ambulation during physical therapy, timed up and going test, and hospital length of stay post-operatively in male vs female patients and in dominant vs non-dominant extremity.

## 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 Martin GM, Crowley M. Total knee arthroplasty. Available from: URL: <https://www.uptodate.com/contents/total-knee-arthroplasty>
- 3 Berger RA, Sanders S, D'Ambrogio E, Buchheit K, Deirmengian C, Paprosky W, Della Valle CJ, Rosenberg AG. Minimally invasive quadriceps-sparing TKA: results of a comprehensive pathway for outpatient TKA. *J Knee Surg* 2006; **19**: 145-148 [PMID: 16642894 DOI: 10.1055/s-0030-1248097]
- 4 Cui Q, Schapiro LH, Kinney MC, Simon P, Poole A, Novicoff WM. Reducing costly falls of total knee replacement patients. *Am J Med Qual* 2013; **28**: 335-338 [PMID: 23322911 DOI: 10.1177/1062860612469440]
- 5 Elkassabany NM, Antosh S, Ahmed M, Nelson C, Israelite C, Badiola I, Cai LF, Williams R, Hughes C, Mariano ER, Liu J. The Risk of Falls After Total Knee Arthroplasty with the Use of a Femoral Nerve Block Versus an Adductor Canal Block: A Double-Blinded Randomized Controlled Study. *Anesth Analg* 2016; **122**: 1696-1703 [PMID: 27007076 DOI: 10.1213/ANE.0000000000001237]
- 6 Li D, Ma GG. Analgesic efficacy and quadriceps strength of adductor canal block versus femoral nerve block following total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 2614-2619 [PMID: 26611901 DOI: 10.1007/s00167-015-3874-3]
- 7 Gao F, Ma J, Sun W, Guo W, Li Z, Wang W. Adductor Canal Block Versus Femoral Nerve Block for Analgesia After Total Knee Arthroplasty: A Systematic Review and Meta-analysis. *Clin J Pain* 2017; **33**: 356-368 [PMID: 27322397 DOI: 10.1097/AJP.0000000000000402]

P- Reviewer: De Sousa K, Erkan S S- Editor: Ji FF  
L- Editor: Filipodia E- Editor: Song H



Retrospective Study

## Screw placement is everything: Risk factors for loss of reduction with volar locking distal radius plates

Herwig Drobetz, Alyce Black, Jonathan Davies, Petra Buttner, Clare Heal

Herwig Drobetz, Alyce Black, Clare Heal, James Cook University School of Medicine and Dentistry, Mackay 4740, Queensland, Australia

Herwig Drobetz, Jonathan Davies, Clare Heal, Mackay Institute of Research and Innovation, Mackay Hospital, Mackay 4740, Queensland, Australia

Herwig Drobetz, Jonathan Davies, Mackay Base Hospital Orthopaedic Department, Mackay Hospital, Mackay 4740, Queensland, Australia

Petra Buttner, Tropical Health Solutions PTY Ltd, Townsville 4810, Queensland, Australia

Petra Buttner, Centre for Chronic Disease Prevention, James Cook University, Cairns 4878, Queensland, Australia

Clare Heal, Anton Breinl Research Centre for Health Systems Strengthening, Townsville 4810, Queensland, Australia

ORCID number: Herwig Drobetz (0000-0003-0837-2696); Alyce Black (0000-0002-8235-7921); Jonathan Davies (0000-0003-4231-8642); Petra Buttner (0000-0002-5418-922X); Clare Heal (0000-0002-5041-2666).

**Author contributions:** Drobetz H, Black A, Davies J, and Heal C developed the study protocol; Drobetz H, Black A, Davies J initiated the study, and performed literature research and proofreading for scientific content; Drobetz H and Black A participated in patient recruitment and follow-up, data collection, and writing of the manuscript; Heal C performed statistical analysis and interpretation, write up of data, preparation of ethics submission, and provided overall oversight of conduct of study; Buttner P performed statistical analysis of raw data, and revised the manuscript for statistical content.

**Institutional review board statement:** This study was reviewed and approved by the Human Research Ethics Committee of Queensland Health, Australia.

**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 declare no conflicts-of-interest related to this article.

**Open-Access:** This is an open-access article that 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:** Herwig Drobetz, MD, PhD, Professor, Director of Orthopaedics, Department of Orthopaedics, Mackay Hospital and Health District, Bridge Road, Mackay 4740, Queensland, Australia. [herwig.dro@gmail.com](mailto:herwig.dro@gmail.com)  
**Telephone:** +61-748-857900  
**Fax:** +61-748-857900

**Received:** April 30, 2018  
**Peer-review started:** April 30, 2018  
**First decision:** May 16, 2018  
**Revised:** June 28, 2018  
**Accepted:** August 20, 2018  
**Article in press:** August 21, 2018  
**Published online:** October 18, 2018

### Abstract

#### AIM

To determine factors correlated with postoperative radial shortening in patients with distal radius fractures treated with volar locking distal radius plates.

#### METHODS

A total of 250 patients with a distal radius fracture sta-

bilised with volar locking plates between January 2010 and December 2014 were included in a multicentre retrospective cohort study. We measured the distance of the distal locking screws to the joint line immediately post-operatively and then measured radial shortening after six to eight weeks using the change in ulnar variance.

### RESULTS

Multivariate linear regression analysis showed that there was a significant linear association between the distance of the screws from the joint line and radial shortening. No other patient, injury, or treatment-related characteristic significantly influenced radial shortening in multivariate analysis.

### CONCLUSION

Distal locking screws should be placed as close as possible to the subchondral joint line to prevent postoperative loss of reduction.

**Key words:** Loss of reduction; Volar locking distal radius plate; Distal radius fracture; Screw placement; Cohort study

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** The aim of this study was to determine risk factors for postoperative radial shortening in patients with distal radius fractures treated with volar locking distal radius plates. Retrospective analysis of 250 X-rays and clinical data determined immediate post-operative distance of the distal locking screws from the joint line and degree of radial shortening 6-8 wk post-operatively. Radial shortening was significantly and linearly correlated with increased distance of locking screws from the joint line. No other factor analysed in the study was significant. We recommend subchondral placement of distal locking screws in order to maintain reduction postoperatively.

Drobetz H, Black A, Davies J, Buttner P, Heal C. Screw placement is everything: Risk factors for loss of reduction with volar locking distal radius plates. *World J Orthop* 2018; 9(10): 203-209 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i10/203.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i10.203>

## INTRODUCTION

Distal radius fractures are the most common type of fracture of the human skeleton<sup>[1-3]</sup>. The treatment of distal radius fractures has undergone a paradigm shift in the last fifteen years, and fixation with volar locking distal radius plates (VLDRP) has become the operative standard<sup>[1,4-6]</sup>, despite lack of clear evidence of benefit over any other treatment modality<sup>[7-10]</sup>. VLDRP do have a distinct advantage over any other treatment method as they allow immediate postoperative mobilisation<sup>[11]</sup>,

provided optimal placement of the plate/screw construct is achieved intraoperatively. Biomechanical studies<sup>[12-15]</sup> and clinical observations<sup>[16-20]</sup> indicate the best placement of the distal locking screws is as close as possible to the subchondral area of the joint to prevent loss of postoperative reduction. The aim of our study was to evaluate the relationship between distal screw placement and postoperative radial shortening in a large consecutive cohort of dorsally displaced distal radius fractures plated with VLDRP. Our hypothesis was that loss of reduction after plating is related to the distance the distal locking screws are placed from the subchondral joint line.

## MATERIALS AND METHODS

### Study design

We performed a longitudinal multicentre retrospective cohort study including patients who underwent VLDRP fixation of a dorsally displaced distal radius fracture. X-rays and charts of patients undergoing surgery at two Australian regional hospitals between January 2010 and December 2014 were assessed (Ethics approval HREC/15/QTHS/10).

### Participants

Consecutive patients with dorsally displaced distal radius fractures managed with VLDRP were included. Ten patients had bilateral wrists fractures - one wrist was randomly chosen for inclusion for each. Patients with Kirschner wires in addition to VLDRP were excluded. Patients without documented follow-up were excluded.

### Data collection

Data were collected from pre-, intra- and post-operative standard anterior-posterior and lateral X-rays. Images were measured using digital radiology software (AGFA<sup>R</sup> HealthCare Impax 6, Belgium). Fracture classification, angle and distance measurements were assessed by the second author. The first author validated all measurements. If there was more than ten percent difference between measurements, a board-certified radiologist repeated the measurement.

We recorded anterior-posterior radial inclination (degrees), ulnar variance (radial length; millimetre) and lateral volar tilt (degrees). The distance of distal locking screws from the deepest point of the subchondral joint line was measured on intra-operative lateral tilted images. The subchondral line was defined as the dense area, which denotes the articular surface. The optimal most distal screw placement was defined as the area just proximal to the subchondral line without breaching it. Radial shortening as a parameter of reduction loss was determined as the change in ulnar variance between six and eight weeks post-operatively (Figure 1). Pre-operative images were used for AO fracture classification<sup>[21]</sup>. Patient age, gender, mechanism of injury (high or low energy), likelihood of osteoporosis and



**Figure 1** Examples of distal screw placement. A: Intraoperative image shows that screws are placed immediate to the subchondral joint line. Postoperative image does not show any loss of reduction; B: Placing the screws at a distance from the subchondral joint line causes postoperative loss of radial length; C: Intraoperative measurement. As the diameter of the screws was known, the distance of the screws was able to be calculated.

comorbidities [American Society of Anaesthesiologists (ASA)] classification<sup>[22]</sup> and postoperative immobilisation were sourced from patient charts.

### Statistical methods

A pilot study including 31 cases was used to calculate the sample size, as variability was unknown. Accounting for eight potential independent characteristics, the  $R^2$  was 0.28 and Cohen's  $f^2$  effect size was 0.39, indicating that 50 fractures would be required to have power in excess of 80% and a level of significance of 0.05.

Bivariate statistical comparisons used unpaired *t*-tests, one-way Analysis of Variance, Pearson's correlation coefficient and Spearman rank correlation coefficient (*r*) to identify factors influencing postoperative radial shortening. Factors included in the analysis were age, sex, mechanism of injury, affected wrist (left or right), AO

classification, time between injury and surgery, VLDRP characteristics including number of distal screw rows, total number of distal screws, distance of the distal locking screws from the subchondral joint line, and whether the wrist was immobilised postoperatively.

Multiple linear regression analysis identified independent factors associated with postoperative radial shortening. A Kolmogorov-Smirnov test verified that the outcome measure was normally distributed ( $P = 0.240$ ). After identifying independent significant factors, the remaining variables were investigated for potential confounding effects. Statistical analysis was conducted using Stata release 12 (StataCorp LP, Texas, United States) and SPSS for Windows, Version 22 (SPSS Inc., Chicago, IL, United States). Statistical analysis was performed by one of the authors, PB, a biostatistician ([www.tropicalhealthsolutions.com/petrabuttner](http://www.tropicalhealthsolutions.com/petrabuttner)).

**Table 1** Description of characteristics of 250<sup>1</sup> patients with 250 dorsally displaced distal radius fractures managed with volar locking distal radius plates documented between 2010 and 2014 at two regional hospitals in north Queensland, Australia

Characteristic	Descriptive statistics
<b>Patient</b>	
Mean age (SD) <sup>2</sup> ; range (yr)	49.1 (16.7); range 16 to 88
Female	63.2% (n = 158)
Comorbidities (ASA classification) <sup>4</sup> (n = 67)	
ASA 1	34.3% (n = 23)
ASA 2	59.7% (n = 40)
ASA 3	6.0% (n = 4)
With Osteoporosis <sup>5</sup> (n = 164)	51.2% (n = 84)
<b>Injury</b>	
High energy mechanism (n = 160)	46.9% (n = 75)
Right wrist fractured (n = 248)	42.3% (n = 105)
AO fracture classification <sup>6</sup>	
A2	14.8% (n = 37)
A3	14.8% (n = 37)
B1	2.8% (n = 7)
B2	4.0% (n = 10)
C1	12% (n = 30)
C2	34.4% (n = 86)
C3	17.2% (n = 43)
Median number of days from injury to surgery (IQR) <sup>3</sup> ; range (n = 164)	6 (1, 16); range 0 to 71
<b>Treatment</b>	
With 1 distal screw row	25.6% (n = 64)
Median number of distal screws (IQR); range	4 (4, 5); range 3 to 8
Median number of distal screws in first row (IQR); range	4 (4, 4.25); range 2 to 5
Median number of distal screws in second row (IQR); range	2 (1, 3); range 1 to 4
With 4 or less distal screws in most distal row	75.2% (n = 188)
Median distance from joint line (IQR); range (mm)	3.1 (2.1, 4.1) range 0 to 11
Postoperative immobilisation <sup>7</sup> (n = 224)	87.9% (n = 197)
<b>Outcome measure</b>	
Mean radial shortening (SD); range (mm)	1.9 (1.3); range 0 to 5.6

<sup>1</sup>n = 250 unless otherwise stated; <sup>2</sup>SD = standard deviation; <sup>3</sup>IQR = interquartile range; <sup>4</sup>ASA classification; <sup>5</sup>osteoporosis was classified as “yes” when chart information was available and in females > 60 years of age with low energy trauma; <sup>6</sup>AO fracture classification. B3 fractures were excluded from the analysis as they are volar shear fractures and follow different biomechanical principles; <sup>7</sup>postoperative immobilisation was either by cast (n = 128) or by thermoplastic splint (n = 77). Duration of immobilisation varied between two and four weeks. ASA: American Society of Anaesthesiologists.

## RESULTS

For detailed results, see Table 1. A total of 250 patients were included from Hospital 1 (n = 141; 56.4%) and Hospital 2 (n = 109; 43.6%). In all, 186 plates (74.4%) had two distal screw rows. Plates used were Medartis<sup>R</sup> Aptus TriMed<sup>R</sup> volar fixed angle plates or Synthes<sup>R</sup> VA. Sixty-four plates (25.6%) had one distal screw row (Synthes<sup>R</sup> volar locking buttress plate 2.4 mm). There was disagreement regarding two fractures. The board-certified radiologist agreed with the first author’s measurements.

## Factors influencing postoperative loss of radial length

Bivariate analysis showed that the mean postoperative loss of radial length was higher for AO type A and C fractures (mean: 2.0, SD: 1.3) and less for AO type B fractures (mean: 1.2, SD: 0.8) (P = 0.033). There was a weak negative correlation between number of distal screws in the most distal screw row and radial shortening (r = -0.13; P = 0.042). There was a strong positive correlation between the distance of the distal locking screws from the subchondral joint line and postoperative loss of radial length (r = 0.61; P < 0.001). None of the other factors (see Table 1 for complete list of factors investigated) was statistically significantly related to radial shortening.

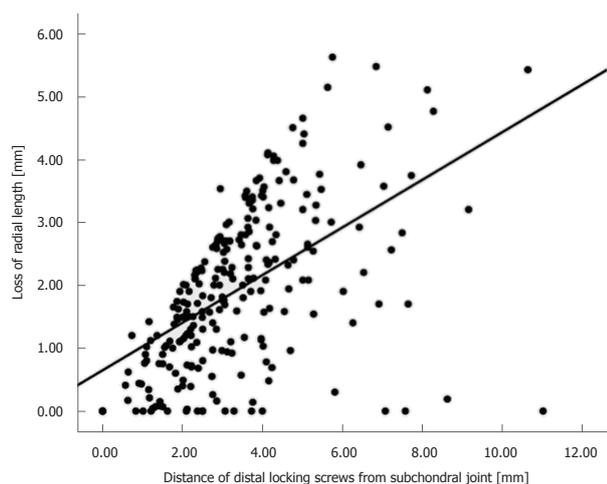
Multiple linear regression analysis showed that the distance of distal locking screws from the subchondral joint line was the only independent factor statistically significantly associated with radial shortening (coefficient 0.379, 95%CI: 0.304-0.454; P < 0.001). No confounding variables were identified. The linear regression line was estimated as radial shortening = 0.7 mm + 0.4 × the distance from joint line (mm) (P < 0.001) (Figure 2). Volar tilt and the change of radial inclination did not change in the postoperative period and were not analysed.

## DISCUSSION

The results of our study show that placement of distal locking screws is the only independent factor significantly associated with postoperative loss of radial length. Postoperative shortening is proportional to the distance of the distal locking screws from the subchondral joint line. The soft metaphyseal bone of the distal radius fragment cannot support the distal locking screws. The distal fragment will settle and “sink through” until the screws are in the hard subchondral area just proximal of the joint. Placing the distal screws as close as possible to the joint line prevents loss of postoperative displacement, independent of age, gender, osteoporosis and immobilisation.

Our study expands on a previous biomechanical study and clinical observations<sup>[13,16,18-20,23]</sup>. Drobtz *et al.*<sup>[13]</sup> found a statistically significant linear association between loss of radial length and distance of the distal locking screws from the subchondral joint line. They also noted that the distal fragment “sank straight” without loss of volar tilt and radial inclination, an observation which was confirmed in our study population. The current study translates these findings into a clinical setting. The clinical relevance of our results is that “distance from the joint line” is a modifiable risk factor. Postoperative loss of reduction therefore seems to be mainly surgeon-dependent.

Our findings also indicate that loss of reduction is independent of the number of distal screws, provided there are at least four distal screws with a minimum diameter of 2.3 mm each (the type of plates we assessed).



**Figure 2** Correlation of loss of radial length (mm) and distance of distal locking screws from the subchondral joint line (mm) of 250 patients with dorsally displaced distal radius fractures managed with volar locking distal radius plates. The linear regression line was: radial shortening = 0.7 mm + 0.38 x distance from joint line (mm) ( $P < 0.001$ ).

A second distal screw row does not have any positive influence on postoperative radial shortening. This is in accordance with biomechanical studies<sup>[12,14,24-26]</sup>.

The clinical and biomechanical advantage of a second distal screw row eludes the authors. According to operation manuals of various implant companies, two screw rows either provide a “three-dimensional scaffold for optimal subchondral support” or “intra-operative solutions for different fracture requirements”, “intra-operative fine contouring of the radial and intermediate columns”, “optional three point support for more stability” or “creation of a scaffold to allow two plane fixation of distal metaphyseal fragments”. Katsunori<sup>[27]</sup> and Kawasaki<sup>[28]</sup> have reported on a double tiered subchondral support (DSS) procedure in which the screws of the second distal screw row are placed long, so that their tips support the dorsal part of the distal radius. Their findings showed less loss of radial length and volar tilt when using the DSS construct compared to placing screws only in the distal row. Other studies<sup>[29-31]</sup>, found that a screw length of 75% of the sagittal distal radius diameter is sufficient to withstand postoperative displacement loads, which somewhat contradicts Katsunori’s and Kawasaki’s findings.

Our findings further demonstrated that immediate postoperative mobilisation did not lead to increased loss of radial length and consequently that postoperative immobilisation did not prevent loss of radial length when the distal screws were placed into the soft metaphyseal bone. Only 12.4% of fractures underwent early mobilisation, the remainder being immobilised by splint or a cast (Table 1). We speculate that this is an ingrained surgeon practice rather than behaviour based on evidence.

Previous studies have identified osteoporosis as a risk factor for radial shortening after plating with VLDRP<sup>[32]</sup>, and it has been postulated that this is due to poor bone quality. This finding was not supported in our study. Age

could be considered to be a surrogate marker for osteoporosis, but this was also not shown to be associated with radial shortening. Our findings highlight that volar locking plates are suitable and effective in this subset of patients. However, it was difficult to diagnose osteoporosis, as chart information was limited and it was not feasible to retrospectively perform bone mineral density measurements on all patients. This is a weakness of our study. Osteoporosis was classified as “yes” when chart information was available and in females > 60 years of age with low energy trauma<sup>[5]</sup>.

There were other limitations in our study. We did not evaluate clinical outcomes in our patient population, but this was not within the scope of our study. However, a recent prospective cohort study<sup>[3]</sup> showed that radial shortening of more than 2 mm was associated with worse patient-reported outcome scores. These findings indirectly indicate the possible clinical relevance of our paper. There are also several other studies which show that “function follows form”, *i.e.*, that good clinical outcomes are associated with healing in near anatomical position<sup>[33-35]</sup>.

The study strengths are adequate sample size and the large number of variables analysed. In addition to measurements performed by two authors independently, the same X-ray departments, machines and viewing program counteracted possible bias. In summary, the distance of the distal screws in relation of the subchondral joint line is the only independent variable associated with postoperative loss of reduction. The loss of reduction is independent of age, gender, osteoporosis, ASA status, fracture severity, immobilisation, number of distal screws and the presence or absence of a second distal screw row. Surgeons using VLDRPs for fixation of distal radius fractures should attempt to place the distal screws as close as possible to the subchondral joint line.

## ARTICLE HIGHLIGHTS

### Research background

Treatment of distal radius fractures with volar locking distal radius plates (VLDRP) has become the most popular treatment method in the last ten years. Biomechanical and clinical studies indicate that distal screw placement as close as possible to the articular surface is crucial to prevent loss of postoperative reduction. To our knowledge, no study has been undertaken that proves or disproves this observation.

### Research motivation

Our hypothesis was that postoperative loss of reduction will occur when the distal VLDRP screws are placed more proximal, in the distal radius fragment metaphysis, rather than in the subchondral hard area close to the articular surface. We also hypothesized that the loss of postoperative reduction is directly related to the distance of the distal screws from the articular surface. We undertook a retrospective study analyzing pre- and postoperative X-rays of 250 consecutive distal radius fractures treated with VLDRP.

### Research objectives

Objectives of the study were to determine factors correlated with postoperative radial shortening in patients with distal radius fractures treated with VLDRPs.

### Research methods

This is a longitudinal multicentre retrospective cohort study including patients who underwent VLDRP fixation of a dorsally displaced distal radius fracture in

which 250 wrist fractures were included. Collected parameters were fracture classification, radial length, radial inclination, volar inclination of the joint surface, patient age, gender, mechanism of injury, likelihood of osteoporosis, comorbidities and postoperative immobilisation. The distance of the distal locking screws to the articular surface was measured on intraoperative lateral tilted X-rays. Radial shortening as a parameter of loss of reduction was measured on X-rays obtained at a minimum of six weeks postoperatively. Bivariate statistical comparisons were used to identify factors influencing postoperative radial shortening. Multiple linear regression analysis then identified independent factors associated with postoperative radial shortening.

### Research results

Multiple linear regression analysis showed that the distance of the distal locking screws from the articular surface was the only independent factor associated with radial shortening. The relationship between shortening and distance of the distal screws to the articular surface was linear and statistically highly significant.

### Research conclusions

Our study showed that in order to prevent postoperative loss of reduction in fractures plated with VLDRP, it is crucial that the distal screws are placed as close as possible to the articular surface. The study further indicated that loss of postoperative reduction is not associated with any other parameters measured - age, gender, osteoporosis, ASA status, fracture severity, immobilisation, number of distal screws and the presence or absence of a second distal screw row.

### Research perspectives

A major advantage of treating distal radius fractures with VLDRP is that patients can be treated without postoperative immobilisation. VLDRP are in fact the only treatment modality that allows for immediate postoperative use of the wrist. Based on the findings of our study and provided that the distal screws are placed as close as possible to the articular surface, immediate postoperative mobilization should be possible without loss of reduction. Future studies should attempt to verify our findings in a clinical setting.

## REFERENCES

- 1 **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]
- 2 **Gehrmann SV**, Windolf J, Kaufmann RA. Distal radius fracture management in elderly patients: a literature review. *J Hand Surg Am* 2008; **33**: 421-429 [PMID: 18343302 DOI: 10.1016/j.jhssa.2007.12.016]
- 3 **Larouche J**, Pike J, Slobogean GP, Guy P, Broekhuysen H, O'Brien P, Lefavre KA. Determinants of Functional Outcome in Distal Radius Fractures in High-Functioning Patients Older Than 55 Years. *J Orthop Trauma* 2016; **30**: 445-449 [PMID: 26978132 DOI: 10.1097/BOT.0000000000000566]
- 4 **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]
- 5 **Bartl C**, Stengel D, Gülke J, Gebhard F. Clinical results following conservative and surgical treatment of osteoporotic distal radius fractures in the elderly: Overview of best available evidence. *Unfallchirurg* 2016; **119**: 723-731 [PMID: 27481355 DOI: 10.1007/s00113-016-0216-y]
- 6 **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]
- 7 **Costa ML**, Achten J, Parsons NR, Rangan A, Griffin D, Tubeuf S, Lamb SE; DRAFFT Study Group. 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]
- 8 **Arora R**, Lutz M, Deml C, Krappinger D, Haug L, Gabl M. A prospective randomized trial comparing nonoperative treatment with volar locking plate fixation for displaced and unstable distal radial fractures in patients sixty-five years of age and older. *J Bone Joint Surg Am* 2011; **93**: 2146-2153 [PMID: 22159849 DOI: 10.2106/JBJS.J.01597]
- 9 **Zong SL**, Kan SL, Su LX, Wang B. Meta-analysis for dorsally displaced distal radius fracture fixation: volar locking plate versus percutaneous Kirschner wires. *J Orthop Surg Res* 2015; **10**: 108 [PMID: 26169601 DOI: 10.1186/s13018-015-0252-2]
- 10 **Mellstrand Navarro C**, Ahrengart L, Tornqvist H, Ponzer S. Volar Locking Plate or External Fixation With Optional Addition of K-Wires for Dorsally Displaced Distal Radius Fractures: A Randomized Controlled Study. *J Orthop Trauma* 2016; **30**: 217-224 [PMID: 26709818 DOI: 10.1097/BOT.0000000000000519]
- 11 **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**: 687-694 [PMID: 27795951 DOI: 10.5312/wjo.v7.i10.687]
- 12 **Drobetz H**, Weninger P, Grant C, Heal C, Muller R, Schuetz M, Pham M, Steck R. More is not necessarily better. A biomechanical study on distal screw numbers in volar locking distal radius plates. *Injury* 2013; **44**: 535-539 [PMID: 23127726 DOI: 10.1016/j.injury.2012.10.012]
- 13 **Drobetz H**, Bryant AL, Pokorny T, Spitaler R, Leixnering M, Jupiter JB. Volar fixed-angle plating of distal radius extension fractures: influence of plate position on secondary loss of reduction--a biomechanical study in a cadaveric model. *J Hand Surg Am* 2006; **31**: 615-622 [PMID: 16632057 DOI: 10.1016/j.jhssa.2006.01.011]
- 14 **Weninger P**, Dall'Ara E, Drobetz H, Nemeš W, Figl M, Redl H, Hertz H, Zysset P. Multidirectional volar fixed-angle plating using cancellous locking screws for distal radius fractures--evaluation of three screw configurations in an extra-articular fracture model. *Wien Klin Wochenschr* 2011; **123**: 4-10 [PMID: 21165706 DOI: 10.1007/s00508-010-1488-9]
- 15 **Hart A**, Collins M, Chhatwal D, Steffen T, Harvey EJ, Martineau PA. Can the use of variable-angle volar locking plates compensate for suboptimal plate positioning in unstable distal radius fractures? A biomechanical study. *J Orthop Trauma* 2015; **29**: e1-e6 [PMID: 24786734 DOI: 10.1097/BOT.0000000000000146]
- 16 **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.jhssa.2008.01.024]
- 17 **Wich M**, Sixto R, Spranger N. Design of distal radius volar locking plates: Anatomical, surgical and biomechanical aspects. *Unfallchirurg* 2016; **119**: 742-746 [PMID: 27444999 DOI: 10.1007/s00113-016-0218-9]
- 18 **Orbay JL**, Fernandez DL. Volar fixation for dorsally displaced fractures of the distal radius: a preliminary report. *J Hand Surg Am* 2002; **27**: 205-215 [PMID: 11901379 DOI: 10.1053/jhsu.2002.32081]
- 19 **Drobetz H**, Kutscha-Lissberg E. Osteosynthesis of distal radial fractures with a volar locking screw plate system. *Int Orthop* 2003; **27**: 1-6 [PMID: 12582800 DOI: 10.1007/s00264-002-0393-x]
- 20 **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]
- 21 **Müller E**, Koch P, Nazarian S, Schatzker J. The Comprehensive classification of fractures of long bones. Berlin, Heidelberg: Springer Berlin Heidelberg; 1990 [DOI: 10.1007/978-3-642-61261-9]
- 22 **Owens WD**, Felts JA, Spitznagel EL Jr. ASA physical status classifications: a study of consistency of ratings. *Anesthesiology* 1978; **49**: 239-243 [PMID: 697077 DOI: 10.1097/0000542-197810000-00003]
- 23 **Berglund LM**, Messer TM. Complications of volar plate fixation for managing distal radius fractures. *J Am Acad Orthop Surg* 2009; **17**: 369-377 [PMID: 19474446 DOI: 10.5435/00124635-200906000-00005]
- 24 **Drobetz H**, Schueller M, Tschegg EK, Heal C, Redl H, Muller R. Influence of screw diameter and number on reduction loss after

- plating of distal radius fractures. *ANZ J Surg* 2011; **81**: 46-51 [PMID: 21299798 DOI: 10.1111/j.1445-2197.2010.05479.x]
- 25 **Moss DP**, Means KR Jr, Parks BG, Forthman CL. A biomechanical comparison of volar locked plating of intra-articular distal radius fractures: use of 4 versus 7 screws for distal fixation. *J Hand Surg Am* 2011; **36**: 1907-1911 [PMID: 22018475 DOI: 10.1016/j.jhssa.2011.08.039]
- 26 **Neuhaus V**, Badri O, Ferree S, Bot AG, Ring DC, Mudgal CS. Radiographic alignment of unstable distal radius fractures fixed with 1 or 2 rows of screws in volar locking plates. *J Hand Surg Am* 2013; **38**: 297-301 [PMID: 23267755 DOI: 10.1016/j.jhssa.2012.10.040]
- 27 **Inagaki K**, Kawasaki K. Distal radius fractures-Design of locking mechanism in plate system and recent surgical procedures. *J Orthop Sci* 2016; **21**: 258-262 [PMID: 27006135 DOI: 10.1016/j.jos.2015.12.022]
- 28 **Kawasaki K**, Nemoto T, Inagaki K, Tomita K, Ueno Y. Variable-angle locking plate with or without double-tiered subchondral support procedure in the treatment of intra-articular distal radius fracture. *J Orthop Traumatol* 2014; **15**: 271-274 [PMID: 24942842 DOI: 10.1007/s10195-014-0292-0]
- 29 **Gabl M**, Arora R, Schmidle G. Biomechanics of distal radius fractures: Basics principles and GPS treatment strategy for locking plate osteosynthesis. *Unfallchirurg* 2016; **119**: 715-722 [PMID: 27445000 DOI: 10.1007/s00113-016-0219-8]
- 30 **Baumbach SF**, Synek A, Traxler H, Mutschler W, Pahr D, Chevalier Y. The influence of distal screw length on the primary stability of volar plate osteosynthesis--a biomechanical study. *J Orthop Surg Res* 2015; **10**: 139 [PMID: 26351239 DOI: 10.1186/s13018-015-0283-8]
- 31 **Wall LB**, Brodt MD, Silva MJ, Boyer MI, Calfee RP. The effects of screw length on stability of simulated osteoporotic distal radius fractures fixed with volar locking plates. *J Hand Surg Am* 2012; **37**: 446-453 [PMID: 22305729 DOI: 10.1016/j.jhssa.2011.12.013]
- 32 **Rhee SH**, Kim J, Lee YH, Gong HS, Lee HJ, Baek GH. Factors affecting late displacement following volar locking plate fixation for distal radial fractures in elderly female patients. *Bone Joint J* 2013; **95-B**: 396-400 [PMID: 23450027 DOI: 10.1302/0301-620X.95B3.30514]
- 33 **Trumble TE**, Culp RW, Hanel DP, Geissler WB, Berger RA. Intra-articular fractures of the distal aspect of the radius. *Instr Course Lect* 1999; **48**: 465-480 [PMID: 10098077]
- 34 **McQueen M**, Caspers J. Colles fracture: does the anatomical result affect the final function? *J Bone Joint Surg Br* 1988; **70**: 649-651 [PMID: 3403617 DOI: 10.1302/0301-620X.70B4.3403617]
- 35 **Kazuki K**, Kusunoki M, Yamada J, Yasuda M, Shimazu A. Cineradiographic study of wrist motion after fracture of the distal radius. *J Hand Surg Am* 1993; **18**: 41-46 [PMID: 8423316 DOI: 10.1016/0363-5023(93)90242-U]

**P- Reviewer:** Liu JY, Emara KM **S- Editor:** Dou Y  
**L- Editor:** Filipodia **E- Editor:** Song H



## Observational Study

**Long-term results of an anatomically implanted hip arthroplasty with a short stem prosthesis (MiniHip™)**

Lars V von Engelhardt, Andreas Breil-Wirth, Christian Kothny, Jörn Bengt Seeger, Christian Grasselli, Joerg Jerosch

Lars V von Engelhardt, Faculty of Health, University of Witten/Herdecke, Witten 58448, Germany

Lars V von Engelhardt, Department of Trauma Surgery Orthopedics and Sports Medicine, Katholisches Karl-Leisner Klinikum, Kleve 47533, Germany

Andreas Breil-Wirth, Christian Grasselli, Joerg Jerosch, Department of Orthopedics, Trauma Surgery and Sports Medicine, Johanna Etienne Hospital, Neuss 41462, Germany

Christian Kothny, Munich Ortho Center, Munich 80802, Germany

Jörn Bengt Seeger, Department of Orthopaedics and Orthopaedic Surgery, University Hospital Giessen and Marburg, Giessen 35392, Germany

Christian Grasselli, Department of Orthopaedics and Traumatology, Waldburg-Zeil Clinic Tett nang, Tett nang 88069, Germany

ORCID number: Lars V von Engelhardt (0000-0002-3181-6163); Andreas Breil-Wirth (0000-0003-1077-1901); Christian Kothny (0000-0002-6992-8670); Jörn Bengt Seeger (0000-0002-6443-8875); Christian Grasselli (0000-0002-9746-4367); Joerg Jerosch (0000-0002-1965-5977).

Author contributions: Jerosch J, Kothny C and Seeger JB contributed to the study conception and design; Seeger JB, Breil-Wirth A, Jerosch J and Grasselli C contributed to the data acquisition, analysis and data interpretation; von Engelhardt LV contributed to the data interpretation, the literature research, the preparation of the figures and the writing of the article which was approved by all authors.

Supported by A sponsorship from Corin (Corin Group, Cirencest, United Kingdom).

Institutional review board statement: The study was reviewed and approved by the local ethical committee of the Medical Association of North Rhine (Ärztekammer Nordrhein) in Düsseldorf (Study No. 2011379).

Informed consent statement: All persons involved in this study gave their informed consent prior to study inclusion. All

details that might disclose the identity of the subjects under study were omitted or anonymized.

Conflict-of-interest statement: This paper's publication fee is paid by a sponsorship from Corin (Corin Group, Cirencest, United Kingdom). Except for Jörn Bengt Seeger, all authors have a paid consultancy/speakers contract for Corin. All authors declare to have no further 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/>

Manuscript source: Unsolicited manuscript

Correspondence to: Lars V von Engelhardt, MD, PhD, Surgeon, Department of Trauma Surgery Orthopedics and Sports Medicine, Katholisches Karl-Leisner Klinikum, Alfred-Herrhausen-Straße 50, Kleve 47533, Germany. [chirurgie.ahk@kkle.de](mailto:chirurgie.ahk@kkle.de)  
Telephone: +49-2821-4901151  
Fax: +49-2821-4901080

Received: May 22, 2018

Peer-review started: May 23, 2018

First decision: June 5, 2018

Revised: June 17, 2018

Accepted: June 28, 2018

Article in press: June 28, 2018

Published online: October 18, 2018

**Abstract****AIM**

To evaluate the clinical and radiological outcome nine

and ten years after short-stemmed, bone preserving and anatomical hip arthroplasty with the MiniHip™ system.

### METHODS

In a prospective study, 186 patients underwent hip arthroplasty with a partial neck preserving short stem (MiniHip™, Corin). Elderly patients were not excluded from this study, thus the mean age at the time of surgery was 59.3 years (range 32 to 82 years). Surgery and the follow-up assessments were performed at two Centers. Up until now, the mean follow-up was 112.5 ± 8.2 mo. The Oxford Hip Score (OHS) and the Hip Dysfunction Osteoarthritis and Outcome Score (HOOS) was assessed pre- and each year after surgery. The clinical follow-up was accompanied by standardized a.p. and axial radiological examinations. Periprosthetic lucencies, hypertrophies within the Gruen zones one to fourteen were assessed. A subsidence of the stem was investigated according to Morray and heterotopic ossifications were assessed according to Brooker.

### RESULTS

The OHS and HOOS improved from 18 ± 3.3 to 46 ± 2.0 and from 30 ± 8.3 to 95 ± 4.6 points,  $P < 0.001$  respectively. There were no differences regarding age, etiology, friction pairings, *etc.*, ( $P > 0.05$ ). Two stems were revised due to a symptomatic subsidence four and twelve months postoperatively. Thus, the survivorship for aseptic loosening at nine to ten years was 98.66%. Including one stem revision due to a symptomatic exostosis, bursitis and thigh pain as well as one revision because of a septic stem loosening, the overall survival for the stem with revision for any reason was 97.32%. Besides one asymptomatic patient, radiological signs of a proximal stress-shielding, such as bone resorptions within the proximal Gruen zones, were not noticed. Findings suggesting a distal loading, *e.g.*, bony hypertrophies or bone appositions of more than 2 mm, were also not detected.

### CONCLUSION

Regarding these first long-term results on the MiniHip™, the implant performed exceedingly well with a high rate of survivorship for aseptic loosening. Our radiological results within the Gruen zones support the design rationale of the Minihip to provide a reliable metaphyseal anchoring with the expected proximal, more physiological load transfer. This might minimize or exclude a stress shielding which might be associated with thigh pain, proximal bone loss and an increased risk of aseptic loosening. The MiniHip™ is a reliable partial-neck retaining prosthesis with good a clinical long-term outcome in younger as well as elderly patients.

**Key words:** Primary hip arthroplasty; Long-term results; Short stem endoprosthesis; Prospective follow-up study; Stress-shielding

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

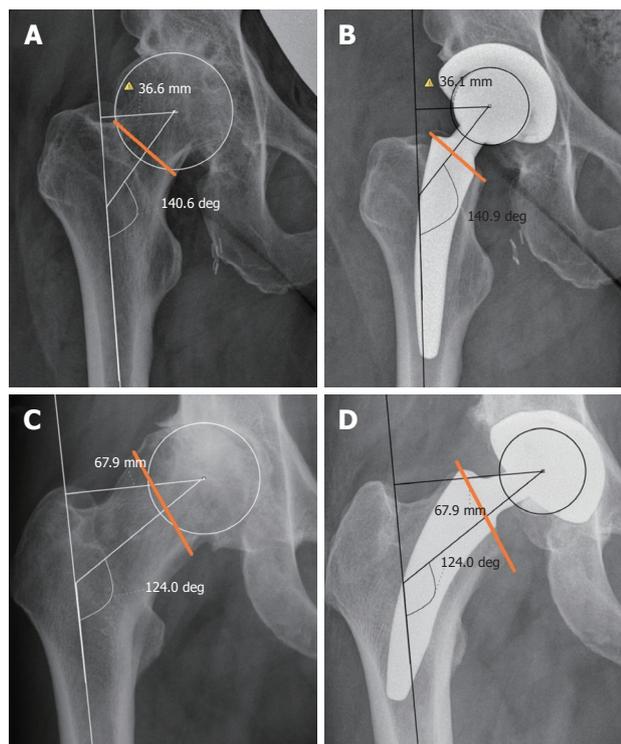
**Core tip:** An innovative aspect of the MiniHip™ short stem prosthesis is that the design provides the possibility to restore the joint geometry by using an individual femoral neck cut. In general, there is an increasing demand for long-term results of newer arthroplasty systems. In contrast to other studies on short stems for hip replacement, this study was explicitly not only conducted in young and active patients. Therefore, this clinical and radiological long-term follow-up study is of particular interest. This study revealed an excellent and lasting clinical outcome, a reliable metaphyseal anchoring with a physiological proximal load transfer and an excellent long-term stem survivorship which is at least comparable to standard prostheses and other short stem concepts.

von Engelhardt LV, Breil-Wirth A, Kothny C, Seeger JB, Grasselli C, Jerosch J. Long-term results of an anatomically implanted hip arthroplasty with a short stem prosthesis (MiniHip™). *World J Orthop* 2018; 9(10): 210-219 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i10/210.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i10.210>

### INTRODUCTION

Short-stemmed cementless hip arthroplasty prostheses have been designed to preserve bone stock, facilitate an eventual revision surgery and achieve a more physiological loading to the proximal part of the femur<sup>[1-4]</sup>. In comparison to conventional cementless stems, short stems are therefore described to reduce the stress shielding around the stem, which might be associated with thigh pain, bone loss and an increased risk of aseptic loosening<sup>[5-8]</sup>.

In different conventional stems as well as short stems, digital planning analysis studies and clinical studies on the radiological outcome frequently demonstrate an inadequate reconstruction of the individual femoral offset<sup>[9,10]</sup>. Such changes in hip geometry often lead to a reduced soft tissue tension as well as a decreased muscular preload. This might be accompanied by an insufficiency of the gluteus muscle group and/or a relevant hip instability<sup>[11,12]</sup>. However, the widely used standardized femoral neck cut of most prosthesis stems leads to a "bottom up strategy" where the restoration of the joint geometry can only be guaranteed by selecting different modular conus components for a modular tapered stem or different designs of a monoblock prosthesis. The MiniHip™ short stem (Corin Group PLC, Cirencester, United Kingdom) is different. Based on a large series of preoperative CT data collected in hip arthroplasty patients, it is designed to allow the use of individual resection levels for the femoral neck<sup>[13]</sup>. According to this concept, the MiniHip™ implant is a partial neck retaining prosthesis. This leads to a "top down concept" which provides a completely different possibility to restore the individ-



**Figure 1** “Top down concept” of the MiniHip™ to restore the individual joint geometry. The individual femoral neck cut and physiological orientation of the partially retained femoral neck allows the reconstruction of the individual joint geometry. A: Valgus hip deformity; B: A deeper femoral neck cut leads a reduction of the femoral offset with an accurate reconstruction of the joint geometry; C: Varus hip; D: A low femoral neck provides a reconstruction of the geometry with an increased femoral offset with an appropriate successfully reconstructed joint geometry.

ual joint geometry. Thus, the physiological orientation of the partially retained femoral neck allows a much easier and reliable reconstruction of the individual anteversion, offset and CCD angle (Figure 1)<sup>[13-15]</sup>. Using 3-dimensional CT scans in cadaver hips, Mihalko *et al.*<sup>[16]</sup> investigated the value of different femoral neck resection levels for the implantation of a short stem prosthesis without modular components. They showed that all geometrical parameters, including the femoral neck anteversion, the CCD angle and the center of the femoral head, were reconstructed within a mean error of 2° and/or 1 mm<sup>[16]</sup>. Moreover, Windhagen *et al.*<sup>[17]</sup> have shown that a short stem partial neck-retaining implant provides a more balanced hip in terms of the surrounding soft tissue structures, whereas a straight stem alters the head position and induces much more non-physiological strains.

Clinical follow-up studies of the MiniHip™ showed a good short-term clinical outcome<sup>[18-20]</sup> as well as good densitometric results with a comparatively lower proximal bone density reduction<sup>[1,21]</sup>. To our knowledge, this is the longest study on this well-established femoral neck retaining metadiaphyseal prosthesis. In contrast to other studies on short stems for hip replacement, this prospective study was explicitly not only conducted in

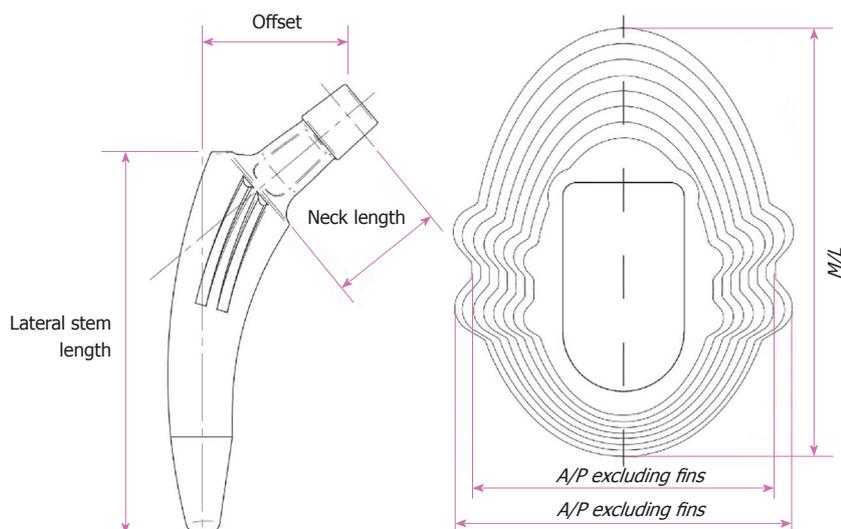
young and active patients. The purpose of the current study was to assess the clinical and radiological long-term outcome of the MiniHip™ in a relatively diverse population with a wide range of patient age.

## MATERIALS AND METHODS

This prospective follow-up examination has been approved by the Ethical Committee of the Medical Association of North Rhine (Ärzttekammer Nordrhein) in Düsseldorf, Germany under the No. 2011379. All patients gave their written informed consent before enrollment in the study. A total of 186 consecutive hip joint arthroplasties (right/left = 97/89) in 186 patients (m/f = 94/92) were included for the follow-up assessment. Fourteen patients received a bilateral hip arthroplasty with the MiniHip™ as a two-staged procedure. Patients’ mean age at the time of surgery was 59.3 years (range 32 to 82 years). Indications for surgery included advanced osteoarthritis arthritis recalcitrant to conservative treatments. All surgeries were carried out between 2008 and 2010 at the Department of Orthopedics, Trauma Surgery and Sports Medicine of the Johanna-Etienne Hospital Neuss ( $n = 108$ ) and at the Munich Ortho Center ( $n = 78$ ) in Germany.

During the subsequent follow-up, 37 patients were excluded from this study. Reasons were an osteosynthesis on the same leg in one patient, one aseptic loosening of the stem on the other side (no MiniHip™), a severe, immobilizing spinal canal stenosis in one case, two severe other diseases, nine patients wanted to quit the study, one patient died and 22 were lost for unknown reasons.

Pre-operative planning of the prosthesis components was performed in all cases on scaled anteroposterior digital radiographs using the MediCAD® software. In all patients, the meta-diaphyseal anchoring short-stem system MiniHip™ (Corin Group PLC, Cirencester, United Kingdom) was implanted. The MiniHip™ was introduced by Jerosch<sup>[13]</sup> in 2008. The stem is designed to fit and fill the retained part of the femoral neck. After the femoral neck cut and the opening of the metadiaphyseal cavity, the implant side is prepared by using impactors with an increasing size. This compression of the metadiaphyseal spongy bone might improve the filling of the metaphysis. Moreover, the MiniHip™ stem is designed to provide an extended contact area with a wide load transfer at the femoral calcar region. The MiniHip™ stem is available in nine sizes, each providing a centrum collum diaphyseal angle of 130° (Figure 2). The material of the stem is an alpha-beta titanium alloy (Ti-6Al-4V) and it is coated by a layer of hydroxyapatite applied over a layer of pure titanium (Bi-coat™). The elevated roughness might contribute to the primary stability of the prosthesis, whereas the additional hydroxyapatite coating may serve as an osseointegrator between bone and prosthesis and therefore enhance the secondary



size	stem length	offset	neck length	A/P diameter excluding fins	A/P diameter including fins	M/L diameter
1	79.5	32.2	25.0	13.6	15.0	22.0
2	84.2	33.3	26.0	15.2	16.7	23.9
3	89.0	34.5	27.0	16.7	18.4	25.8
4	93.8	35.6	28.0	18.3	20.2	27.6
5	98.5	36.8	29.0	19.8	21.8	29.5
6	103.3	37.9	30.0	21.4	23.6	31.4
7	108.0	39.1	31.0	22.9	25.2	33.3
8	112.8	40.2	32.0	24.5	27.0	35.1
9	117.5	41.4	33.0	26.0	28.6	37.0

Figure 2 Dimensions (mm) of the different sizes of the MiniHip™ stem.

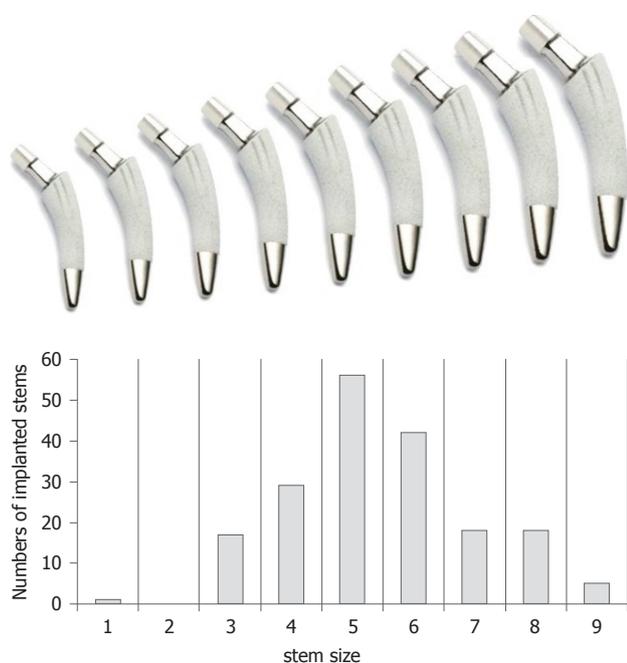


Figure 3 Frequencies of the implanted stem sizes used in this study. The distribution of sizes used in this study is similar to a Gauss curve. The increasing dimensions of the conus according to the nine different sizes of the implant are depicted. The distal bullet tip of the prosthesis is polished. This design might prevent a fixation in this area and therefore reduce the risk of thigh pain.

stem stability. The stem is intended to be used with 12/14 taper heads of different lengths. The distal tip of the prosthesis is polished and is designed to prevent a fixation in this area. This feature is expected to reduce the risk of anterior thigh pain (Figure 3). The frequencies of implanted stem sizes used in this study are depicted in Figure 3. At the Johanna-Etienne Hospital Neuss, surgery was performed in the supine position using the antero-lateral minimal invasive (ALMI) for supine position described by Jerosch<sup>[22]</sup>. This approach protects the abductor muscles to facilitate the post-operative rehabilitation. The exposure of the femur and the acetabulum as well as the positioning of the patient allows an excellent orientation which is mandatory for an optimal positioning of the prosthesis components. At the Munich Ortho Center, two approaches were used. In 60 patients, a standard direct anterior approach through the intermuscular plane was performed. Similarly to the ALMI approach, this approach has been described to preserve the hip abductor muscles<sup>[23,24]</sup>. In 18 patients, a lateral, transgluteal approach with a splitting of the gluteus medius muscle was used<sup>[25]</sup>. During the implantation of the MiniHip™, the stem follows the curvature of the medial calcar. Therefore, an individual femoral neck can be used to restore the joint geometry<sup>[15]</sup>. The height of the femoral neck cut is planned on the preoperative X-ray. In a valgus hip,

a deep resection leads to an increased CCD angle and a smaller offset, whereas a high cut near to the head neck junction is used to reconstruct the low CCD angle of a varus hip (Figure 1). Intraoperatively, the landmark for the femoral cut is the piriformis fossa, which is easy to visualize when a minimally invasive approach is used. The cut is made parallel to the head neck junction and at 90° to the femoral neck. Then, the implant side is prepared by using different impactors of increasing size. The postoperative and rehabilitative treatment was started in all patients on the first postoperative day. Patients started weight-bearing as tolerated with two crutches for six weeks. If there were no contraindications, Ibuprofen was recommended for ten days as prophylaxis for heterotopic ossifications.

The follow-up examinations were performed preoperatively and annually by two independent examiners. The preoperative and follow-up clinical evaluations included the Oxford Hip Score (OHS)<sup>[26]</sup>, and the Hip Dysfunction Osteoarthritis and Outcome Score (HOOS)<sup>[27]</sup>. Both the HOOS and the OHS are validated and reliable scores used to assess the functional and symptomatic results after total hip arthroplasty<sup>[26,27]</sup>. First descriptive statistics were used to compare our data to the literature. To assess predictors such as sex, age, friction pairings, etc. which might influence the outcome scoring, we used a linear mixed model analysis.

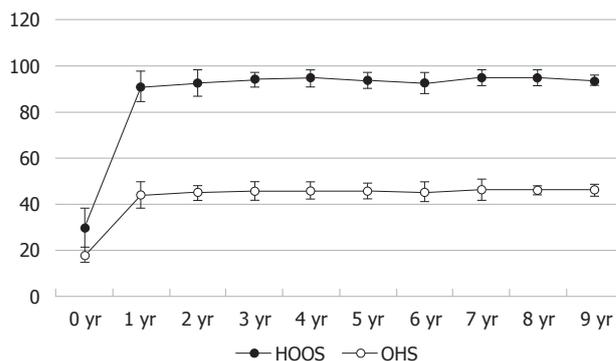
The X-ray assessments were performed preoperatively, postoperatively immediately after the initial mobilization and at the follow-up appointments. Standardized standing antero-posterior (AP) and lateral radiographs of the proximal femur were taken. To assess the bone remodeling around the prosthesis, radiographs were inspected within the Gruen zones for the presence of radiolucencies, bony hypertrophies or atrophies, reactive lines and pedestal formation according to the criteria by Engh *et al.*<sup>[28]</sup>. A change of the stem position was investigated according to Morray by using the osteotomy as a bony reference<sup>[29]</sup>. A subsidence of the stem as a detectable pathology was documented for a position change of at least 2 mm. Ossifications were analyzed according to the Brooker classification<sup>[30]</sup>. All complications related to the prosthesis such as a septic or aseptic loosening, infection, subsidence, dislocation and all operative revision were documented.

Data analyses were reviewed and supported by a biomedical statistician. Analyses were performed with Excel Statistics software (Microsoft, Redmond, WA, United States) and SPSS Statistics software 22.0 (SPSS Inc., Chicago, IL, United States).

## RESULTS

### Functional outcome

One year after surgery, both, the HOOS and OHS improved significantly from a mean of  $30 \pm 8.3$  to  $91 \pm 6.7$  and from  $18 \pm 3.3$  to  $44 \pm 5.8$  points,  $P < 0.001$ ,

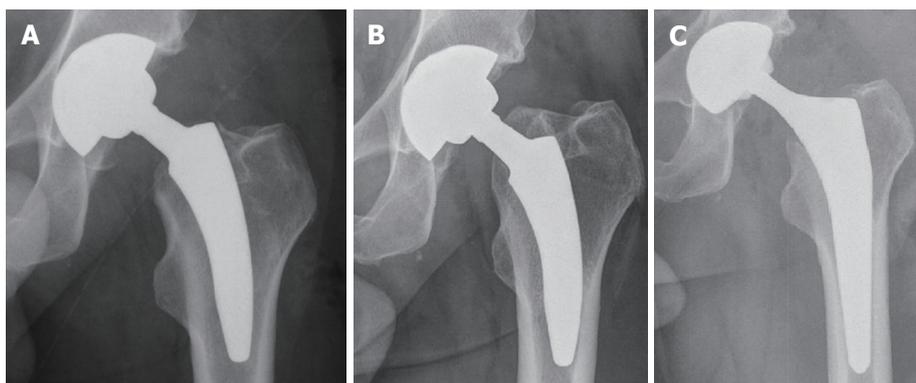


**Figure 4 Outcome at the Hip Dysfunction Osteoarthritis and Outcome Score and Oxford Hip Score scoring over ten years.** After the initial improvement after one year, the subsequent scorings at our follow-up investigations two to ten years after the implantation showed only slight increases, which were not significant,  $P > 0.05$  respectively. HOOS: Hip Dysfunction Osteoarthritis and Outcome Score; OHS: Oxford Hip Score.

respectively. After this initial improvement after one year, the scorings at the follow-up investigations two to ten years after the implantation stayed on the same level or showed only slight increases, which were not significant,  $P > 0.05$  respectively (Figure 4). A further linear mixed model analysis revealed that there were no significant differences regarding sex, age, component sizes, etiology and friction pairings ( $P > 0.05$ ).

### Revisions and complications

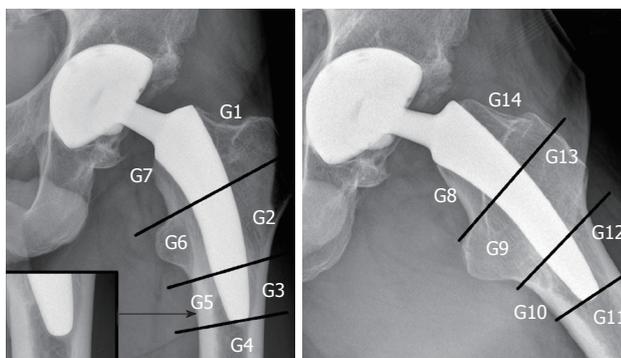
The primary outcome measure was the stem revision for loosening as the failure endpoint of the stem. In our series, we noticed two cases with an aseptic stem loosening four and twelve months after surgery with a symptomatic subsidence of 12 and 15 mm (Figure 5). In these patients, a one-stage revision to a conventional stem was conducted. Thus, the survivorship for aseptic loosening at nine to ten years is 98.66% (147 of 149). Another patient had a symptomatic exostosis with a chronic bursitis and thigh pain. Besides the removal of the exostosis a revision of the stem was performed. One patient suffered a septic stem loosening with the detection of propioni bacteria 20 mo postoperatively. Therefore, the overall survival for the stem with revision for any reason was 97.32% (145 of 149). Another important outcome measure was the number of cup revisions for any reason as the failure endpoint for the cup. In our series, we had one patient with an aseptic cup loosening four months postoperative. Another patient had a symptomatic iliopsoas impingement at the anterior border of the cup which showed an early loosening three weeks postoperatively. These early revisions lead to an overall survival for the cup with revision for any reason of 98.66% (147 of 149). Other major complications, such as dislocations, periprosthetic fractures, a deep venous thrombosis and nerve injuries were not observed during the immediate postoperative inpatient care and the subsequent follow-



**Figure 5** Exemplary X-ray of one of the two cases with a symptomatic subsidence. A: Postoperative X-ray; B: Subsidence of 15 mm twelve months after surgery; C: X-ray of the one-stage revision to a conventional stem.



**Figure 6** Exemplary X-ray of one of the nine cases with a heterotopic ossifications grade I according to Brooker.



**Figure 7** Periprosthetic bone resorptions or bony hypertrophies were assessed within the Gruen zones 1-14. A small ostolysis of less than 2 mm outlined by a discrete sclerotic margin was detected in a large number of patients around the tip of the stem. Being detected exclusively around the polished tip of the stem, it might be indicative for a fibrous ingrowth at the bullet polished tip of the stem. Further radiological and/or clinical signs of a loosening were not noticed in these cases.

up investigations.

### Radiological results

A subsidence was investigated according to Morray<sup>[29]</sup>. Besides the patients with a symptomatic subsidence mentioned above, we documented one asymptomatic

sintering of the stem at the one-year control. The subsidence measured 6 mm and remained unchanged during our subsequent follow-up investigations.

Heterotopic ossifications were assessed according to Brooker *et al.*<sup>[30]</sup>. Radiologically, we saw nine cases of heterotopic ossifications, three with a Brooker grade II and six cases with a grade I finding (Figure 6).

In a further investigation, periprosthetic bone resorptions or bony hypertrophies within the Gruen zones were assessed (Figure 7). One patient showed a bony atrophy with an ostolysis of more than 2 mm in Gruen zones 1, 2, 8 and 14 (Table 1). Further patients with extended bony resorptions of more than 2 mm were not detected. A small ostolysis of less than 2 mm outlined by a discrete sclerotic margin was detected in a large number of patients around the tip of the stem. This finding was only noticed in the distal Gruen zones 3, 4, 5, 10, 11, 12 (Table 1). Because this finding was exclusively noticed around the polished tip of the stem, it might be indicative for a fibrous ingrowth at the polished tip of the stem. Further radiological and/or clinical signs of a loosening were not noticed in these cases (Figure 7). Bony hypertrophies of less than 2 mm were detected in three cases in Gruen zone 3 and in one case in Gruen zone 5 (Table 1). Further cortical hypertrophies, neocortex formations or a spot welding with new bone formations between the endosteal surface and the stem were not noticed in our series.

## DISCUSSION

The bi-coating and an optimized initial press fit within an extended contact area at the proximal femur is expected to provide a solid primary and secondary fixation of the MiniHip™<sup>[13-15,18,31]</sup>. This might provide a good long-term survival. Searching for data on the survival in short stems, short- and mid-term but only a few long-term results are published<sup>[18,32-35]</sup>. In a review article by van Oldenrijk *et al.*<sup>[35]</sup>, the majority of the studies had a follow-up of less than 5 years. Out of 49 studies on 19 short stems, midterm result were only reported for the Mayo (Zimmer Inc., Warsaw,

**Table 1 Periprosthetic bone density changes within the Gruen zones (G1-14) detected in standardized a.p. and axial X-rays**

a.p.	Axial
G1: 1 × bony atrophy > 2 mm	G8: 1 × bony atrophy > 2 mm
G2: 1 × bony atrophy > 2 mm	G9: No abnormality
G3: 3 × bony hypertrophy < 2 mm 16 × RL <sup>1</sup>	G10: 36 × RL <sup>1</sup>
G4: 47 × RL	G11: 21 × RL <sup>1</sup>
G5: 1 × bony hypertrophy < 2 mm 54 × RL <sup>1</sup>	G12: 31 × RL <sup>1</sup>
G6: No abnormality	G13: No abnormality
G7: No abnormality	G14: 1 × bony atrophy > 2 mm

<sup>1</sup>Small radiolucency < 2 mm with discrete sclerotic margin.

United States), Metha (B.Braun Aesculap, Tuttlingen, Germany) and CFP stem (Collum Femoris Preserving, Waldemar Link GmbH, Hamburg, Germany). In contrast to this relatively poor data pool, an increasingly large number of different short stem designs are currently available. Thus, we have to notice a strong need for follow-up studies. For the Minihip™ stem, an overall survival of 98.16%, 97.26% and 99.3% was reported after 60, 18 and 37 mo, respectively<sup>[18-20]</sup>. These short- and mid-term results are encouraging. The present study is the first one in the Minihip™ after a follow-up of nine to ten years. Two of 186 stems subsided within the first year and required revision (Figure 5). Both patients reported a severe thigh pain. A third case of a subsidence of 6 mm at the first-year follow up was asymptomatic. During the following radiological controls, the stem remained stable without any further subsidence and/or loosening. Further cases with a subsidence of more than 2 mm were not noticed. Thus, the rate of aseptic stem loosening as an important outcome measure showed an overall survivorship of 98.66%. This rate is similar to a recent seven year follow-up study in the monoblock design of the Metha stem, where the revision rate was 1%. Zero point five percent were revised for aseptic loosening and 0.4% because of a femoral fracture during the postoperative follow-up. It is important to mention that the revision rate for the modular design of this stem was 9.4% for the titanium and 4.6% for the cobalt chrome neck<sup>[34]</sup>. Thus, the adapter fractures of the modular Metha stem lead to much higher stem revision rates, whereas the revision rates for the monoblock were similar compared to conventional stems. This supports our preference for a short monoblock prosthesis which we combine with our "top down" concept for an exact joint geometry reconstruction<sup>[13]</sup>. In the present study, one late infection and one exostosis with thigh pain lead to two further stem revisions. Therefore, the overall survivorship, including all revisions for any reasons was 97.32%. Regarding these long-term results, the implant performed exceedingly well. This is in accordance with the clinical outcome showing a lasting

improvement at the OHS and HOOS scorings (Figure 4). Corresponding to these clinical data, the assessment of bone resorptions within the Gruen zones demonstrate good long-term results. Nonetheless, regarding the distal Gruen zones (Table 1) the large number of small (< 2 mm) radiolucencies outlined by a discrete sclerotic margin has to be mentioned (Figure 7). These findings were always noticed around the polished bullet tip of the stem and are indicative for a fibrous interface membrane without any bony ingrowth. This special radiological finding has frequently been documented in uncemented polished taper designs and never been described to be indicative for a loosening or as any other detrimental condition<sup>[36,37]</sup>. On the contrary, this finding has to be recognized differently. According to the design rationale of the Minihip™, the polished bullet tip is expected to minimize endosteal abutment. This way, pressure peaks and/or a bony ingrowth at the tip of the stem are expected to be avoided. Moreover, this might decrease the stiffness of the implant and prevent the occurrence of thigh pain at the tip of the stem<sup>[38]</sup>. Another aspect is the more proximal and therefore more physiological load transfer to the metaphysis of the femur. This proximal load transfer, which is an important goal of the design of the Minihip™, should not be affected by the tip of the prosthesis. Therefore, the absence of a bony ingrowth around the polished bullet tip is a desirable finding for the Minihip™ stem. Our investigations on bone density changes within the proximal Gruen zones (Table 1) might support our thesis that this principle of a proximal load might actually work. Besides one single patient, where we documented an asymptomatic bone atrophy of more than 2 mm in Gruen zones 1, 2, 8 and 14, further resorptions were not detected within these proximal areas. In regard to these findings, a distal load transfer leading to a stress shielding and bone resorptions within the proximal zones appears quite unlikely. Moreover, bony hypertrophies within the distal Gruen zones, which might be indicative for an unphysiological distal load transfer, were only detected in one patient. For the CLS Spotorno stem (Zimmer, US), in contrast, bony hypertrophies and/or appositions within the distal zones with or without a bone loss within the proximal areas have been described after a 2-4 years in 53% of the cases<sup>[39]</sup>. For the Hipstar (Stryker, Duisburg, Germany) and the Zweymueller stem (SL-Plus®-Plus Orthopedics AG, Rotkreuz, Switzerland) similar findings were detected already after one year in 60% and 87% of the cases<sup>[40]</sup>. These findings are indicative for an unphysiological distal load with correspondingly high rates of a proximal stress-shielding. As a logical consequence, the authors discussed, if a progression of these proximal bone resorptions may influence the clinical results and the survival of the implant<sup>[40]</sup>. Our radiological long-term results showing a more physiological proximal load transfer and a reduced stress-

shielding, have been confirmed by several densitometric studies comparing the bone remodeling between different short and conventional straight stems<sup>[41,42]</sup>. For the MiniHip™ but also for other stems, an initial bone resorption in all periprosthetic zones is a typical finding immediately after the implantation<sup>[1,21]</sup>. However, in studies on the MiniHip™, the initial bone resorption within the first months had a much lesser extend compared to different conventional stems<sup>[13,41-43]</sup>. More important is that a relatively strong subsequent bone remodelling within the proximal Gruen zones was documented during the following years. Thus, compared to conventional straight stems, a much lower proximal bone density loss was noticed<sup>[1,21]</sup>. Because of this process of bone formation, which continued till the second year, the bone-friendly design of the MiniHip™ as a representative of a partially neck-sustaining stem has been discussed<sup>[21]</sup>. Similar results were demonstrated on other partially neck-retaining prostheses, demonstrating a significant bone remodeling leading to a markedly lower bone density reduction in the proximal Gruen zones<sup>[44,45]</sup>. Taken together, all these radiographic and osteodensitometric data support the thesis of a more physiological proximal load. Regarding these convincing data, it is not surprising that a lower frequency of thigh pain was reported in short stems compared to straight, conventional stem types<sup>[46]</sup>.

Short stems have become increasingly utilized in younger patients<sup>[38]</sup>. This may reflect the surgeon's desire to conserve bone stock in these patients. Because of the lack of long-term studies, this may also reflect some concerns regarding the achievement of a lasting stable fixation in elderly patients. In regard to studies reporting an increased intraoperative fracture risk with advanced age<sup>[47]</sup>, worries about such complications might further influence the indication of a short stem in elderly patients. Therefore, the wide range of patients' ages between 32 and 82 years is an interesting feature of this study. The analysis of the outcome scorings revealed no significant differences regarding the patients' age. Intraoperative fractures were not noticed and a loosening of the stem with a subsidence was a rare and early occurring complication in two patients of a mean age. Thus, in comparison to conventional stems as a current benchmark level<sup>[48]</sup>, the MiniHip™ short stem might also be a reliable alternative in elderly patients.

In conclusion, this long-term study revealed an excellent and long-lasting clinical outcome, low complication rates, a reliable metaphyseal anchoring with a more physiological proximal load transfer and an excellent long-term stem survivorship. Therefore, the MiniHip™ might be a convincing concept for a partial-neck retaining prosthesis in a wide range of patients.

## ARTICLE HIGHLIGHTS

### Research background

In contrast to a poor scientific data pool, an increasingly large number of different short stem designs are currently available. Thus, we have to notice a

strong need for follow-up studies especially on long-term results of these stems. Regarding the MiniHip™ stem, previous short-term results are encouraging, whereas long-term studies are lacking. Thus, the present study is the first one after a follow-up period of nine to ten years. In contrast to studies on short-stemmed hip replacements, which are mainly conducted in relatively young and active patients, this study included a wide range of patients including elderly persons.

### Research motivation

The MiniHip™ monoblock stem is designed to fit and fill the retained part of the femoral neck and the metaphysis. Using an individual femoral neck cut, the implant is normally used as a partial neck retaining prosthesis. This leads to a "top down concept" which provides a completely different possibility to restore the joint geometry. Using this concept, the physiological orientation of the partially retained femoral neck allows an easy and reliable reconstruction of the individual anteversion, CCD angle and offset. Moreover, this might lead to a more physiological loading of the proximal femur. The key question is, if these design features are useful to reduce the stress shielding around the stem with its' complications such as thigh pain, bone loss and aseptic loosening. Thus, this concept might possibly solve or reduce some typical problems of conventional hip arthroplasty. Our optimistic expectation is that this might also secure a good long-term outcome of such prostheses.

### Research objectives

The design of the MiniHip™ prosthesis seems to provide some reasonable advantages. The main objective was to assess the long-term clinical and radiological outcome and the complication rates of this prosthesis in a relatively diverse study cohort with a wide range of patients' age. This might support the understanding in recent developments of partial-neck retaining, short-stemmed hip prostheses, which provide a metaphyseal anchoring as well as a more physiological proximal load transfer to the femur.

### Research methods

This study on the MiniHip™ is the first one after such a long mean follow-up period of nine to ten years. 186 patients, with a comparatively wide age range between 32 and 82 years, were included. Hip arthroplasty with the MiniHip™ prosthesis was performed at two Centers. The clinical follow-up, which included the Oxford Hip Score (OHS) and the Hip Dysfunction Osteoarthritis and Outcome Score (HOOS), was accompanied by standardized p.a. and axial radiological examinations. The radiological evaluation included the assessment of periprosthetic lucencies, hypertrophies within the Gruen zones, the assessment of a possible stem subsidence and the detection of heterotopic ossifications.

### Research results

The OHS and HOOS score improved significantly from 18 to 46 and from 30 to 95 points. Stem related complications included two cases with a symptomatic subsidence after four and twelve months. The survivorship for aseptic loosening remained unchanged after the subsequent follow-up of nine to ten years. Thus, the final survivorship was 98.66%. Including one stem revision due to a symptomatic exostosis, bursitis and thigh pain as well as one revision because of a septic stem loosening, the overall survival for the stem with revision for any reason was 97.32%. Besides one asymptomatic patient, signs of a proximal stress shielding, such as corresponding bone resorptions within the proximal Gruen zones, were not noticed. Bony hypertrophies and/or bone appositions which might be indicative for a distal loading, were also not noticed.

### Research conclusions

This study is the first one on the MiniHip™ prosthesis evaluating the long-term outcome in patients with a wide range of ages. This study revealed a convincing and lasting clinical outcome. The radiological findings suggest a physiological proximal load transfer with a reliable metaphyseal anchoring and an excellent long-term stem survivorship, which is at least comparable to standard prostheses and other short stem concepts. The MiniHip™ is designed to fit and fill the retained part of the femoral neck. During surgery, the implant side is prepared and compressed by using impactors with an increasing size. Moreover, the MiniHip™ stem is designed to provide an extended contact

area and an optimized filling with a wide load transfer at the femoral calcar region. This new concept is expected to provide a solid fixation. Moreover, a porous coating of a hip stem leads to an elevated roughness and an additional hydroxyapatite coating may serve as an osteoconductor between bone and prosthesis. All these features of this partial neck-retaining prosthesis might enhance the primary as well as secondary stem stability, provide an optimized proximal loading and finally provide a good long-term survival of this prosthesis. We hope that this concept might solve or reduce some typical problems of conventional hip arthroplasty stems. Short-stemmed, partial neck retaining hip arthroplasty seems to realize a more physiological proximal load transfer with a reliable metaphyseal anchoring and an excellent long-term stem survivorship. Partial neck retaining hip arthroplasty using the MiniHip™ stem might be a convincing concept for a wide range of patients. The study presented here was a necessary step in exploring this prosthesis, which seems to provide reasonable advantages. Short-stemmed, partial neck retaining hip arthroplasty by using an individual femoral neck cut provides a physiological proximal load transfer and an excellent long-term stem survivorship, which is at least comparable to other prosthesis concepts. This might be a contributory factor to the convincing and lasting clinical outcome demonstrated in this study. This study includes a population with a wide range of ages. The follow-up comprises a long-term period of nine to ten years. The radiological assessment included typical changes of the periprosthetic bone within the Gruen zones as well as the detection of a possible stem subsidence. In contrast to other studies on short stems for hip replacement, this study was explicitly not only conducted in young and active patients. Therefore, this clinical and radiological long-term follow-up study might be of particular interest and might provide a better understanding of such partial neck retaining prostheses. This long-term study on the MiniHip™ revealed an overall survivorship for an aseptic stem loosening of 98.66%. The promising clinical and radiological outcome was proved to be lasting in a wide range of patients. The radiological findings within the Gruen zones suggest a more physiological proximal load transfer and a reliable proximal metaphyseal anchoring. This might explain the excellent long-term stem survivorship of the MiniHip™ prosthesis. In our future clinical practice, we will follow this concept of a proximal, metaphyseal anchored partial-neck retaining prosthesis. Especially the concept of the MiniHip™, which allows an individual femoral neck cut and which recommends a compression of the implant side by using different impactors, might provide some reasonable advantages to achieve such reliable and long-lasting results. Moreover, this concept might be interesting in a wide range of patients including those with an advanced age.

### Research perspectives

In consideration of conventional stems as a current benchmark for survival rates and for typical complications occurring intraoperatively, but also in the long-term follow-up, a proximal-metaphyseal anchored partial-neck retaining prosthesis might be a reliable alternative in younger as well as elderly patients. Further clinical outcome studies in larger study populations might be useful to find out limitations regarding the indication for this short-stemmed, partial neck retaining hip prosthesis. Perhaps the indication for such short-stemmed prostheses will be reconsidered in the future. Regarding our initial long-term results, signs for an upcoming implant failure based on a material failure or a mechanical mismatch of implant and bone structure are not imminent. Ongoing assessments with longer follow-up periods will evaluate the durability of these first nine to ten year results. Follow-up studies with larger cohorts and longer follow-up periods will be a useful method for the future research.

### REFERENCES

- 1 **Ercan A**, Sokkar SM, Schmid G, Filler TJ, Abdelkafy A, Jerosch J. Periprosthetic bone density changes after MiniHip™ cementless femoral short stem: one-year results of dual-energy X-ray absorptiometry study. *SICOT J* 2016; **2**: 40 [PMID: 27855776 DOI: 10.1051/sicotj/2016033]
- 2 **Falez F**, Casella F, Panegrossi G, Favetti F, Barresi C. Perspectives on metaphyseal conservative stems. *J Orthop Traumatol* 2008; **9**: 49-54 [PMID: 19384482 DOI: 10.1007/s10195-008-0105-4]
- 3 **Leali A**, Fetto J, Insler H, Elfenbein D. The effect of a lateral flare feature on implant stability. *Int Orthop* 2002; **26**: 166-169 [PMID: 12073110 DOI: 10.1007/s00264-002-0355-3]
- 4 **Tanner KE**, Yettram AL, Loeffler M, Goodier WD, Freeman

- MA, Bonfield W. Is stem length important in uncemented endo-prostheses? *Med Eng Phys* 1995; **17**: 291-296 [PMID: 7633757 DOI: 10.1016/1350-4533(95)90854-5]
- 5 **Brinkmann V**, Radetzki F, Delank KS, Wohlrab D, Zeh A. A prospective randomized radiographic and dual-energy X-ray absorptiometric study of migration and bone remodeling after implantation of two modern short-stemmed femoral prostheses. *J Orthop Traumatol* 2015; **16**: 237-243 [PMID: 25666724 DOI: 10.1007/s10195-015-0335-1]
- 6 **Chen HH**, Morrey BF, An KN, Luo ZP. Bone remodeling characteristics of a short-stemmed total hip replacement. *J Arthroplasty* 2009; **24**: 945-950 [PMID: 18848420 DOI: 10.1016/j.arth.2008.07.014]
- 7 **Kim YH**, Choi Y, Kim JS. Comparison of bone mineral density changes around short, metaphyseal-fitting, and conventional cementless anatomical femoral components. *J Arthroplasty* 2011; **26**: 931-940.e1 [PMID: 21130598 DOI: 10.1016/j.arth.2010.10.001]
- 8 **Yan SG**, Weber P, Steinbrück A, Hua X, Jansson V, Schmidutz F. Periprosthetic bone remodelling of short-stem total hip arthroplasty: a systematic review. *Int Orthop* 2017; Epub ahead of print [PMID: 29178044 DOI: 10.1007/s00264-017-3691-z]
- 9 **Jerosch J**, Funken S. Change of offset after implantation of hip alloarthroplasties. *Unfallchirurg* 2004; **107**: 475-482 [PMID: 15197454 DOI: 10.1007/s00113-004-0758-2]
- 10 **Wedemeyer C**, Quitmann H, Xu J, Heep H, von Knoch M, Saxler G. Digital templating in total hip arthroplasty with the Mayo stem. *Arch Orthop Trauma Surg* 2008; **128**: 1023-1029 [PMID: 17994244 DOI: 10.1007/s00402-007-0494-5]
- 11 **Asayama I**, Chamnongkitch S, Simpson KJ, Kinsey TL, Mahoney OM. Reconstructed hip joint position and abductor muscle strength after total hip arthroplasty. *J Arthroplasty* 2005; **20**: 414-420 [PMID: 16124955 DOI: 10.1016/j.arth.2004.01.016]
- 12 **Matsushita A**, Nakashima Y, Jingushi S, Yamamoto T, Kuraoka A, Iwamoto Y. Effects of the femoral offset and the head size on the safe range of motion in total hip arthroplasty. *J Arthroplasty* 2009; **24**: 646-651 [PMID: 18534445 DOI: 10.1016/j.arth.2008.02.008]
- 13 **Jerosch J**. Kurzschaftprothesen an der Hüfte. 1<sup>st</sup> ed. Springer-Verlag GmbH, Germany, 2017; 197-233 [DOI: 10.1007/978-3-662-52744-3]
- 14 **Buttaro M**, Nally F, Diaz F, Stagnaro J, Rossi L, Comba F, Zanotti G, Piccaluga F. Which prosthetic system restores hip biomechanics more effectively? ICJR World Arthroplasty Congress, 2015 Apr 16-18; Paris, France
- 15 **Jerosch J**, Grasselli C, Kothny PC, Litzkow D, Hennecke T. Reproduction of the anatomy (offset, CCD, leg length) with a modern short stem hip design--a radiological study. *Z Orthop Unfall* 2012; **150**: 20-26 [PMID: 21487992 DOI: 10.1055/s-0030-1270965]
- 16 **Mihalko WM**, Assaf D, Sungu M. Reproducing the hip center with a femoral neck-retaining implant. *Orthopedics* 2015; **38**: S21-S26 [PMID: 25826628 DOI: 10.3928/01477447-20150215-52]
- 17 **Windhagen H**, Chincisan A, Choi HF, Thorey F. Soft-tissue balance in short and straight stem total hip arthroplasty. *Orthopedics* 2015; **38**: S14-S20 [PMID: 25826627 DOI: 10.3928/01477447-20150215-51]
- 18 **Breil-Wirth A**, von Engelhardt LV, Grasselli C, Jerosch J. 5- to 6-years-results of a cementless short stem hip joint endoprosthesis [Article in German]. *Orthopädische und Unfallchirurgische Praxis* 2016; **6**: 370-375
- 19 **Dettmer M**, Pourmoghaddam A, Kreuzer SW. Comparison of Patient-Reported Outcome from Neck-Preserving, Short-Stem Arthroplasty and Resurfacing Arthroplasty in Younger Osteoarthritis Patients. *Adv Orthop* 2015; **2015**: 817689 [PMID: 26101669 DOI: 10.1155/2015/817689]
- 20 **Teoh KH**, Lee PY, Woodnutt DJ. Our early experience of the Corin Minihip prosthesis. *Hip Int* 2016; **26**: 265-269 [PMID: 27034100 DOI: 10.5301/hipint.5000343]
- 21 **Shafy TA**, Sayed A, Abdelazeem AH. Study of the bone behavior around a neck preserving short stem implant: bone densitometric analysis over a span of two years. *SICOT J* 2016; **2**: 31 [PMID:

- 27716459 DOI: 10.1051/sicotj/2016025]
- 22 **Jerosch J**, Theising C, Fadel ME. Antero-lateral minimal invasive (ALMI) approach for total hip arthroplasty technique and early results. *Arch Orthop Trauma Surg* 2006; **126**: 164-173 [PMID: 16523344 DOI: 10.1007/s00402-006-0113-x]
  - 23 **Matta JM**, Shahrard 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]
  - 24 **Oinuma K**, Eingartner C, Saito Y, Shiratsuchi H. Total hip arthroplasty by a minimally invasive, direct anterior approach. *Oper Orthop Traumatol* 2007; **19**: 310-326 [PMID: 17728988 DOI: 10.1007/s00064-007-1209-3]
  - 25 **Bauer R**, Kerschbaumer F, Poisel S, Oberthaler W. The transgluteal approach to the hip joint. *Arch Orthop Trauma Surg* 1979; **95**: 47-49 [PMID: 526126 DOI: 10.1007/BF00379169]
  - 26 **Dawson J**, Fitzpatrick R, Carr A, Murray D. Questionnaire on the perceptions of patients about total hip replacement. *J Bone Joint Surg Br* 1996; **78**: 185-190 [PMID: 8666621 DOI: 10.1302/0301-620X.78B2.0780185]
  - 27 **Klässbo M**, Larsson E, Mannevik E. Hip disability and osteoarthritis outcome score. An extension of the Western Ontario and McMaster Universities Osteoarthritis Index. *Scand J Rheumatol* 2003; **32**: 46-51 [PMID: 12635946 DOI: 10.1080/0300974031000409]
  - 28 **Engl CA**, Massin P, Suthers KE. Roentgenographic assessment of the biologic fixation of porous-surfaced femoral components. *Clin Orthop Relat Res* 1990; 107-128 [PMID: 2199114 DOI: 10.1097/0003086-199008000-00022]
  - 29 **Morrey BF**, Adams RA, Kessler M. A conservative femoral replacement for total hip arthroplasty. A prospective study. *J Bone Joint Surg Br* 2000; **82**: 952-958 [PMID: 11041581 DOI: 10.1302/0301-620X.82B7.10420]
  - 30 **Brooker AF**, Bowerman JW, Robinson RA, Riley LH Jr. Ectopic ossification following total hip replacement. Incidence and a method of classification. *J Bone Joint Surg Am* 1973; **55**: 1629-1632 [PMID: 4217797 DOI: 10.2106/00004623-197355080-00006]
  - 31 **Castellini I**, Andreani L, Parchi PD, Bonicoli E, Piolanti N, Risoli F, Lisanti M. Hydroxyapatite in total hip arthroplasty. Our experience with a plasma spray porous titanium alloy/hydroxyapatite double-coated cementless stem. *Clin Cases Miner Bone Metab* 2016; **13**: 221-227 [PMID: 28228786 DOI: 10.11138/ccmbm/2016.13.3.221]
  - 32 **Hauer G**, Vielgut I, Amerstorfer F, Maurer-Ertl W, Leithner A, Sadoghi P. Survival Rate of Short-Stem Hip Prostheses: A Comparative Analysis of Clinical Studies and National Arthroplasty Registers. *J Arthroplasty* 2018; **33**: 1800-1805 [PMID: 29428465 DOI: 10.1016/j.arth.2018.01.017]
  - 33 **Kendoff DO**, Citak M, Egidy CC, O'Loughlin PF, Gehrke T. Eleven-year results of the anatomic coated CFP stem in primary total hip arthroplasty. *J Arthroplasty* 2013; **28**: 1047-1051 [PMID: 23523502 DOI: 10.1016/j.arth.2012.10.013]
  - 34 **Schnurr C**, Schellen B, Dargel J, Beckmann J, Eysel P, Steffen R. Low Short-Stem Revision Rates: 1-11 Year Results From 1888 Total Hip Arthroplasties. *J Arthroplasty* 2017; **32**: 487-493 [PMID: 27639304 DOI: 10.1016/j.arth.2016.08.009]
  - 35 **van Oldenrijk J**, Molleman J, Klaver M, Poolman RW, Haverkamp D. Revision rate after short-stem total hip arthroplasty: a systematic review of 49 studies. *Acta Orthop* 2014; **85**: 250-258 [PMID: 24694271 DOI: 10.3109/17453674.2014.908343]
  - 36 **Pluot E**, Davis ET, Revell M, Davies AM, James SL. Hip arthroplasty. Part 2: normal and abnormal radiographic findings. *Clin Radiol* 2009; **64**: 961-971 [PMID: 19748001 DOI: 10.1016/j.crad.2009.05.002]
  - 37 **Vanrusselt J**, Vansevanant M, Vanderschueren G, Vanhoenacker F. Postoperative radiograph of the hip arthroplasty: what the radiologist should know. *Insights Imaging* 2015; **6**: 591-600 [PMID: 26487647 DOI: 10.1007/s13244-015-0438-5]
  - 38 **Khanuja HS**, Vakil JJ, Goddard MS, Mont MA. Cementless femoral fixation in total hip arthroplasty. *J Bone Joint Surg Am* 2011; **93**: 500-509 [PMID: 21368083 DOI: 10.2106/JBJS.J.00774]
  - 39 **Robinson RP**, Lovell TP, Green TM. Hip arthroplasty using the cementless CLS stem. A 2-4-year experience. *J Arthroplasty* 1994; **9**: 177-192 [PMID: 8014649 DOI: 10.1016/0883-5403(94)90067-1]
  - 40 **Bergschmidt P**, Bader R, Finze S, Gankovych A, Kundt G, Mittelmeier W. Cementless total hip replacement: a prospective clinical study of the early functional and radiological outcomes of three different hip stems. *Arch Orthop Trauma Surg* 2010; **130**: 125-133 [PMID: 19526245 DOI: 10.1007/s00402-009-0907-8]
  - 41 **Freitag T**, Hein MA, Werner D, Reichel H, Bieger R. Bone remodelling after femoral short stem implantation in total hip arthroplasty: 1-year results from a randomized DEXA study. *Arch Orthop Trauma Surg* 2016; **136**: 125-130 [PMID: 26613788 DOI: 10.1007/s00402-015-2370-z]
  - 42 **Koyano G**, Jinno T, Koga D, Yamauchi Y, Muneta T, Okawa A. Comparison of Bone Remodeling Between an Anatomic Short Stem and a Straight Stem in 1-Stage Bilateral Total Hip Arthroplasty. *J Arthroplasty* 2017; **32**: 594-600 [PMID: 27554784 DOI: 10.1016/j.arth.2016.07.016]
  - 43 **Roth A**, Richartz G, Sander K, Sachse A, Fuhrmann R, Wagner A, Venbrocks RA. Periprosthetic bone loss after total hip endoprosthesis. Dependence on the type of prosthesis and preoperative bone configuration. *Orthopade* 2005; **34**: 334-344 [PMID: 15726320 DOI: 10.1007/s00132-005-0773-1]
  - 44 **Lerch M**, von der Haar-Tran A, Windhagen H, Behrens BA, Wefstaedt P, Stukenborg-Colsman CM. Bone remodelling around the Metha short stem in total hip arthroplasty: a prospective dual-energy X-ray absorptiometry study. *Int Orthop* 2012; **36**: 533-538 [PMID: 21935621 DOI: 10.1007/s00264-011-1361-0]
  - 45 **Zeh A**, Pankow F, Röllinshoff M, Delank S, Wohlrab D. A prospective dual-energy X-ray absorptiometry study of bone remodeling after implantation of the Nanos short-stemmed prosthesis. *Acta Orthop Belg* 2013; **79**: 174-180 [PMID: 23821969]
  - 46 **Banerjee S**, Pivec R, Issa K, Harwin SF, Mont MA, Khanuja HS. Outcomes of short stems in total hip arthroplasty. *Orthopedics* 2013; **36**: 700-707 [PMID: 24024994 DOI: 10.3928/01477447-20130821-06]
  - 47 **Zhao R**, Cai H, Liu Y, Tian H, Zhang K, Liu Z. Risk Factors for Intraoperative Proximal Femoral Fracture During Primary Cementless THA. *Orthopedics* 2017; **40**: e281-e287 [PMID: 27874909 DOI: 10.3928/01477447-20161116-06]
  - 48 **Rometsch E**, Bos PK, Koes BW. Survival of short hip stems with a "modern", trochanter-sparing design - a systematic literature review. *Hip Int* 2012; **22**: 344-354 [PMID: 22878970 DOI: 10.5301/HIP.2012.9472]

**P- Reviewer:** Li JM, Robertson GA **S- Editor:** Ji FF  
**L- Editor:** A **E- Editor:** Song H



## Observational Study

## Does ethnicity and education influence preoperative disability and expectations in patients undergoing total knee arthroplasty?

Madeline Therese Kudibal, Thomas Kallemose, Anders Troelsen, Henrik Husted, Kirill Gromov

Madeline Therese Kudibal, Anders Troelsen, Henrik Husted, Kirill Gromov, Department of Orthopedic Surgery, Copenhagen University Hospital Hvidovre, Hvidovre 2650, Denmark

Thomas Kallemose, Clinical Research Centre, Copenhagen University Hospital Hvidovre, Hvidovre 2650, Denmark

ORCID number: Madeline Therese Kudibal (0000-0002-3490-3625); Thomas Kallemose (0000-0002-7356-6481); Anders Troelsen (0000-0003-0132-8182); Henrik Husted (0000-0002-6878-7503); Kirill Gromov (0000-0002-8114-5193).

**Author contributions:** Kudibal MT, Troelsen A, Husted H, and Gromov K contributed to study conception and design; Kudibal MT, Kallemose T, and Gromov K to data acquisition, analysis and interpretation; Kudibal MT and Gromov K contributed to writing the article; all authors contributed to editing, reviewing and final approval of article.

**Supported by** the Danish Rheumatism Association, No. R111-A2587.

**Institutional review board statement:** No approval from the National Ethics Committee was necessary as this was a non-interventional observational study. Permission to store and review patient data was obtained from the Danish Data Protection Agency Jr, No. 2007-58-0015.

**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 conflicts of interest.

**STROBE statement:** the STROBE checklist was adopted in preparation of 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:** Unsolicited manuscript

**Correspondence to:** Madeline Therese Kudibal, MD, Doctor, Department of Orthopedic Surgery, Copenhagen University Hospital Hvidovre, Hvidovre, Kettegård alle 30, Hvidovre 2650, Denmark. [madelinetherese@hotmail.com](mailto:madelinetherese@hotmail.com)  
Telephone: +45-53-669073

**Received:** April 28, 2018

**Peer-review started:** April 28, 2018

**First decision:** June 15, 2018

**Revised:** June 22, 2018

**Accepted:** June 27, 2018

**Article in press:** June 27, 2018

**Published online:** October 18, 2018

### Abstract

#### AIM

To investigate whether minority ethnicity and the duration of education influence preoperative disability and expectations in patients undergoing total knee arthroplasty.

#### METHODS

We prospectively included 829 patients undergoing primary unilateral total knee arthroplasty (TKA) from April 2013 to December 2014 at a single centre. Patients filled in pre-operative questionnaires with information regarding place of birth, duration of education, expectations for outcome of surgery and baseline characteristics. Patients were stratified based on ethnicity. Majority ethnicity was defined as born in

the study country and minority ethnicity was defined as born in any other country. Similarly, patients were stratified based on duration of education in groups defined as < 9 years, 9-12 years and > 12 years, respectively.

## RESULTS

We found that 92.2% of patients were of majority ethnicity. We found that 24.5%, 44.8% and 30.8% of patients had an education of < 9 years, 9-12 years and > 12 years, respectively. The mean preoperative (pre-OP) oxford knee score (OKS) in the total population was 23.6. Patients of minority ethnicity had lower mean pre-OP OKS (18.6 *vs* 23.9,  $P < 0.001$ ), higher pain levels (VAS 73.0 *vs* 58.7,  $P < 0.001$ ), expected higher levels of post-OP pain (VAS 14.1 *vs* 6.1,  $P = 0.02$ ) and of overall symptoms (VAS 16.6 *vs* 6.4,  $P = 0.006$ ). Patients with > 12 years education had lower mean pre-OP OKS (21.5 *vs* 23.8 and 24.6,  $P < 0.001$ ) and higher pre-OP VAS pain (65.4 *vs* 59.2 and 56.4,  $P < 0.001$ ) compared to groups with shorter education. One year post-operative (post-OP) patients of minority ethnicity had lower mean OKS, higher pain and lower QoL. One year post-OP patients with > 12 years education reported higher pain compared to patients with shorter educations. However, the response-rate was low (44.6%), and therefore post-OP results were not considered to be significant.

## CONCLUSION

Minority ethnicity and the duration of education influence preoperative disability and expectation in patients undergoing TKA. This should be taken into account when patients are advised pre-operatively.

**Key words:** Socioeconomic factors; Ethnicity; Education; Expectations to surgery; Preoperative disability; Total knee arthroplasty

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** We investigated whether minority ethnicity and duration of education influence preoperative disability and expectations in patients undergoing total knee arthroplasty. We prospectively included 829 patients scheduled to undergo primary total knee arthroplasty in a single centre. We found that patients of minority ethnicity suffer from more severe preoperative symptoms and expect a poorer post-operative outcome compared to patients of majority ethnicity. We also found that patients with > 12 years education have more severe preoperative symptoms compared to patients with shorter educations. This information can assist surgeons in appropriate treatment plans and preoperative consultation for all patients.

Kudibal MT, Kallemose T, Troelsen A, Husted H, Gromov K. Does ethnicity and education influence preoperative disability

and expectations in patients undergoing total knee arthroplasty? *World J Orthop* 2018; 9(10): 220-228 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i10/220.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i10.220>

## INTRODUCTION

Thousands of patients undergo total knee arthroplasty (TKA) every year worldwide. In recent years, pre-operative (pre-OP) planning and patient information has been streamlined by using the fast-track concept<sup>[1]</sup>. This operation has excellent results in terms of survival, with a reported ten-year prosthetic survival of close to 95% (National Hospital Discharge Survey 2010); however, patient satisfaction remains a challenge, with up to 20% of patients being dissatisfied with their one-year post-operative (post-OP) outcomes<sup>[2,3]</sup>.

Outcome is known to be influenced by patient-related factors that include age, pre-OP symptoms<sup>[4-6]</sup>, comorbidities and mental health status, such as depression and anxiety<sup>[7]</sup>. Previous studies have shown that patient satisfaction can be influenced by both surgery-related factors, such as implant alignment<sup>[8-10]</sup>, implant brand and hospital type<sup>[8]</sup>, as well as patient-related factors including age, pre-OP symptoms and expectations<sup>[2]</sup>. Other less well-defined factors have also been shown to influence outcome following TKA and THA, such as socioeconomic factors<sup>[11,12]</sup> and duration of education<sup>[13]</sup>. Understanding the way that ethnicity and the duration of education influence both pre-OP symptoms and post-OP outcome in TKA patients will assist healthcare providers in determining specific areas of possible improvement and adjusting treatment options appropriately. Furthermore, it will assist in more accurate comparisons of study populations in future research.

The purpose of the study was to investigate whether minority ethnicity and duration of education influence pre-OP disability and expectations in patients undergoing TKA.

## MATERIALS AND METHODS

We conducted a prospective cohort study that included all patients undergoing primary TKA at our institution from April 1<sup>st</sup> 2013 to December 8<sup>th</sup> 2014. Exclusion criteria were simultaneous bilateral TKA and missing data on education/country of origin. Prior to surgery, patients were asked to fill in a questionnaire regarding patient demographics, pre-OP symptoms and expectations about surgery outcome. All patients were asked to fill in another questionnaire one year post-OP *via* email or regular mail, and 370 patients completed a one-year follow-up questionnaire (Figure 1). A clinical control was not conducted. Patients filled in the questionnaire independently or with help from

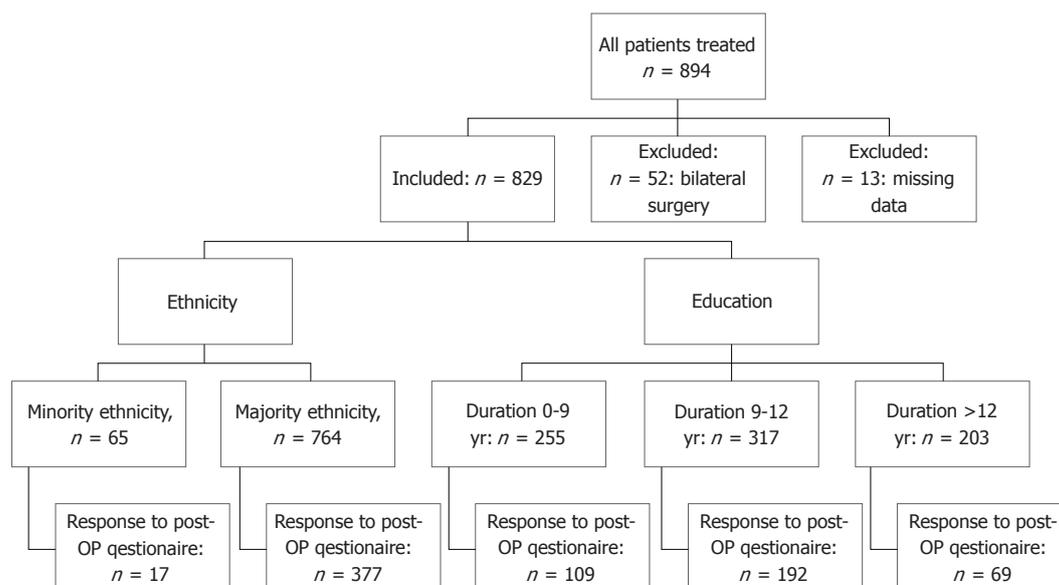


Figure 1 Flowchart of patient distribution.

family members. All surgeries were performed in a standardized fast-track setup<sup>[1]</sup> by experienced surgeons specializing in arthroplasty surgery, each having performed > 100 primary TKAs annually. The standard surgical protocol for TKA includes spinal analgesia, standardized fluid management, use of preoperative intravenous tranexamic acid, preoperative single-shot high-dose methylprednisolone<sup>[14]</sup> and absence of drains. All TKAs were performed with a standard medial parapatellar approach without the use of tourniquet, with an application of local infiltration analgesia (LIA)<sup>[15]</sup> and postoperative compression bandaging<sup>[16]</sup>. Post-operative opioid-sparing pain treatment consisted of celecoxib 200 mg/12 h and paracetamol 1 g/6 h with rescue analgesics [administered if visual analogue scale (VAS) > 50 mm at rest] consisting of 10 mg oral morphine as needed. Physiotherapy was started on the day of surgery and continued until discharge. Rivaroxaban (Bayer, Denmark) was used as oral thromboprophylaxis starting 6 to 8 h postoperatively and continued daily until discharge<sup>[17]</sup>. Mechanical thromboprophylaxis and extended oral thromboprophylaxis were not used. Patients were discharged to their own home upon fulfilling functional discharge criteria<sup>[18]</sup>.

Preoperative disability was measured by Oxford knee score (OKS), self-reported quality of life (QoL)<sup>[19]</sup>, knee pain during activity measured on VAS, and overall symptoms and expectations. OKS ranges from 0 to 48, with lower numbers indicating more severe symptomatic disease. All VAS scales in this study range from 0 to 100. For pain and symptoms, higher values represent the worst conditions, while high values on the scale for QoL represent the best conditions. Patients were stratified based on duration of education and place of birth. Ethnicity was divided into two groups, majority and minority ethnicity. Majority ethnicity was defined

as patients born in Denmark (the study country), and minority ethnicity was defined as all patients born outside Denmark. As the level of education varies between countries, education was stratified based on duration (< 9 years, 9-12 years and > 12 years of education). Preoperatively, we registered baseline-characteristics including alcohol consumption, smoking, BMI and comorbidity. Comorbidity was registered as heart disease, lung disease, previous stroke, kidney disease, liver disease, diabetes and autoimmune disease. We also registered symptoms (OKS, use of walking aids, walking distance, pain on VAS score during rest and activity) self-reported QoL, and expectations for post-OP symptoms and QoL. Finally, we registered self-reported post-OP symptoms and self-reported QoL using the one-year post-op questionnaire.

As all our results are based on patient reported outcome measures, we take into account the minimal clinically important difference (MCID). For OKS, this is acknowledged to be four-five<sup>[20,21]</sup>. For VAS scales in knee arthritis patients, MCID has been reported to be around 20 points<sup>[22]</sup>.

### Statistical analysis

All data were processed in R 3.2.2. All measurements were reported as mean with standard deviation (SD) for continues variables and number with percent for categorical variables. Tests for association of minority ethnicity with continues interest variables was done by *t*-test or for non-normal distributed variables by Wilcoxon sum rank test. Association with categorical interest variables was done by chi-squared or, in cases with expected values below 5, Fishers exact test. Associations between education duration groups and the interest variables were done for continues variables by uni-

**Table 1** Characteristics of the total patient population *n* (%)

	All patients
Baseline characteristics	
BMI (mean ± SD)	29.7 ± 5
Age (mean ± SD)	66.8 ± 10
Gender	
Male	308 (36.6)
Female	534 (63.4)
Smoking	
Non-smoker	492 (58.6)
Former smoker	213 (25.4)
Active smoker	134 (16)
Duration of education	
More than 12 yr	255 (30.8)
9-12 yr	371 (44.8)
0-9 yr	203 (24.5)
Ethnicity	
Born in Denmark	764 (92.2)
Born outside Denmark	65 (7.8)
Preoperative level of function and symptoms	
Walking aid outside the home:	
None	597 (71.2)
One cane	133 (15.9)
Two canes	34 (4.1)
Wheeled walker	69 (8.2)
Do not leave the home	6 (0.7)
Oxford knee score (mean ± SD)	23.6 ± 8
Knee pain during activity <sup>1</sup> , median (range)	63 (0:100)
Quality of life <sup>1</sup> , median (range)	47 (0:100)
Level of symptoms <sup>1</sup> , median (range)	50 (0:100)
Preoperative expectations	
Knee pain 1 yr after surgery <sup>1</sup> , median (range)	2 (0:100)
Quality of life 1 yr post-OP <sup>1</sup> , median (range)	94 (0:100)
Level of symptoms. 1 yr post-OP <sup>1</sup> , median (range)	3 (0:99)

<sup>1</sup>Visual analogue scale 0-100. BMI: Body mass index.

variable linear regression with TYPE III test or Kruskal-Wallis sum rank test for non-normal distributed variables, and for categorical variables chi-square and Fishers exact test. Additionally, to adjust for multiple testing, a Bonferroni correction was done for all *P*-values, and the correction scale was given by the number of tests performed within each outcome group. The adjusted *P*-value was calculated by multiplying the original *P*-values by the given scale. *P* < 0.05 was considered significant.

## RESULTS

We included 894 consecutive and unselected patients undergoing TKA at our institution. The following were excluded: simultaneous bilateral TKA (*n* = 52) and missing data on education/country of origin (*n* = 13), thus leaving 829 patients for analysis.

For the total population, mean ± SD at time of surgery was 66.8 (10) years, 63.4% were female and 764 (92.2%) of patients were of majority ethnicity. Specifically, 24.5% of patients had an education of < 9 years, 44.8% of 9-12 years and 30.8% > 12 years (Table 1). Mean pre-OP OKS (SD) was 23.6 (8). Patients of minority ethnicity were younger compared to patients of majority ethnicity (*P* = 0.045) and had

a shorter education (72.3% had an education of 0-9 years while only 20.4% of patients with majority ethnicity had an education of this length (*P* < 0.001) (Table 2). Patients of minority ethnicity had a lower pre-OP OKS (*P* < 0.005), higher knee pain during activity (*P* < 0.001), and a significantly larger proportion were dependent on a walking aid (*P* = 0.026) (Table 2). Furthermore, this patient group had a significantly lower expectation to their post-OP pain during activity (*P* = 0.016) and overall symptoms (*P* = 0.016). Patients with an education of > 12 years were older at the time of surgery, with a mean age of 67.7 years compared to 64.8 years for patients with an education of 0-9 years (*P* < 0.001). Patients with an education > 12 years reported a lower pre-OP OKS compared to the groups with 9-12 years and < 9 years of education (*P* < 0.001). Concurrent to this, patients with an education > 12 years had a higher pre-OP VAS for knee pain during activity compared to the other groups (*P* = 0.002, expectation measures also differed between the education groups (all *P* ≤ 0.008)). Women composed a higher proportion of the highly educated group, with 73.4% compared to 57.1% and 63.0% in the middle and low education groups, respectively (*P* = 0.003) (Table 3).

Response-rates to the post-OP questionnaire were 44.6% (*n* = 370). We found a higher response-rate for patients of majority ethnicity (46.2% vs 26.2% for minority ethnicity patients). We also found that responders overall had a longer duration of education, the biggest difference seen in education of 0-9 years (29.2% for non-responders vs 18.6% for responders, *P* < 0.001). The differences between responders and non-responders for other parameters was not statistically significant.

Patients of minority ethnicity had significantly lower mean OKS one year post-OP compared with patients of majority ethnicity (*P* = 0.002). Patients of minority ethnicity also reported higher pain during activity (*P* = 0.001), a significantly lower QoL (*P* = 0.001) and significantly higher overall symptom score (*P* = 0.001) compared with patients of majority ethnicity. Although patients of minority ethnicity had higher post-OP pain, we also found a larger difference between pre-OP and post-OP pain compared to patients of majority ethnicity (*P* = 0.049) (Table 2). Patients with educations > 12 years had significantly higher knee pain post-OP (*P* = 0.006), however there was also a larger difference between pre-OP and post-OP pain during activity (*P* = 0.069) and QoL (*P* = 0.017) (Table 3).

## DISCUSSION

In this prospective study, we found that patients of minority ethnicity report more severe pre-OP symptoms (lower OKS and higher overall pain level) and have lower expectations for post-OP outcome compared to patients of majority ethnicity. Patients of minority

**Table 2** Significance of ethnicity *n* (%)

	Majority ethnicity	Minority ethnicity	<i>P</i> value (adjusted)
Baseline characteristics			
BMI (mean ± SD)	29.7 ± 5	29.9 ± 4	0.702 (3.508)
Age (mean ± SD)	67.0 ± 10	64.0 ± 9	0.009 (0.045)
Gender			
Male	294 (37.36)	11 (15.22)	< 0.001 (0.004)
Female	470 (62.64)	54 (84.78)	
Smoking			
Non-smoker	430 (56.3)	55 (84.6)	< 0.001 (< 0.001)
Former smoker	207 (27.1)	4 (6.5)	
Active smoker	127 (16.6)	6 (9.2)	
Duration of education			
More than 12 yr	248 (32.5)	7 (10.8)	< 0.001 (< 0.001)
9-12 yr	369 (47.1)	11 (16.9)	
0-9 yr	156 (20.4)	47 (72.3)	
Preoperative level of function and symptoms			
Walking aid outside the home:			
None	556 (72.8)	34 (52.3)	0.005 (0.026)
One cane	111 (14.9)	20 (30.8)	
Two canes	30 (3.9)	3 (4.6)	
Wheeled walker	61 (8)	8 (12.3)	
Do not leave the home	6 (0.8)	0 (0)	
Oxford knee score (mean ± SD)	23.9 ± 7	18.6 ± 8	< 0.001 (< 0.001)
Knee pain during activity <sup>1</sup> , median (range)	61.0 (0:100)	76 (13:100)	< 0.001 (< 0.001)
Quality of life before surgery <sup>1</sup> , median (range)	47.0 (0:100)	38 (0:100)	0.388 (1.938)
Level of symptoms before surgery <sup>1</sup> , median (range)	50.0 (0:100)	61 (0:100)	0.276 (1.380)
Preoperative expectations			
Expectations to knee pain caused by use of hip 1 yr after surgery <sup>1</sup> , median (range)	2.0 (0:100)	4 (0:99)	0.005 (0.016)
Expectations to quality of life 1 yr after surgery <sup>1</sup> , median (range)	94.0 (0:100)	92 (0:100)	0.296 (0.888)
Expectations to level of symptoms 1 yr after surgery <sup>1</sup> , median (range)	3.0 (0:99)	6 (0:99)	0.005 (0.016)
Postoperative level of function and symptoms:			
Oxford knee score, median (range)	39.0 (3.0:48.0)	24.0 (10.0:47.0)	< 0.001 (0.002)
Knee pain during act <sup>1</sup> , median (range)	18.0 (0.0:100.0)	62.0 (5.0:90.0)	< 0.001 (< 0.001)
Quality of life <sup>1</sup> , median (range)	71.5 (0.0:100.0)	40.0 (0.0:95.0)	< 0.001 (0.001)
Level of symptoms <sup>1</sup> , median (range)	21.0 (0.0:100.0)	62.0 (10.0:90.0)	< 0.001 (0.001)
Difference in outcome parameters:			
Difference in Pain <sup>1</sup> , median (range)	13.0 (90.0:100.0)	47.0 (37.0:90.0)	0.008 (0.0499)
Difference in Quality of life after surgery <sup>1</sup> , median (range)	15.0 (100.0:98.0)	44.0 (99.0:38.0)	0.013 (0.078)
Difference in level of symptoms <sup>1</sup> , median (range)	17 (56.0:100.0)	46.0 (36.0:88.0)	0.299 (1.796)

<sup>1</sup>Visual analogue scale 0-100. BMI: Body mass index.

ethnicity also report more severe symptoms post-OP, however our response rate was too low to regard the results as significant. Patients with an education > 12 years report more severe pre-OP symptoms (OKS and overall pain level) compared to patients with both < 9 years and 9-12 years of education. Post-OP, we found that patients with an education > 12 years reported higher overall pain.

It is generally acknowledged that patient's overall health is associated with socioeconomic factors<sup>[23]</sup>. Recently, Lavernia *et al*<sup>[11]</sup> showed that expectations and the knowledge of prosthetic surgery in patients with knee and hip arthritis depend on ethnicity. The same observation was made by Krupic *et al*<sup>[12]</sup>, who showed that patients born outside of Sweden had a poorer outcome after total hip replacement than patients born within Sweden. This is concurrent with our results, as we find that patients born outside the country have greater preoperative disability (lower OKS and higher VAS for pain). However, the studies describing the

correlations between ethnicity and surgery are few and based on short-term observation.

In general, minority groups in western countries are less likely to undergo knee replacement than their locally-born counterparts<sup>[24-26]</sup>. Our data show that patients of minority ethnicity have lower expectations for surgery and suffer from more severe symptoms pre-OP than patients of majority ethnicity. The reason for this difference is unknown, but we could speculate that patients of minority ethnicity might seek doctors at a more progressed stage of the disease compared to patients of majority ethnicity due to cultural or language barriers. Shahid *et al*<sup>[25]</sup> reports that racial disparities in African Americans compared to Caucasian Americans are caused by patient preferences, patients education/knowledge of osteoarthritis (OA) and expectations for post-OP outcome. Minority Americans were found to have lower expectations of the overall effect of OA surgery and higher expectations of post-OP pain<sup>[24,27-29]</sup>. This supports our findings that patients of minority ethnicity

**Table 3** Significance of duration of education *n* (%)

	Education 0-9 yr	Education 9-12 yr	Education > 12 yr	P value (adjusted)
Baseline characteristics				
BMI, mean ± SD	28.7± 5	30.0 ± 6	30.5 ± 5	< 0.001 (0.007)
Age, mean ± SD	64.8 ± 10	67.8 ± 10	67.7 ± 11	< 0.001 (0.005)
Gender				
Male	92 (36.1)	159 (42.9)	54 (26.6)	< 0.001 (0.003)
Female	163 (63.9)	212 (57.1)	149 (73.4)	
Ethnicity				
Majority ethnicity	248 (97.3)	360 (97)	156 (76.8)	< 0.001 (< 0.001)
Minority ethnicity	7 (2.7)	11 (3)	47 (23.2)	
Smoking:				
Non-smoker	155 (60.8)	207 (55.8)	123 (60.6)	0.003 (0.017)
Former smoker	74 (29)	100 (27)	37 (18.2)	
Active smoker	26 (10.2)	64 (17.3)	43 (21.2)	
Preoperative level of function and symptoms				
Walking aid outside the home				
None	198 (77.6)	273 (73.6)	119 (58.6)	0.005 (0.002)
One cane	35 (13.7)	55 (14.8)	41 (20.2)	
Two canes	11 (4.3)	12 (3.2)	10 (4.9)	
Wheeled walker housebound	10 (3.9)	27 (7.3)	32 (15.8)	
	1 (0.4)	4 (1.1)	1 (0.5)	
Oxford knee score, mean ± SD	24.6 ± 8	23.8 ± 7	21.5 ± 8	< 0.001 (< 0.001)
Knee pain during activity <sup>1</sup> , median (range)	59 (0:99)	63 (0:100)	67 (6:100)	< 0.001 (0.002)
Quality of life before surgery <sup>1</sup> , median (range)	45 (0:100)	47 (0:100)	50 (0:100)	0.634 (3.170)
Level of symptoms before surgery <sup>1</sup> , median (range)	51 (0:100)	50 (0:100)	50 (0:100)	0.634 (3.171)
Preoperative expectations				
Expectations to knee pain caused by use of hip 1 yr after surgery <sup>1</sup> , median (range)	4 (0:95)	2 (0:96)	2 (0:100)	0.003 (0.008)
Expectations to quality of life 1 yr after surgery <sup>1</sup> , median (range)	90 (0:100)	94 (0:100)	96 (0:100)	< 0.001 (0.002)
Expectations to level of symptoms 1 yr after surgery <sup>1</sup> , median (range)	4 (0:82)	2 (0:99)	2 (0:99)	< 0.001 (0.001)
Postoperative level of function and symptoms:				
Oxford knee score, median (range)	40 (8.0:47.0)	37 (3.0:48.0)	37.5 (7.0:48.0)	0.240 (0.960)
Knee pain during activity, Post-OP <sup>1</sup> , median (range)	12 (0.0:90.0)	20 (0.0:100.0)	26 (0.0:97.0)	0.002 (0.006)
Quality of life after surgery <sup>1</sup> , median (range)	77.5 (13.0:98.0)	70 (0.0:100.0)	69 (0.0:100.0)	0.055 (0.219)
Level of symptoms after surgery <sup>1</sup> , median (range)	21 (0.0:94.0)	23 (0.0:100.0)	31 (0.0:95.0)	0.182 (0.728)
Difference in outcome parameters:				
Difference in Pain <sup>1</sup> , median (range)	8 (-11.0:84.0)	15 (-90.0:100.0)	21 (-48.0:97.0)	0.012 (0.069)
Difference in Quality of life Post-OP <sup>1</sup> , median (range)	-7 (-67.0:95.0)	-20 (-100.0:98.0)	-18 (-99.0:98.0)	0.003 (0.017)
Difference in level of symptoms <sup>1</sup> , median (range)	15 (-14.0:89.0)	17 (-56.0:100.0)	18 (-41.0:95.0)	0.532 (3.193)

<sup>1</sup>Visual analogue scale 0-100. BMI: Body mass index.

have lower pre-OP expectations. African Americans have been found to be less knowledgeable regarding OA, to have a lesser understanding of the risks and benefits of surgery compared to White Americans<sup>[30,31]</sup>, and to have a lower preference for surgical treatment<sup>[25]</sup>. This could explain our finding of more severe pre-OP symptoms in patients of minority ethnicity, as patient preference has been associated with referral from GP to orthopaedic evaluation in OA patients<sup>[25]</sup>. Many American-based studies report that minorities are more likely to undergo surgery at low volume hospitals and that this is a cause for poorer outcome. This does not apply in Denmark, as most patients are treated in the public system and all our data are based on patients treated in one high-volume public institution. Severity of pre-OP symptoms has been shown to influence outcome<sup>[4-6]</sup>. Although our post-OP response rate was too low to make any conclusions, we did find that the overall outcome for patients born outside

the country was poorer compared to patients born in the country, which is concurrent with the reportings of Krupic *et al*<sup>[12]</sup>. Similar findings have been reported in American patients, where minorities are reported to have a higher post-OP complication rate, mortality and longer hospital stay compared to white Americans<sup>[25,26]</sup>.

The duration of education is key to how individuals seek and handle information<sup>[32]</sup>, and therefore important with regard to how patients cope with medical treatment. We found that patients with > 12 years of education had more severe pre-OP symptoms than those with shorter educations. This result is not concurrent with findings in previous studies, as these have found more severe symptoms in patients with shorter education; an educational level less than high school in the United States has been associated with greater pre-OP pain and lower function in TKA patients by Lopez-Olivo *et al*<sup>[33]</sup>. Although we found significant *P*-values

for these parameters, the differences of OKS was only three, two and nine on VAS, thus both below MCID and not convincingly clinically-relevant. High education has previously been found to be a predictor for better post-OP outcomes by Greene *et al.*<sup>[13]</sup>, while others report no significance<sup>[34]</sup>. We found that patients with short educations reported a lower post-OP pain severity (MCID below cut-off level), and could find no other significant influence of education on other outcome parameters. Although statistically significant, Greene *et al.*<sup>[13]</sup> also found very small differences that were not clinically relevant. It is thus uncertain whether education can be used as an outcome predictor for TKA patients. Combined with our low response rate, no findings regarding education and post-OP outcome were convincing.

Our study has several limitations, as this is a purely descriptive and hypothesis-generating study. External validation is a major limitation for our study, as both ethnicity and education differ between countries. Education differs greatly across the world; we have, however, tried to accommodate this by dividing patients into three groups based on their number of education years rather than completed degrees. Ethnic minority groups within a country are of course different across the world. In this study, we try to address the issues that arise in healthcare for people born outside their residential country and not the health care behaviour of specific ethnic groups. We believe that our results can contribute to the knowledge base for how to approach racial disparities within a population.

Our results are based on regression analysis, adjusting for patient-related factors such as gender, smoking, alcohol consumption, co-morbidities, symptoms, self-reported QoL and expectations as shown in the Tables. Residual confounders include the missing evaluation of radiologic status/alignment. Surgical factors have been shown to influence patient satisfaction in other studies, and this is unaccounted for in our study; however, all patients were treated by the same high-volume surgeons in a well-defined fast-track setup with standardized treatment for pain, mobilisation and post-OP care, as described in the Methods section<sup>[1]</sup>. All treatments in Denmark are free of charge, and therefore socioeconomic factors do not affect the choice of implant in our population. Only 44.6% of patients responded to our post-OP questionnaire, and response rate was even lower for patients born outside the country (26.2% vs 46.2% for patients born in the country). We therefore make no conclusions regarding significance of either ethnicity or education on post-OP measurements. In this study, we have only evaluated results based on patient-reported outcome measures, and not other outcome measures such as the length of hospital stay, infection rate or other complication rates.

In conclusion, minority ethnicity and duration of education influence pre-OP disability and expectations in patients undergoing TKA. This should be taken into

account when patients are advised pre-operatively.

## ARTICLE HIGHLIGHTS

### Research background

The background, present status, and significance of the study should be described in detail. It is known that patient-related factors, socioeconomic factors and education influence patient outcomes in general, however this area is difficult to investigate and thus these factors are often confounding in scientific work. These factors are also known to be of significance in patients scheduled to undergo total knee arthroplasty (TKA), and this study provides information regarding the significance of education and ethnicity in these patients.

### Research motivation

During recent years, a trend towards optimized care, standardized patient evaluations and fast-track surgery has been influencing orthopaedic surgery. Although beneficial in many ways, this concept may not be appropriate for all patients. Levels of education and ethnicity is known to influence patients, and understanding the significance of these factors in TKA patients will assist healthcare providers in optimizing treatment plans for individual patients.

### Research objectives

The objectives of this study were to determine if level of education and ethnicity influence the preoperative status of patients undergoing primary TKA or patient expectations for surgery. The significance of ethnicity and level of education on outcome following TKA is still uncertain and should be an objective for future research.

### Research methods

We prospectively included 829 patients undergoing TKA. Patients filled in pre-operative questionnaires with information regarding place of birth, duration of education, expectations for outcome of surgery and baseline characteristics. Statistical analyses were performed to identify the significance of ethnicity and level of education.

### Research results

We find that patients undergoing TKA in a country different to where they were born report more severe preoperative symptoms and lower expectations for postoperative outcome. We also found that patients with a longer duration of education report more severe pre-operative symptoms. We found that patients of minority ethnicity and with an education > 12 years had more severe symptoms post-operatively. However, due to a low response rate, we cannot draw generalizable conclusions about these results. The significance of ethnicity and education on post-operative results remain to be sufficiently described.

### Research conclusions

Minority ethnicity and duration of education influence preoperative disability and expectations in patients undergoing TKA. Patients undergoing TKA in a country different to where they were born need individualised evaluation to accommodate potential differences from the general patient population. Patients of minority ethnicity report more severe pre-operative symptoms before undergoing TKA and lower expectations for post-operative outcome. Patients with educations longer than 12 years report more severe symptoms before undergoing TKA. Minority ethnicity and duration of education influence preoperative disability and expectations in patients undergoing TKA. Ethnicity and education influence patients' perception of disease. Socioeconomic factors should be considered when evaluating patients.

### Research perspectives

Our study provides knowledge regarding the significance of ethnicity and education on preoperative disability and expectations of outcome. This information is key for healthcare professionals when evaluating patients prior

to TKA, as it allows for the identification of individuals who may not be suitable for a standardized information regimen. It is important to investigate the significance of socioeconomic factors on outcome following TKA.

## REFERENCES

- 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]
- Bourne RB,** Chesworth BM, Davis AM, Mahomed NN, Charron KD. Patient satisfaction after total knee arthroplasty: who is satisfied and who is not? *Clin Orthop Relat Res* 2010; **468**: 57-63 [PMID: 19844772 DOI: 10.1007/s11999-009-1119-9]
- Klit J,** Jacobsen S, Rosenlund S, Sonne-Holm S, Troelsen A. Total knee arthroplasty in younger patients evaluated by alternative outcome measures. *J Arthroplasty* 2014; **29**: 912-917 [PMID: 24269097 DOI: 10.1016/j.arth.2013.09.035]
- Núñez M,** Núñez E, Segur JM, Maculé F, Sanchez A, Hernández MV, Vilalta C. Health-related quality of life and costs in patients with osteoarthritis on waiting list for total knee replacement. *Osteoarthritis Cartilage* 2007; **15**: 258-265 [PMID: 16962795 DOI: 10.1016/j.joca.2006.07.011]
- Petersen KK,** Simonsen O, Laursen MB, Nielsen TA, Rasmussen S, Arendt-Nielsen L. Chronic postoperative pain after primary and revision total knee arthroplasty. *Clin J Pain* 2015; **31**: 1-6 [PMID: 25485953 DOI: 10.1097/AJP.0000000000000146]
- Sakellariou VI,** Poultsides LA, Ma Y, Bae J, Liu S, Sculco TP. Risk Assessment for Chronic Pain and Patient Satisfaction After Total Knee Arthroplasty. *Orthopedics* 2016; **39**: 55-62 [PMID: 26730683 DOI: 10.3928/01477447-20151228-06]
- Alattas SA,** Smith T, Bhatti M, Wilson-Nunn D, Donell S. Greater pre-operative anxiety, pain and poorer function predict a worse outcome of a total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 3403-3410 [PMID: 27734110 DOI: 10.1007/s00167-016-4314-8]
- Baker PN,** van der Meulen JH, Lewsey J, Gregg PJ; National Joint Registry for England and Wales. The role of pain and function in determining patient satisfaction after total knee replacement. Data from the National Joint Registry for England and Wales. *J Bone Joint Surg Br* 2007; **89**: 893-900 [PMID: 17673581 DOI: 10.1302/0301-620X.89B7.19091]
- Choong PF,** Dowsey MM, Stoney JD. Does accurate anatomical alignment result in better function and quality of life? Comparing conventional and computer-assisted total knee arthroplasty. *J Arthroplasty* 2009; **24**: 560-569 [PMID: 18534397 DOI: 10.1016/j.arth.2008.02.018]
- Longstaff LM,** Sloan K, Stamp N, Scaddan M, Beaver R. Good alignment after total knee arthroplasty leads to faster rehabilitation and better function. *J Arthroplasty* 2009; **24**: 570-578 [PMID: 18534396 DOI: 10.1016/j.arth.2008.03.002]
- Lavernia CJ,** Contreras JS, Parvizi J, Sharkey PF, Barrack R, Rossi MD. Do patient expectations about arthroplasty at initial presentation for hip or knee pain differ by sex and ethnicity? *Clin Orthop Relat Res* 2012; **470**: 2843-2853 [PMID: 22733183 DOI: 10.1007/s11999-012-2431-3]
- Krupic F,** Eisler T, Garellick G, Kärrholm J. Influence of ethnicity and socioeconomic factors on outcome after total hip replacement. *Scand J Caring Sci* 2013; **27**: 139-146 [PMID: 22616899 DOI: 10.1111/j.1471-6712.2012.01013.x]
- Greene ME,** Rolfson O, Nemes S, Gordon M, Malchau H, Garellick G. Education attainment is associated with patient-reported outcomes: findings from the Swedish Hip Arthroplasty Register. *Clin Orthop Relat Res* 2014; **472**: 1868-1876 [PMID: 24549772 DOI: 10.1007/s11999-014-3504-2]
- Bugada D,** Allegri M, Gemma M, Ambrosoli AL, Gazzero G, Chiumento F, Dongu D, Nobili F, Fanelli A, Ferrua P, Berruto M, Cappelleri G. Effects of anaesthesia and analgesia on long-term outcome after total knee replacement: A prospective, observational, multicentre study. *Eur J Anaesthesiol* 2017; **34**: 665-672 [PMID: 28767456 DOI: 10.1093/bja/aeq333]
- Andersen LØ,** Husted H, Otte KS, Kristensen BB, Kehlet H. High-volume infiltration analgesia in total knee arthroplasty: a randomized, double-blind, placebo-controlled trial. *Acta Anaesthesiol Scand* 2008; **52**: 1331-1335 [PMID: 19025523 DOI: 10.1111/j.1399-6576.2008.01777.x]
- 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]
- Jørgensen CC,** Jacobsen MK, Soeballe K, Hansen TB, Husted H, Kjærsgaard-Andersen P, Hansen LT, Laursen MB, Kehlet H. Thromboprophylaxis only during hospitalisation in fast-track hip and knee arthroplasty, a prospective cohort study. *BMJ Open* 2013; **3**: e003965 [PMID: 24334158 DOI: 10.1136/bmjopen-2013-003965]
- Husted H,** Lunn TH, Troelsen A, Gaarn-Larsen L, Kristensen BB, Kehlet H. Why still in hospital after fast-track hip and knee arthroplasty? *Acta Orthop* 2011; **82**: 679-684 [PMID: 22066560 DOI: 10.3109/17453674.2011.636682]
- Berliner JL,** Brodke DJ, Chan V, SooHoo NF, Bozic KJ. Can Preoperative Patient-reported Outcome Measures Be Used to Predict Meaningful Improvement in Function After TKA? *Clin Orthop Relat Res* 2017; **475**: 149-157 [PMID: 26956248 DOI: 10.1007/s11999-016-4770-y]
- Clement ND,** MacDonald D, Simpson AH. The minimal clinically important difference in the Oxford knee score and Short Form 12 score after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 1933-1939 [PMID: 24253376 DOI: 10.1007/s00167-013-2776-5]
- Beard DJ,** Harris K, Dawson J, Doll H, Murray DW, Carr AJ, Price AJ. Meaningful changes for the Oxford hip and knee scores after joint replacement surgery. *J Clin Epidemiol* 2015; **68**: 73-79 [PMID: 25441700 DOI: 10.1016/j.jclinepi.2014.08.009]
- Tubach F,** Ravaut P, Baron G, Falissard B, Logeart I, Bellamy N, Bombardier C, Felson D, Hochberg M, van der Heijde D, Dougados M. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. *Ann Rheum Dis* 2005; **64**: 29-33 [PMID: 15208174 DOI: 10.1136/ard.2004.022905]
- Costa-Font J,** Hernández-Quevedo C. Measuring inequalities in health: what do we know? What do we need to know? *Health Policy* 2012; **106**: 195-206 [PMID: 22607941 DOI: 10.1016/j.healthpol.2012.04.007]
- Katz JN.** Persistence of Racial and Ethnic Differences in Utilization and Adverse Outcomes of Total Joint Replacement. *J Bone Joint Surg Am* 2016; **98**: 1241-1242 [PMID: 27489313 DOI: 10.2106/JBJS.16.00623]
- Shahid H,** Singh JA. Racial/Ethnic Disparity in Rates and Outcomes of Total Joint Arthroplasty. *Curr Rheumatol Rep* 2016; **18**: 20 [PMID: 26984804 DOI: 10.1007/s11926-016-0570-3]
- Zhang W,** Lyman S, Boutin-Foster C, Parks ML, Pan TJ, Lan A, Ma Y. Racial and Ethnic Disparities in Utilization Rate, Hospital Volume, and Perioperative Outcomes After Total Knee Arthroplasty. *J Bone Joint Surg Am* 2016; **98**: 1243-1252 [PMID: 27489314 DOI: 10.2106/JBJS.15.01009]
- Groeneveld PW,** Kwok CK, Mor MK, Appelt CJ, Geng M, Gutierrez JC, Wessel DS, Ibrahim SA. Racial differences in expectations of joint replacement surgery outcomes. *Arthritis Rheum* 2008; **59**: 730-737 [PMID: 18438917 DOI: 10.1002/art.23565]
- Lavernia CJ,** Alcerro JC, Rossi MD. Fear in arthroplasty surgery: the role of race. *Clin Orthop Relat Res* 2010; **468**: 547-554 [PMID: 19763716 DOI: 10.1007/s11999-009-1101-6]
- Weng HH,** Kaplan RM, Boscardin WJ, Maclean CH, Lee IY, Chen W, Fitzgerald JD. Development of a decision aid to address racial disparities in utilization of knee replacement surgery. *Arthritis Rheum* 2007; **57**: 568-575 [PMID: 17471558 DOI: 10.1002/art.22670]
- Figaro MK,** Williams-Russo P, Allegante JP. Expectation and outlook: the impact of patient preference on arthritis care among African Americans. *J Ambul Care Manage* 2005; **28**: 41-48 [PMID: 15682960 DOI: 10.1097/00004479-200501000-00006]

- 31 **Ibrahim SA**. Racial and ethnic disparities in hip and knee joint replacement: a review of research in the Veterans Affairs Health Care System. *J Am Acad Orthop Surg* 2007; **15** Suppl 1: S87-S94 [PMID: 17766799 DOI: 10.5435/00124635-200700001-00019]
- 32 **Hankins FH**, American Sociological Association. WC-L, American Sociological Society. American Sociological Review. Vol 60. American Sociological Society; 1995
- 33 **Lopez-Olivo MA**, Landon GC, Siff SJ, Edelstein D, Pak C, Kallen MA, Stanley M, Zhang H, Robinson KC, Suarez-Almazor ME. Psychosocial determinants of outcomes in knee replacement. *Ann Rheum Dis* 2011; **70**: 1775-1781 [PMID: 21791452 DOI: 10.1136/ard.2010.146423]
- 34 **Noiseux NO**, Callaghan JJ, Clark CR, Zimmerman MB, Sluka KA, Raket BA. Preoperative predictors of pain following total knee arthroplasty. *J Arthroplasty* 2014; **29**: 1383-1387 [PMID: 24630598 DOI: 10.1016/j.arth.2014.01.034]

**P- Reviewer:** Lin JA, Surace MF **S- Editor:** Cui LJ  
**L- Editor:** Filipodia **E- Editor:** Song H



## Total knee arthroplasty in patients with Paget's disease of bone: A systematic review

Ravi Popat, Konstantinos Tsitskaris, Steven Millington, Sebastian Dawson-Bowling, Sammy A Hanna

Ravi Popat, Department of Trauma and Orthopaedic Surgery, the Hillingdon Hospitals NHS Foundation Trust, Uxbridge UB8 3NN, United Kingdom

Konstantinos Tsitskaris, Steven Millington, Sebastian Dawson-Bowling, Sammy A Hanna, Department of Trauma and Orthopaedic Surgery, Barts Health NHS Trust, London E1 1BB, United Kingdom

ORCID number: Ravi Popat (0000-0002-2385-651X); Konstantinos Tsitskaris (0000-0002-5062-4255); Steven Millington (0000-0001-5143-3074); Sebastian Dawson-Bowling (0000-0002-0756-9238); Sammy A Hanna (0000-0001-7381-701X).

**Author contributions:** Popat R and Tsitskaris K designed the research, performed the research and analysed the data; Popat R, Tsitskaris K and Hanna SA wrote the paper; Dawson-Bowling S and Millington S supervised the paper; all authors read and approved the final manuscript.

**Conflict-of-interest statement:** All the authors declare that they have no competing interests

**PRISMA 2009 Checklist statement:** The guidelines of the PRISMA 2009 statement have been adopted.

**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:** Ravi Popat, MBBS, Doctor, Specialist Registrar, Department of Trauma and Orthopaedic Surgery, the Hillingdon Hospitals NHS Foundation Trust, Pield Heath Road, Uxbridge UB8 3NN, United Kingdom. [r.popat14@imperial.ac.uk](mailto:r.popat14@imperial.ac.uk)  
Telephone: +44-798-5694033

Received: April 19, 2018

Peer-review started: April 19, 2018

First decision: June 15, 2018

Revised: June 28, 2018

Accepted: July 10, 2018

Article in press: July 10, 2018

Published online: October 18, 2018

### Abstract

#### AIM

To determine the functional outcomes, complications and revision rates following total knee arthroplasty (TKA) in patients with Paget's disease of bone (PDB).

#### METHODS

A systematic review of the literature was performed. Four studies with a total of 54 TKAs were included for analysis. Functional outcomes, pain scores, complications and revision rates were assessed. The mean age was 72.0 years and the mean follow-up was 7.5 years.

#### RESULTS

All studies reported significant improvement in knee function and pain scores following TKA. There were 2 cases of aseptic loosening, with one patient requiring revision of the femoral component 10 years after the index procedure. Malalignment, bone loss, soft tissue contractures were the most commonly reported intra-operative challenges. There were five cases (9%) that were complicated by intra-operative patellar tendon avulsion.

#### CONCLUSION

The findings support the use of TKA in patients with PDB. The post-operative functional outcomes are largely similar to other patients, however there are specific perioperative challenges that have been highlighted, in particular the high risk for patellar tendon avulsion.

**Key words:** Total knee arthroplasty; Paget's disease of

bone; Revision; Loosening; Paget's disease

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Patients with Paget's disease of the bone commonly develop significant mal-alignment, structural bone deformities and soft tissue contractures, making total knee arthroplasty (TKA) in this patient group challenging. In addition, exposure of the knee joint can prove particularly difficult, with this review demonstrating a high incidence of patella tendon avulsion. This systematic review has demonstrated that TKA improves pain and functional outcomes in patients with Paget's disease of the bone. The rate of loosening and revision in this patient group appears comparable to other patients undergoing TKA.

Popat R, Tsitskaris K, Millington S, Dawson-Bowling S, Hanna SA. Total knee arthroplasty in patients with Paget's disease of bone: A systematic review. *World J Orthop* 2018; 9(10): 229-234 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i10/229.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i10.229>

## INTRODUCTION

Sir James Paget first described Paget's disease of bone (PDB) as "osteitis deformans" in 1877<sup>[1]</sup>. PDB is a bone disorder that typically manifests in middle-aged patients and affects approximately 2%-4% of people older than 40 years. It is a chronic affliction of adult bone, which undergoes aggressive osteoclast-mediated bone resorption, followed by abnormal osteoblast-mediated bone repair<sup>[2]</sup>.

Although the exact etiology is still unknown, PDB is thought to result from a viral infection in genetically predisposed individuals<sup>[3]</sup>. The disease process evolves through three distinct phases. Initially, there is an osteolytic phase with a collection of destructive osteoclasts spreading to encompass the entire bone. This is followed by a mixed osteolytic and osteoblastic phase, and finally by the osteoblastic or sclerotic phase<sup>[4]</sup>. This process results in bone that is mechanically weaker, larger, less compact, more vascular and more susceptible to fracture than normal adult lamellar bone<sup>[3]</sup>.

PDB is slightly more common in men and more prevalent in Europe, North America and Australasia<sup>[5,6]</sup>. It can affect any bone but is most commonly found in the pelvis, skull, lumbosacral spine, femur or tibia, and is polyostotic in 75% of cases<sup>[7]</sup>.

PDB is usually asymptomatic and only 5%-10% of patients with the disease experience any symptoms, most commonly poorly localized bone pain. Patients may also present with bone deformity, fracture, skin temperature changes, or neurological complications<sup>[8]</sup>. Concurrent symptomatic osteoarthritis of the knee affects 10%-12% of individuals with PDB<sup>[8]</sup>. Differ-

entiating the pain of PDB from osteoarthritis of the knee joint can be challenging as both can give a dull ache that may worsen with weight bearing<sup>[2]</sup>. An intra-articular injection with local anaesthetic can help solve the diagnostic conundrum, as relief of the symptoms would suggest osteoarthritis as the source of pain. Similarly, pain due to PDB can be improved with medication, such as bisphosphonates and calcitonin, further assisting in clarifying the diagnosis.

The non-operative management of osteoarthritis in patients with PDB involves activity and lifestyle modifications, physical therapy, analgesics, functional bracing and anti-Paget's medication. If these fail to alleviate the pain, surgical intervention in the form of total knee arthroplasty (TKA) is indicated. The disease process characterized by bone expansion, softening, cortical thickening and hypervascularity can lead to sclerotic bone, deformity and soft tissue contractures around the knee joint<sup>[9]</sup>. Marked bone loss and large bone cysts have also been described. These morphological changes can present specific technical challenges when performing TKA in patients with PDB.

With the number of TKAs performed each year growing rapidly, there is a high likelihood that arthroplasty surgeons will increasingly need to perform TKA in patients with PDB. Understanding the challenges associated with this group of patients is, hence, very important. We have, therefore, performed a systematic review of the literature to determine the functional outcomes, failure rates and complication rates of TKA in patients with PDB of the knee.

## MATERIALS AND METHODS

### Search strategy

A search of Medline and EMBASE was performed on 01/03/2018. The keywords used for the searches were "total knee arthroplasty" or "total knee replacement" and "Paget's disease". All relevant studies in the English literature describing the results of TKA in patients with PDB, between 1986 and 2017, were identified in accordance with the PRISMA statement. We also identified relevant studies or reviews by assessing the bibliographies of all papers that were included.

### Eligibility criteria

All papers that described the results of TKA in patients with PDB published in the English language were included. All the articles adhered to the PICO Criteria for systematic reviews (Population, Intervention, Comparison and Outcomes).

### Data extraction

One reviewer (Ravi Popat) scrutinised the articles and collected the data using a standardised data collection form. All information relating to the number of patients, their demographics, follow-up period, complications, revision rates and functional outcomes were entered in a spreadsheet. Another reviewer (KT) checked the accuracy

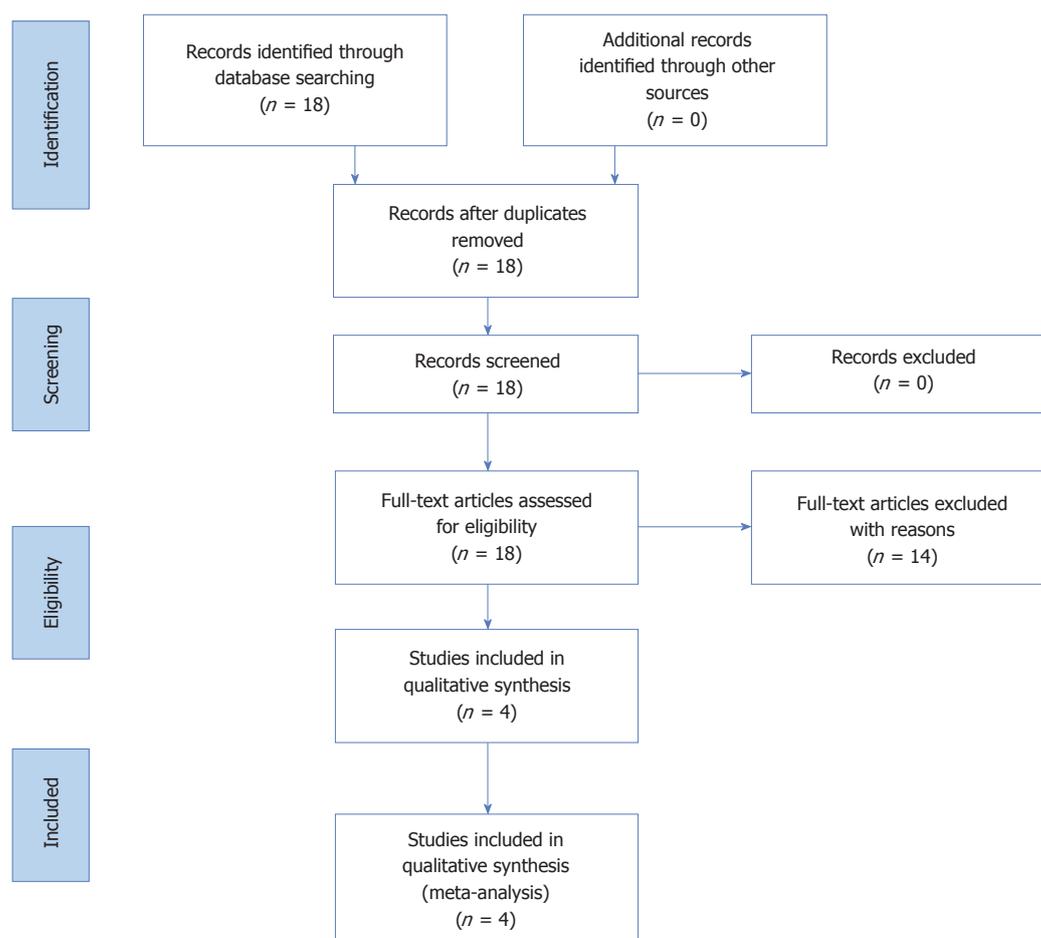


Figure 1 PRISMA flowchart illustrating the search strategy and number of records screened and included.

of the data collection. There were no inconsistent results.

### Statistical analysis

The results were summarized using descriptive statistics for continuous variables, and frequencies and percentages for categorical variables. Microsoft Excel, 2016 version (Microsoft Corporation, Redmond, Washington) was used for data analysis.

## RESULTS

### Search results

The literature search identified 18 articles. The full text of each article was reviewed. A total of 4 studies satisfied the eligibility criteria. Figure 1 outlines the search strategy.

### Quality assessment

All studies were small to medium retrospective case series ( $n = 7-21$  patients) describing the outcome of TKA in patients with PDB. The range of follow-up in these studies was from 2 to 20 years.

### Cohort characteristics

The studies included 54 TKAs performed in patients with

PDB. These patients had a mean age of 72 years (range, 57-86 years) with an average follow-up of 7.5 years (range, 2-20 years). Table 1 summarises the patient demographics.

### Outcome analysis

**Functional outcome:** All the studies reported improvement in knee function following TKA. Two studies reported a pre and post-operative comparison of the Knee Society Score (KSS) and demonstrated an average improvement of 42 points post-operatively<sup>[8,10]</sup>. Schai *et al*<sup>[11]</sup> provided post-operative functional scores only, with a mean of 62.

**Pain outcome:** All the studies reported an improvement in pain scores post-operatively. Two studies demonstrated an average improvement of 46 points post-operatively<sup>[8,10]</sup>. The average pain score for patients in Schai *et al*<sup>[11]</sup> was 83. Five out of 7 patients in the cohort from Broberg *et al*<sup>[12]</sup> reported no post-operative pain. The remaining patients reported mild pain.

### Aseptic loosening and revision

There were 2 cases of aseptic loosening out of a total of 54 cases. There was one revision of the femoral

**Table 1 Demographics of the patients included in the studies and a summary of the results**

Ref.	No. of knees	Age (yr)	Follow up (yr)	Complications	Revision rate	Functional outcomes
Lee <i>et al</i> <sup>[10]</sup> , 2005, United States	21	71 (57-85)	9 (2-20)	Patellar tendon avulsion (3/21)	1 (4.8%)	Knee Society Pain Score 41 to 87
Gabel <i>et al</i> <sup>[8]</sup> , 1991, United States	15	72 (61-85)	7 (2-15)	Aseptic loosening (1/15) Patella tendon avulsion (1/16) Femoral notching (2/21)	0	Knee Society Pain Score 42 to 88 Knee Society Functional Score 33 to 86
Schai <i>et al</i> <sup>[11]</sup> , 1999, United States	11	75 (59-86)	5.7 (2-16)	Patellar tendon avulsion (1/11) Necrosis of patella (1/11)	0	Knee Society Pain Score 83 (post-op only) Knee Society Functional Score 62 (post-op only)
Broberg <i>et al</i> <sup>[12]</sup> , 1986, United States	7	71 (66-85)	6.6 (3-12)	Partial patellar tendon avulsion (1/7)	0	No pain - 5 Mild Pain - 2 (post-operatively)

component, 10 years after the index procedure.

**Patellar tendon avulsion**

Difficulties during the surgical approach, soft tissue contractures and thickening of the patellar tendon were described in all studies. A total of 5 out of 54 patients (9.3%) had patellar tendon avulsion intra-operatively.

**DISCUSSION**

TKA has been shown to be a generally successful procedure in patients with PDB. All the studies that were included in this systematic review reported a post-operative improvement in knee function and pain scores. Furthermore, the overall rate of aseptic loosening was 3.7% in 7.5 years, and the revision rate was 1.85%, with one revision of the femoral component 10 years after the index procedure. This failure rate is comparable to other patients undergoing TKA. According to the most up to date report of the National Joint Registry, a revision rate of 1.85% at 7.5 years is considered reasonable<sup>[13]</sup>.

The overall reported incidence of patellar tendon avulsion was 9.3%. This is an extraordinarily high incidence for this complication and surgeons undertaking TKA in the context of PDB should be aware of interventions that can help prevent it. We are discussing such interventions in a dedicated paragraph later in this review. Conversely, although the incidence of heterotopic bone (HO) formation has been reported to be as high as 46% following total hip arthroplasty for PDB, HO does not appear to be a concern following TKA<sup>[14]</sup>.

The studies included in this review reported on a variety of TKA implants with variable levels of constraint. Some of these implants are also historical. Due to the small number of cases and the wide variation of implant type and constraint, further analysis of potential subgroups, such as cruciate retaining vs posterior stabilised, or cemented vs uncemented, was not feasible.

The main challenges when performing TKA in the context of PDB are malalignment (more commonly varus), extensive bone loss, soft tissue contractures and thickening of the patellar tendon. With the steadily increasing number of TKAs performed annually, it is reasonable to expect that there will be a proportional increase in the burden of PDB cases. It is, therefore,

important to employ a systematic approach in order to ensure optimal outcomes.

**Per-operative considerations**

Initially, it is very important to isolate articular pain from the deep and aching pain that is associated with the later stages of Paget's disease. The use of intra-articular injections can help to identify and delineate whether the patient's pain is from an intra-articular source, providing greater certainty that an arthroplasty procedure will alleviate the patient's symptoms.

Good quality, full-length radiographs are recommended to establish the type of alignment of the affected limb and to assist in pre-operative planning. Long leg views can also identify potential deformity in the femur, which needs to be considered when using intra-medullary cutting guides. The use of CT scans has grown in popularity in the last two decades and can display information related to bony morphology that is not available on plain radiographs.

Pre-operative assessment and optimisation of haemoglobin and cardiac function is recommended. The hypervascularity of pagetoid bone means that these patients are in a high cardiac output state, which can have implications for the anaesthetic intervention. The use of bisphosphonates or calcitonin can reduce the disease activity and theoretically reduce blood loss, however, this has not been established. Pre-operative autologous blood donations may also be considered.

**Intra-operative considerations**

The morphological changes that occur in bones affected by PDB may require intra-operative adaptations and pre-emptive precautionary measures. PDB around the knee is characterised by enlarged bones and correspondingly larger joint surfaces. A size mismatch between the femoral and tibial components is often encountered, especially in cases where there is isolated involvement of either the tibia or the femur. Additionally, the arthritic changes may be more pronounced, with extensive bone loss, large bone cysts and tight collateral ligaments<sup>[8,11]</sup>.

Exposure of the knee joint can prove particularly challenging because of joint stiffness, particularly in case of thickening of the patellar tendon. Patellar eversion can result in avulsion of the patellar tendon and this

was described as a complication in 5 out of 54 patients. Schai *et al.*<sup>[11]</sup> recommended that the patellar preparation should be performed early during the procedure to allow for improved exposure. Vail and Callaghan<sup>[14]</sup> also advised for early patellar preparation, but also performed lateral releases to help achieve adequate exposure. Pre-emptive measures to protect the patellar tendon insertion are essential, especially in cases where there is pagetoid involvement of the tibial tuberosity.

Significant varus or valgus malalignment in this patient group presents challenges both due to the respective bone loss and in achieving optimal soft tissue balancing. Extensive medial or lateral releases may be required in order to achieve adequate exposure as well as to help balance the joint, although the latter may not be feasible with low-constraint implants.

Disease-involvement of the femur, especially in the context of increased varus angulation of the distal femur can present a challenge when intra-medullary guides are used to plan the distal femoral cuts<sup>[15]</sup>. It has been previously reported that intramedullary guidance may lead to mal-positioning of the femoral components. It has been recommended that extra-medullary guides are preferable for the preparation of both the femur and tibia<sup>[8]</sup>.

On the tibial side, there can be significant anterior tibial bowing and the use of an extra-medullar tibial cutting guide may lead to excessive bone loss. In order to preserve tibial bone, Gabel *et al.*<sup>[8]</sup> have recommended utilising a tibial cutting guide with 10 degrees of posterior slope and then using a flat tibial component.

Hard sclerotic bone can often be found in the proximal tibia and the use of a tibial punch during preparation of the bone may lead to fractures. It has been recommended that a high-speed burr should be utilised for the preparation of the proximal tibia, instead of a tibial punch<sup>[16]</sup>. Additionally, the presence of sclerotic bone and its tendency to bleed, may have a bearing on cement interdigitation.

Due to bone hypervascularity and the high cardiac output state present in many of these patients, the use of tranexamic acid and blood salvage techniques should be considered.

### Post-operative considerations

Bisphosphonate therapy should continue if disease activity is high (as measured using ALP levels). The main limitation of this review is that it included largely historical studies. Three of the papers were published in the 20<sup>th</sup> century and the fourth more than a decade ago. Nevertheless, the overall results were still favourable. With the number of arthroplasty procedures performed each year increasing rapidly, and with PDB being relatively common, we feel that this review is relevant to current and future clinical practice.

The findings of this review support the use of TKA to alleviate the functional limitation and pain due to osteoarthritis in patients with PDB. Post-operative pain

relief and functional improvement appear to be significant and comparable to other patients. Surgeons that treat this unique group of patients need to be aware of the particular challenges and interventions that are essential for optimal outcomes.

## ARTICLE HIGHLIGHTS

### Research background

Paget's disease of bone (PDB) affects approximately 2%-4% of people older than 40 years. With an ageing population and the number of TKAs performed each year growing rapidly, there is a high likelihood that arthroplasty surgeons will need to perform total knee arthroplasty (TKA) in patients with PDB.

### Research motivation

Patients with PDB can develop significant mal-alignment, structural bone deformities and soft tissue contractures. Understanding the problems and challenges associated with performing TKA in patient with PDB is key to achieving successful outcomes.

### Research objectives

To aid appropriate consenting of patients and to assist surgeons in achieving the best outcomes for their patients, it is important to understand the outcomes that have previously been achieved following TKA in patients with PDB.

### Research methods

A systematic review of the literature was performed. A total of 54 TKAs were included for analysis. Functional outcomes, pain scores, complications and revision rates were assessed.

### Research results

All studies demonstrated a substantial improvement in function and pain following TKA in patients with PDB. The mean follow-up was 7.5 years. There were two cases of aseptic loosening, with one patient requiring a revision TKA at 10 years. Five cases (9%) of intra-operative patellar tendon avulsion were reported, suggesting that exposure of the knee joint in patient with PDB can be particularly challenging.

### Research conclusions

This systematic review supports the use of TKA to improve function and alleviate pain in patients with Paget's disease around their knee joints. The post-operative functional outcomes appear to be similar to those experienced by patients that do not have PDB. At an average of 7.5 years follow-up, implant survival appears comparable with patients that receive TKA for primary OA. Pain scores also improve substantially in this patient group. Morphological changes that occur secondary to PDB, may require intra-operative adaptations and a high rate of patella tendon avulsion (9%) suggests additional care needs to be taken when gaining access to the knee joint, especially in case where there is Pagetoid involvement of the patella/tibial tuberosity.

### Research perspectives

Surgeons treating patients with PDB need to be aware of the particular challenges posed by this patient group, with intra-operative adaptations potentially required to avoid complications. Further studies that compare functional, pain and revision outcomes in patient with PDB around the knee, against a matched control group, with the use of modern TKA implants, will provide further information about the results that can be expected in this patient group.

## REFERENCES

- 1 **Paget J.** On a Form of Chronic Inflammation of Bones (Osteitis Deformans). *Med Chir Trans* 1877; **60**: 37-64.9 [PMID: 20896492]
- 2 **Whyte MP.** Clinical practice. Paget's disease of bone. *N Engl J Med* 2006; **355**: 593-600 [PMID: 16899779 DOI: 10.1056/NEJMc060278]

- 3 **Rebel A**, Basle M, Poupard A, Malkani K, Filmon R, Lepatezour A. Towards a viral etiology for Paget's disease of bone. *Metab Bone Dis Relat Res* 1981; **3**: 235-238 [PMID: 6762481 DOI: 10.1016/0221-8747(81)90038-2]
- 4 **Lander PH**, Hadjipavlou AG. A dynamic classification of Paget's disease. *J Bone Joint Surg Br* 1986; **68**: 431-438 [PMID: 2942548 DOI: 10.1302/0301-620X.68B3.2942548]
- 5 **Doyle T**, Gunn J, Anderson G, Gill M, Cundy T. Paget's disease in New Zealand: evidence for declining prevalence. *Bone* 2002; **31**: 616-619 [PMID: 12477577 DOI: 10.1016/S8756-3282(02)00876-1]
- 6 **van Staa TP**, Selby P, Leufkens HG, Lyles K, Sprafka JM, Cooper C. Incidence and natural history of Paget's disease of bone in England and Wales. *J Bone Miner Res* 2002; **17**: 465-471 [PMID: 11878305 DOI: 10.1359/jbmr.2002.17.3.465]
- 7 **Kanis JA**. Pathophysiology and treatment of Paget's disease of bone. 2<sup>nd</sup> ed. London: Martin Dunitz, 1998: 310
- 8 **Gabel GT**, Rand JA, Sim FH. Total knee arthroplasty for osteoarthritis in patients who have Paget disease of bone at the knee. *J Bone Joint Surg Am* 1991; **73**: 739-744 [PMID: 2045399 DOI: 10.2106/00004623-199173050-00013]
- 9 **Smith SE**, Murphey MD, Motamedi K, Mulligan ME, Resnik CS, Gannon FH. From the archives of the AFIP. Radiologic spectrum of Paget disease of bone and its complications with pathologic correlation. *Radiographics* 2002; **22**: 1191-1216 [PMID: 12235348 DOI: 10.1148/radiographics.22.5.g02se281191]
- 10 **Lee GC**, Sanchez-Sotelo J, Berry DJ. Total knee arthroplasty in patients with Paget's disease of bone at the knee. *J Arthroplasty* 2005; **20**: 689-693 [PMID: 16139702 DOI: 10.1016/j.arth.2004.11.007]
- 11 **Schai PA**, Scott RD, Younger AS. Total knee arthroplasty in Paget's disease: technical problems and results. *Orthopedics* 1999; **22**: 21-25 [PMID: 9925194]
- 12 **Broberg MA**, Cass JR. Total knee arthroplasty in Paget's disease of the knee. *J Arthroplasty* 1986; **1**: 139-142 [PMID: 3559582 DOI: 10.1016/S0883-5403(86)80052-3]
- 13 **National Joint Registry Annual Report**. National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. Available from: URL: <http://www-new.njrcentre.org.uk/njrcentre/Home/tabid/36/Default.aspx>
- 14 **Vail TP**, Callaghan JJ. Total knee replacement with patella magna and pagetoid patella. *Orthopedics* 1995; **18**: 1174-1177 [PMID: 8749297]
- 15 **Parvizi J**, Klein GR, Sim FH. Surgical management of Paget's disease of bone. *J Bone Miner Res* 2006; **21** Suppl 2: P75-P82 [PMID: 17229013 DOI: 10.1359/jbmr.06s214]
- 16 **Cameron HU**. Total knee replacement in Paget's disease. *Orthop Rev* 1989; **18**: 206-208 [PMID: 2927959]

**P- Reviewer:** Angoules A, Drosos GI, Georgiev GPP

**S- Editor:** Ji FF **L- Editor:** A **E- Editor:** Song H





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 November 18; 9(11): 235-284



**EDITORIAL**

- 235 Hip hemi-arthroplasty for neck of femur fracture: What is the current evidence?  
*Robertson GA, Wood AM*

**REVIEW**

- 245 Biomechanics of posterior shoulder instability - current knowledge and literature review  
*Bäcker HC, Galle SE, Maniglio M, Rosenwasser MP*

**MINIREVIEWS**

- 255 Recently highlighted nutraceuticals for preventive management of osteoarthritis  
*Ravalli S, Szychlinska MA, Leonardi RM, Musumeci G*

**SYSTEMATIC REVIEW**

- 262 Should antibiotics be administered before arthroscopic knee surgery? A systematic review of the literature  
*Carney J, Heckmann N, Mayer EN, Alluri RK, Vangsness Jr. CT, Hatch III GF, Weber AE*
- 271 Analysis of a ten step protocol to decrease postoperative spinal wound infections  
*Elgafy H, Raberding CJ, Mooney ML, Andrews KA, Duggan JM*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Achim Elfering, PhD, Professor, Department of Work and Organizational Psychology, University of Bern, Bern 3012, Switzerland

**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 abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), China National Knowledge Infrastructure (CNKI), and Superstar Journals Database.

**EDITORS FOR THIS ISSUE**

**Responsible Assistant Editor:** *Xiang Li*  
**Responsible Electronic Editor:** *Yun-XiaoJian Wu*  
**Proofing Editor-in-Chief:** *Lian-Sheng Ma*

**Responsible Science Editor:** *Ying Dou*  
**Proofing Editorial Office Director:** *Jin-Lei Wang*

**NAME OF JOURNAL**  
*World Journal of Orthopedics*

**ISSN**  
 ISSN 2218-5836 (online)

**LAUNCH DATE**  
 November 18, 2010

**FREQUENCY**  
 Monthly

**EDITOR-IN-CHIEF**  
**Bao-Gan Peng, MD, PhD, Professor**, Department of Spinal Surgery, General Hospital of Armed Police Force, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com/2218-5836/editorialboard.htm>

**EDITORIAL OFFICE**  
 Jin-Lei Wang, Director

*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f0publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f0publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 November 18, 2018

**COPYRIGHT**  
 © 2018 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.f0publishing.com>

## Hip hemi-arthroplasty for neck of femur fracture: What is the current evidence?

Greg AJ Robertson, Alexander M Wood

Greg AJ Robertson, Edinburgh Orthopaedic Trauma Unit, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh, Scotland EH16 4SA, United Kingdom

Alexander M Wood, Orthopaedic Department, Leeds General Infirmary, Great George St, Leeds LS1 3EX, United Kingdom

ORCID number: Greg AJ Robertson (0000-0002-9152-7144); Alexander M Wood (0000-0001-7917-7498).

Author contributions: Robertson GA and Wood AM wrote and edited the manuscript.

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: Greg AJ Robertson, BSc, MBChB, MSc, Surgeon, Edinburgh Orthopaedic Trauma Unit, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh, Scotland EH16 4SA, United Kingdom. [greg\\_robertson@live.co.uk](mailto:greg_robertson@live.co.uk)  
Telephone: +44-131-2423545  
Fax: +44-131-2423541

Received: July 10, 2018

Peer-review started: July 10, 2018

First decision: July 31, 2018

Revised: August 7, 2018

Accepted: October 9, 2018

Article in press: October 9, 2018

Published online: November 18, 2018

### Abstract

This editorial reviews and summarises the current

evidence (meta-analyses and Cochrane reviews) relating to the use of hip hemi-arthroplasty for neck of femur fractures. Regarding the optimal surgical approach, two recent meta-analyses have found that posterior approaches are associated with: higher rates of dislocation compared to lateral and anterior approaches; and higher rates of re-operation compared to lateral approaches. Posterior approaches should therefore be avoided when performing hip hemi-arthroplasty procedures. Assessing the optimal prosthesis head component, three recent meta-analyses and one Cochrane review have found that while unipolar hemi-arthroplasty can be associated with increased rates of acetabular erosion at short-term follow-up (up to 1 year), there is no significant difference between the unipolar hemi-arthroplasty and bipolar hemi-arthroplasty for surgical outcome, complication profile, functional outcome and acetabular erosion rates at longer-term follow-up (2 to 4 years). With bipolar hemi-arthroplasty being the more expensive prosthesis, unipolar hemi-arthroplasty is the recommended option. With regards to the optimal femoral stem insertion technique, three recent meta-analyses and one Cochrane Review have found that, while cemented hip hemi-arthroplasties are associated with a longer operative time compared to uncemented Hip Hemi-arthroplasties, cemented prostheses have lower rates of implant-related complications (particularly peri-prosthetic femoral fracture) and improved post-operative outcome regarding residual thigh pain and mobility. With no significant difference found between the two techniques for medical complications and mortality, cemented hip hemi-arthroplasty would appear to be the superior technique. On the topic of wound closure, one recent meta-analysis has found that, while staples can result in a quicker closure time, there is no significant difference in post-operative infections rates or wound healing outcomes when comparing staples to sutures. Therefore, either suture or staple wound closure techniques appear equally appropriate for hip hemi-arthroplasty procedures.

**Key words:** Hemi-arthroplasty; Prosthesis; Stem; Head; Hip; Femoral; Neck; Fracture; Cement

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** From the current evidence on hip hemi-arthroplasty, the following conclusions can be drawn: posterior approaches are associated with higher rates of dislocation and should be avoided; there is no significant difference between unipolar and bipolar hemi-arthroplasty for surgical outcome, complication profile, functional outcome and long-term acetabular-erosion rates, therefore unipolar hemi-arthroplasty, the cheaper prosthesis, is the recommended option; cemented hemi-arthroplasty, the recommended option, has lower rates of implant-related complications and residual thigh pain compared to uncemented hemi-arthroplasty, with no significant difference in medical complications or mortality; there is no significant difference in wound-infections rates or healing outcomes between staples and sutures.

Robertson GA, Wood AM. Hip hemi-arthroplasty for neck of femur fracture: What is the current evidence? *World J Orthop* 2018; 9(11): 235-244 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i11/235.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i11.235>

## INTRODUCTION

Hip fractures in the elderly represent a major public health concern<sup>[1-7]</sup>. These account for a quarter of all fractures in patients aged 75 years and over<sup>[3]</sup>. With a global incidence of 1.7 million hip fractures in 1990, this is targeted to reach 6.3 million in 2050<sup>[7]</sup>.

The management of hip fractures is based on the location of the fracture: the two main categories being intra and extra-capsular fractures<sup>[8]</sup>. Intra-capsular fractures comprise around 60% of all hip fractures, with up to 80% of these being displaced<sup>[1,9]</sup>. Fracture displacement increases the risk of disruption to the femoral head blood supply, and so, is associated with increased rates of osteo-necrosis of femoral head, non-union, delayed union and failure of fracture fixation procedures<sup>[10-15]</sup>. As such, the current treatment guidelines for hip fractures advise that "displaced intracapsular neck of femur fractures be treated with arthroplasty procedures"<sup>[16]</sup>. There are two main arthroplasty procedures available for the treatment of displaced intracapsular neck of femur fractures: hip hemi-arthroplasty and total hip replacement<sup>[17-22]</sup>. Hip hemi-arthroplasty is the recommended option in the frail, low mobility population as the large diameter hemi-arthroplasty "head" component reduces the risk of dislocation: total hip replacement is the recommended option in the more active population as it can provide a better functional outcome<sup>[17-22]</sup>. The current guidelines from the "National Institute for Health and Care Excellence" (NICE) advice for orthopaedic surgeons to consider total hip

arthroplasty over hip hemi-arthroplasty as treatment of displaced neck of femur fractures in patients who are: independently mobile out-doors, requiring one stick or less for support; cognitively intact; and considered suitably healthy to undergo the operation by both the orthopaedic and anaesthetic teams. When such criteria are not met, a hip hemi-arthroplasty is indicated<sup>[16]</sup>. The current registry data suggests that around 90% of displaced intra-capsular fractures are treated with hip hemi-arthroplasty, with 10% treated with total hip replacements<sup>[1,2,23]</sup>.

Despite the perceived simplicity of the hip hemi-arthroplasty procedure, there are a number of variations to the procedure<sup>[15,24-26]</sup>. These include the approach<sup>[26-28]</sup>, the type of prosthesis head<sup>[25,29-31]</sup>, the method of stem insertion<sup>[25,32-34]</sup>, and the type of prosthesis assembly<sup>[35]</sup>. The optimal selection for each of these factors remains to be determined<sup>[15,24-26]</sup>.

This editorial reviews and summarises the current evidence (meta-analyses and Cochrane reviews) relating to the use of hip hemi-arthroplasty for neck of femur fractures.

## SURGICAL APPROACH - LATERAL VS POSTERIOR VS ANTERIOR APPROACHES

Surgical approaches to the hip for hip hemi-arthroplasty can be divided into three main categories: lateral approaches (LA), posterior approaches (PA) and anterior approaches (AA).

LAs commonly involve (partial or complete) division or retraction of the hip abductor muscles (gluteus medius and minimus) to enable access to the hip capsule<sup>[26,27]</sup>. These include the Hardinge (direct lateral), the transgluteal and the Watson-Jones (anterolateral) approach<sup>[26,27]</sup>.

PAs commonly involve a trans-gluteus-maximus approach, followed by division of the tendons of the short external rotators, to enable access to the hip joint<sup>[26,27]</sup>. These include the Moore, the Southern, the true posterior and the posterolateral approaches<sup>[26,27]</sup>.

AAs commonly involve use the inter-nervous plane between the femoral and the superior gluteal nerves (the superficial interval between sartorius and tensor fasciae latae; and the deep interval between rectus femoris and gluteus medius) to enable access to the anterior hip capsule<sup>[26-28]</sup>. These include the direct anterior and the Smith-Petersen approaches<sup>[26-28]</sup>.

There are two recent meta-analyses<sup>[27,28]</sup> and one Cochrane review<sup>[26]</sup> comparing outcomes of hip hemi-arthroplasty by type of approach used.

The most recent meta-analysis is that by van der Sijp *et al*<sup>[27]</sup>. The authors performed a systematic database search, until October 2017, to identify all studies on hip hemi-arthroplasty for fracture, which compared outcome by approach used<sup>[27]</sup>. Twenty-one studies were included in the meta-analysis [3 randomized controlled trials (RCT), 7 prospective and 11 retrospective cohort studies],

with a synthesis cohort of 61487 patients<sup>[27]</sup>. On meta-analysis, PAs were found to have a significantly higher rate of dislocation compared to AAs (OR = 2.61; 95%CI: 1.26 to 5.43;  $P < 0.01$ ); and LAs (OR = 2.90; 95%CI: 1.63 to 5.14;  $P < 0.0003$ )<sup>[27]</sup>. PAs also had a higher risk of re-operation (*i.e.*, revision procedures, relocation of dislocations, intra-operative fracture fixation, and repair of capsule for repetitive instability) compared to LAs (OR = 1.25; 95%CI: 1.12 to 1.41;  $P < 0.0001$ ); however no significant difference was found when comparing the re-operation rates of LAs and AAs (OR = 1.54; 95%CI: 0.50 to 4.77;  $P = 0.45$ )<sup>[27]</sup>. There was insufficient data to allow meta-analysis comparison of the re-operation rates of PAs and AAs<sup>[27]</sup>. On further meta-analysis between the three approaches, no significant differences were found for rates of surgical site infection, intra-operative fracture, and length of hospital stay<sup>[27]</sup>. It was not possible to perform meta-analysis on the "functional outcome" data between the three approaches<sup>[27]</sup>. The authors concluded that PAs are associated with a higher rate of dislocation and further operations in comparison to LAs and AAs in hip hemiarthroplasty for fracture<sup>[27]</sup>.

The other recent meta-analysis is that by Kunkel *et al.*<sup>[28]</sup>: this compared the direct anterior approach (DAA) for hip hemi-arthroplasty to all other approaches for this procedure. The authors performed a systematic database search, until October 2016, identifying RCTs and cohort studies on hip hemi-arthroplasty for fracture, which compared the DAA to other surgical approaches (lateral, anterolateral, posterior, posterolateral)<sup>[28]</sup>. Nine studies were included in the meta-analysis (3 prospective randomised studies, 3 prospective non-randomised studies and 3 retrospective cohort studies)<sup>[28]</sup>. The synthesis cohort comprised a total of 698 hips (direct anterior approach  $n = 330$ ; posterior approach  $n = 108$ , posterolateral approach  $n = 114$ ; anterolateral approach  $n = 57$ ; lateral approach  $n = 89$ )<sup>[28]</sup>. On meta-analysis, PAs were found to have a significantly higher dislocation rate compared to the DAA (OR = 0.18; 95%CI: 0.05 to 0.63;  $P = 0.007$ )<sup>[28]</sup>. However, there was no significant difference in dislocation rate between the DAA and LAs (OR = 0.19; 95%CI: 0.01 to 4.03;  $P = 0.29$ )<sup>[28]</sup>. On further meta-analysis, no significant difference was found between the approaches for intra-operative blood loss, perioperative fracture, duration of procedure, post-operative pain levels, length of hospital stay, post-operative infection rate, further operation rate, total complication rate and mortality<sup>[28]</sup>. The authors concluded that for fracture-related hip hemiarthroplasty, PAs are associated with a significantly higher rate of dislocation in comparison to the DAA<sup>[28]</sup>.

Prior to this, Parker *et al.*<sup>[26]</sup> performed a Cochrane review in 2002 assessing the influence of surgical approaches on outcome from hip hemiarthroplasty. The authors performed a systematic database search, until February 2002, to identify all RCTs comparing outcome from different surgical approaches in fracture-related hip hemi-arthroplasty<sup>[26]</sup>. Only one RCT was identified that was suitable for inclusion: this comprised 114 hip

fracture patients who were managed with a cemented Thompson hemi-arthroplasty, either through an anterolateral or a posterior approach<sup>[26]</sup>. Unfortunately, the study was found to be of sub-optimal quality to allow for reliable analysis, owing to selection bias, insufficient patient follow-up and insufficient results reporting<sup>[26]</sup>. The authors concluded that, at that time, the evidence from RCTs was inadequate to decide which approach was most effective for hip hemi-arthroplasty in femoral neck fractures<sup>[26]</sup>.

Of the available National Guidelines which provide recommendations on the practice of hip hemiarthroplasty for hip fracture: the NICE Guidelines currently advise clinicians to favour the anterolateral approach over the posterior approach for hip hemiarthroplasty surgery<sup>[16]</sup>; and the Scottish Intercollegiate Guidelines Network (SIGN) Guidelines advise "the anterolateral approach is recommended for hemiarthroplasty surgery"<sup>[36]</sup>.

The current evidence would suggest that, in hip hemi-arthroplasty for fracture, PAs are associated with a higher rate of post-operative dislocation compared to LAs and AAs, and a higher risk of reoperation compared to LAs. There appears no significant difference between LAs and AAs in terms of post-operative dislocation rates and re-operation rates. Thus, PAs should be avoided when performing hip hemi-arthroplasty for femoral neck fracture.

## PROSTHESIS HEAD COMPONENT

### - UNIPOLAR VS BIPOLAR HEMI-ARTHROPLASTY

There are two main categories of hemi-arthroplasty prosthesis, when assessing head component utilised: unipolar hemi-arthroplasty (UH) (Figure 1A) and bipolar arthroplasty (BH) (Figure 1B)<sup>[25,29-31]</sup>. An UH comprise a large single endo-prosthetic head component, while BH has both an endo-prosthetic "bipolar" head component and an inner metal bearing<sup>[25,29-31]</sup>. The theoretical benefit of the BH design, with its mobile bearing concept, is to reduce component-induced wear on the acetabulum<sup>[25,29-31]</sup>. Other theoretical benefits include improved range of hip motion, decreased risk of dislocation and improved hip function, to provide a better clinical outcome over UH<sup>[25,29-31]</sup>. However, the proven benefits of BH over UH remain to be confirmed<sup>[25,29-31]</sup>.

There are three recent meta-analyses<sup>[29-31]</sup> and one Cochrane review<sup>[25]</sup> which compare the outcomes of unipolar to bipolar hip hemi-arthroplasties for femoral neck fracture.

The most recent meta-analysis is by Zhou *et al.*<sup>[29]</sup>. The authors performed a systematic database search, till April 2014, to identify all RCTs which compare UH to BH, as treatment of displaced femoral neck fractures<sup>[29]</sup>. Eight RCTs were included in the meta-analysis, providing a synthesis cohort of 1100 patients<sup>[29]</sup>. On meta-analysis, no significant difference was found

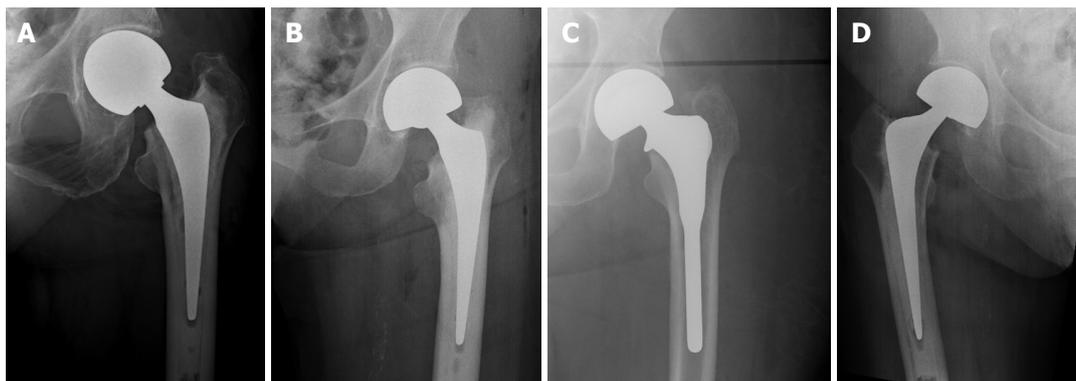


Figure 1 A hip hemi-arthroplasty with a unipolar component head (A); a hip hemi-arthroplasty with a bipolar component head (B); a hip hemi-arthroplasty with an uncemented femoral stem (C); and a hip hemi-arthroplasty with a cemented femoral stem (D).

between UH and BH for acetabular erosion rates (RR = 2.29; 95%CI: 0.85 to 6.12;  $P = 0.10$ ), rate of dislocation (RR = 1.20; 95%CI: 0.47 to 3.07;  $P = 0.71$ ), rate of reoperation (RR = 0.64; 95%CI: 0.33 to 1.26;  $P = 0.19$ ), mortality (RR = 0.85; 95%CI: 0.63 to 1.13;  $P = 0.26$ ), post-operative complication rates (RR = 1.05; 95%CI: 0.70 to 1.56;  $P = 0.82$ ), and post-operative Harris Hip Scores (WMD -1.32; 95%CI: 3.29 to 0.65;  $P = 0.19$ )<sup>[29]</sup>. The authors concluded that there was no apparent difference in clinical results between UH and BH, when used as treatment for displaced intra-capsular neck of femur fractures<sup>[29]</sup>.

The second of the recent meta-analyses was that by Jia *et al.*<sup>[30]</sup>. The authors performed a systematic literature search, until April 2014, to identify all RCTs which compared UH to BH as treatment of displaced intra-capsular neck of femoral fractures<sup>[30]</sup>. The meta-analysis comprised ten RCTs, providing a synthesis cohort of 1190 patients<sup>[30]</sup>. On systematic review of the included studies, the authors found descriptive evidence that BH was superior to UH for post-operative hip function, quality of life and post-operative hip pain; however on meta-analysis, there was no significant difference in post-operative Harris Hip Scores between UH and BH (MD, -0.51, 95%CI: -4.43 to 3.42,  $P = 0.80$ )<sup>[30]</sup>. UH was also found to have increased rates of acetabulum erosions at one year post-surgery, in comparison to BH (RR = 0.24; 95%CI: 0.06 to 0.89;  $P = 0.03$ ): however there was no significant difference between the two groups for acetabular erosion rates at four months post-surgery (RR = 0.35; 95%CI: 0.10 to 1.21;  $P = 0.10$ ), two years post-surgery (RR = 0.46; 95%CI: 0.20 to 1.10;  $P = 0.08$ ), or four years post-surgery (RR = 0.48; 95%CI: 0.20 to 1.19;  $P = 0.12$ )<sup>[30]</sup>. On further meta-analysis, no significant difference was found between UH and BH for: mortality (RR = 0.92; 95%CI: 0.59 to 1.44;  $P = 0.71$ ); reoperation rates (RR = 0.98; 95%CI: 0.42 to 2.27;  $P = 0.95$ ); dislocation rates (RR = 0.76; 95%CI: 0.30 to 1.93;  $P = 0.57$ ); implant-related complications (RR = 0.84; 95%CI: 0.39 to 1.81;  $P = 0.66$ ); general complications (RR = 0.65; 95%CI: 0.28 to 1.49;  $P = 0.31$ )<sup>[30]</sup>. Furthermore,

two of the RCTs which reported on cost of prosthesis both noted that BH was more expensive than UH<sup>[30]</sup>. The authors concluded that, comparing UH to BH, no significant difference could be found between post-operative result and longer term rates of acetabular erosion; however BH was consistently noted to be the more expensive implant<sup>[30]</sup>.

The last of the recent meta-analyses was that by Yang *et al.*<sup>[31]</sup>. The authors performed a systematic database search, till July 2013, to identify all prospective RCTs that compare UH to BH for the treatment of neck of femur fractures in patients aged 65 years and over<sup>[31]</sup>. Six RCTs were included in the meta-analysis, with a combined cohort of 982 patients<sup>[31]</sup>. On meta-analysis, the acetabular erosion rates was noted to be significantly increased in the UH group (5.5%) compared to the BH group (1.2%) (OR = 0.22; 95%CI: 0.07 to 0.74;  $P = 0.01$ )<sup>[31]</sup>. However, there was no significant difference between the two groups for: rate of mortality (OR = 1.08; 95%CI: 0.71 to 1.65;  $P = 0.72$ ), overall post-operative complication rates (OR = 1.00; 95%CI: 0.67 to 1.50;  $P = 1.00$ ), post-operative rate of dislocation (OR = 0.87; 95%CI: 0.29 to 2.60;  $P = 0.80$ ), rate of infection (OR = 1.36; 95%CI: 0.60 to 3.09;  $P = 0.47$ ), rate of reoperation (OR = 1.56; 95%CI: 0.66 to 3.68;  $P = 0.31$ ), Harris hip scores (SMD -0.03; 95%CI: -0.23 to 0.17;  $P = 0.76$ ) and return to pre-fracture function (OR = 1.36; 95%CI: 0.94 to 1.96;  $P = 0.10$ )<sup>[31]</sup>. The authors concluded that there was no significant difference noted in clinical outcome for UH compared to BH when used as treatment of displaced intra-capsular neck of femur fractures in patients aged 65 or over<sup>[31]</sup>. Given the similar clinical outcomes, they advised that unipolar implants appear the more economical prosthesis<sup>[31]</sup>.

Lastly, the most recent Cochrane review on the topic is that Parker *et al.*<sup>[25]</sup>. The authors performed a systematic database search till September 2008, to identify all RCTs and quasi-RCTs comparing the use of different arthroplasty prostheses as management of femoral neck fractures<sup>[25]</sup>. In total, twenty-three studies were included, with a synthesis cohort of 2861

patients<sup>[25]</sup>. A sub-group analysis was performed, assessing all studies which compared UH to BH: this comprised seven studies, with a combined cohort of 857 patients (863 fractures<sup>[25]</sup>). On meta-analysis, no significant differences was found between UH and BH for: dislocation rate (RR = 1.09; 95%CI: 0.36 to 3.31;  $P = 0.88$ ), acetabular erosion rate (RR = 3.83; 95%CI: 0.81 to 18.15;  $P = 0.090$ ), acetabular erosions requiring revision (RR = 2.97; 95%CI: 0.47 to 18.85;  $P = 0.25$ ), rate of deep wound infection (RR = 1.34; 95%CI: 0.50 to 3.62;  $P = 0.56$ ), reoperation rate (RR = 1.41; 95%CI: 0.54 to 3.69;  $P = 0.49$ ), deep vein thrombosis (RR = 0.71; 95%CI: 0.03 to 16.45), mortality at 6 months (RR = 1.13; 95%CI: 0.73 to 1.76;  $P = 0.58$ ); mortality at 1 to 2 years (RR = 0.90; 95%CI: 0.64 to 1.26;  $P = 0.54$ ) and recovery of pre-fracture mobility (RR = 0.94; 95%CI: 0.40 to 2.16)<sup>[25]</sup>. The authors concluded that from the available evidence, UH and BH implants demonstrated no significant clinical difference when used as treatment for displaced femoral neck fractures<sup>[25]</sup>.

Of the current National Guidelines, the SIGN Guidelines recommend that "BH should not be performed in preference to UH, as there is limited evidence of any clinical benefit"<sup>[2]</sup>. In keeping with this, data from the recent English hip fracture audit has found that 79% of all hip hemi-arthroplasties performed in England in 2017 were UH<sup>[1]</sup>.

From the current evidence, it would appear, that while UH can be associated with increased rates of acetabular erosion at short-term follow-up (up to 1 year), there is no significant difference between the two prosthesis types for surgical outcome, complication profile, functional outcome and acetabular erosion rates at longer-term follow-up (2 to 4 years). Thus, with BH being the more expensive prosthesis, UH would appear to be the recommended option.

## TECHNIQUE OF FEMORAL STEM INSERTION - CEMENTED VS UNCEMENTED HEMI-ARTHROPLASTY

The optimal technique for femoral stem implantation, using either an uncemented (Figure 1C) or a cemented (Figure 1D) femoral stem remains another keenly debated topic<sup>[25,32-34]</sup>. In theory, a cemented femoral stem is more uniformly and more securely fixed within the femoral canal; this has been postulated to result in lower rates of post-operative thigh pain and reduced revision rates from aseptic loosening<sup>[25,32-34]</sup>. However, the use of cement intra-operatively potentially confers the risks of cardiac arrhythmias and cardio-respiratory compromise, secondary to fat embolism and cement reaction phenomena<sup>[25,32-34]</sup>. Revision of a cemented hemi-arthroplasty is also considered more challenging than that of an uncemented hemi-arthroplasty<sup>[25,32-34]</sup>. Uncemented hemi-arthroplasties theoretically incur a shorter operating time, due to the lack of cementation

required; they also have been noted to be the cheaper of the two prosthesis types<sup>[25,32-34]</sup>. As such, the optimal technique for femoral stem insertion remains to be decided<sup>[25,32-34]</sup>.

There are three recent meta-analyses<sup>[32-34]</sup> and one Cochrane review<sup>[25]</sup> which compare the outcomes of cemented to uncemented hip hemi-arthroplasties for femoral neck fracture.

The most recent meta-analysis is that by Veldman *et al.*<sup>[32]</sup>. The authors performed a systematic database search, till April 2016, to identify all RCTs comparing outcomes for cemented versus uncemented hemi-arthroplasties for femoral neck fracture, which used contemporary generation femoral stems only<sup>[32]</sup>. Five RCTs were included in the meta-analysis, with a synthesis cohort of 950 patients (950 hips)<sup>[32]</sup>. Complications were categorised as: prosthesis-related (dislocation, aseptic prosthesis loosening, peri-prosthetic fractures); cardiovascular-related; local (deep and superficial wound infections); and other general complications<sup>[32]</sup>. On meta-analysis, cementless hemi-arthroplasties had higher rates of overall complications compared cemented hemi-arthroplasties (OR = 1.61; 95%CI: 1.12 to 2.31;  $P = 0.01$ ), especially implant-related complications (OR = 3.15; 95%CI: 1.55 to 6.41;  $P = 0.002$ )<sup>[32]</sup>. However, cementless hemi-arthroplasties were associated with a shorter operating time compared to cemented hemi-arthroplasties (WMD -9.96 mins; 95%CI: -12.93 to -6.98;  $P < 0.001$ )<sup>[32]</sup>. On further meta-analysis, there was no significant difference between the two methods of femoral stem insertion for: cardio-vascular complications (OR = 0.54; 95%CI: 0.24 to 1.20;  $P = 0.13$ ); local complications (OR = 0.71; 95%CI: 0.27 to 1.86;  $P = 0.49$ ); general complications (OR = 1.09; 95%CI: 0.62 to 1.91;  $P = 0.76$ ); number of re-operations (OR = 1.24; 95%CI: 0.53 to 2.88;  $P = 0.62$ ); length of hospital stay (WMD 0.36 d; 95%CI: -1.13 to 1.85;  $P = 0.63$ ); intra-operative blood loss (WMD -36.19 mL; 95%CI: -89.45 to 17.07;  $P = 0.18$ )<sup>[32]</sup>. It was not possible to perform meta-analysis on the "functional outcome" data<sup>[32]</sup>. The authors concluded that, for fracture-related hip hemiarthroplasty using contemporary femoral stems, cemented hemi-arthroplasties were associated with fewer prosthesis-related complications, though with similar mortality rates, as compared to uncemented hemi-arthroplasties<sup>[32]</sup>.

However, it must be noted that the data regarding implant-related complications, in this meta-analysis, was heterogeneous<sup>[32]</sup>. Review of the three studies, which reported on implant-related complications, revealed the most common complication was peri-prosthetic femoral fracture<sup>[32]</sup>. However, no formal break-down of the individual implant-related complications was provided in the meta-analysis<sup>[32]</sup>. As such, a more detailed meta-analysis is required to properly define the increased risk posed by uncemented prostheses. Nevertheless, the current evidence suggests that the cemented technique is safer.

The second most recent meta-analysis is that by

Ning *et al*<sup>[33]</sup>. The authors performed a systematic database search, till March 2012, to identify all RCTs which compared cemented to uncemented hemi-arthroplasty for fracture, including all available prosthesis types<sup>[33]</sup>. Twelve RCTs were included in the meta-analysis, providing a synthesis cohort of 1805 patients<sup>[33]</sup>. On meta-analysis, cemented hip hemi-arthroplasties were associated with a prolonged operative time when compared to uncemented hemi-arthroplasties (SMD -0.43; 95%CI: -0.56 to -0.30;  $P < 0.001$ )<sup>[33]</sup>. However, no significant difference was found between the two techniques for: intra-operative blood loss (SMD -0.12; 95%CI: -0.33 to 0.10;  $P = 0.291$ ); length of hospital stay (SMD -1.21; 95%CI: -0.05 to 0.22;  $P = 0.224$ ), overall complications (OR = 0.82; 95%CI 0.63 to 1.08;  $P = 0.163$ ); post-operative pain (OR = 1.42; 95%CI: 0.99 to 2.03;  $P = 0.056$ ) and mortality rates (OR = 1.08; 95%CI: 0.88 to 1.34;  $P = 0.469$ )<sup>[33]</sup>. The authors concluded that the outcomes of uncemented and cemented hip hemiarthroplasty for femoral neck fracture, showed no significant difference<sup>[33]</sup>.

The last of the recent meta-analyses was that by Luo *et al*<sup>[34]</sup>. The authors performed a systematic database search, till December 2010, to identify all RCTs comparing uncemented and cemented hip hemiarthroplasty (all prosthesis types included), as treatment for neck of femur fractures<sup>[34]</sup>. Eight RCTs were included in the meta-analysis, providing a synthesis cohort of 1175 hips<sup>[34]</sup>. On meta-analysis, uncemented hemi-arthroplasties were noted to have higher rates of post-operative pain 1-year post-surgery compared to cemented hemi-arthroplasties (RR = 0.69; 95%CI: 0.53 to 0.90;  $P = 0.007$ ). There was however no significant difference between the two techniques for: peri-operative mortality (RR = 0.92; 95%CI: 0.58 to 1.45;  $P = 0.71$ ), 1-year mortality (RR = 0.89; 95%CI: 0.73 to 1.09;  $P = 0.26$ ), rates of reoperation (RR = 0.75; 95%CI: 0.44 to 1.25;  $P = 0.27$ ), general medical complications (RR = 0.83; 95%CI: 0.61 to 1.14;  $P = 0.25$ ) and local complications (comprising dislocation, wound infection, periprosthetic fracture and radiographic prosthesis loosening) (RR = 0.85; 95%CI: 0.58 to 1.23;  $P = 0.38$ )<sup>[34]</sup>. Meta-analysis could not be performed for the "functional outcome" data<sup>[34]</sup>. The authors concluded that, while the cemented prostheses were associated with lower rates of post-operative pain as compared to the uncemented prostheses, the two types of hemi-arthroplasty showed no significant difference in complication rates, reoperation rates and mortality rates<sup>[34]</sup>.

Lastly, the most recent Cochrane review on the topic is by Parker *et al*<sup>[25]</sup>, as described in "Prosthesis Head Component" section. On sub-group analysis, six studies were identified which compared cemented to uncemented hemi-arthroplasties for neck of femur fracture, providing a synthesis cohort of 899 participants<sup>[25]</sup>. All prosthesis types were included in the review<sup>[25]</sup>. On meta-analysis, cemented hemi-arthroplasties had a significantly prolonged operation time (MD 7.24 min; 95%CI: 4.75

to 9.73 min;  $P < 0.00001$ ), though had reduced rates peri-operative of femoral fracture (RR = 0.09; 95%CI: 0.02 to 0.44;  $P = 0.0031$ ), lower rates of residual hip pain at both three-month follow-up (RR = 0.77; 95%CI: 0.60 to 0.98;  $P = 0.034$ ) and longer term follow-up (RR = 0.55; 95%CI: 0.40 to 0.75;  $P = 0.00017$ ), and improved recovery of post-operative mobility scores (RR = -0.80; 95%CI: -1.23 to -0.37)<sup>[25]</sup>. No significant difference was found between the two techniques in mortality rates at any of the follow-up time intervals: 1-mo post-surgery (RR = 0.84; 95%CI: 0.38 to 1.84;  $P = 0.66$ ); one to three months post-surgery (RR = 0.98; 95%CI: 0.68 to 1.41;  $P = 0.90$ ); 1-year post-surgery (RR = 0.90; 95%CI: 0.71 to 1.13;  $P = 0.35$ ); and 3-years post-surgery (RR = 1.13; 95%CI: 0.76 to 1.67)<sup>[25]</sup>. Similarly, no significant difference was found between the two techniques for: peri-operative blood loss (RR = 49.00; 95%CI: -22.10 to 120.10); requirement of blood transfusion (RR = 0.12; 95%CI: -0.04 to 0.27;  $P = 0.13$ ); occurrence of medical complications (RR = 0.82; 95%CI: 0.59 to 1.13;  $P = 0.23$ ); rate of re-operation (RR = 0.55; 95%CI: 0.27 to 1.14;  $P = 0.11$ ); duration of hospital stay (RR = -1.42; 95%CI: -3.15 to 0.32;  $P = 0.11$ ); percentage of patients who were able to return to their pre-injury place of residence (RR = 0.62; 95%CI: 0.34 to 1.12;  $P = 0.11$ ) and restore their pre-injury mobility levels (RR = 0.84; 95%CI: 0.64 to 1.11;  $P = 0.23$ )<sup>[25]</sup>. The authors concluded that cemented hip hemi-arthroplasties can reduce the risk of peri-operative femoral fracture, reduce post-operative pain levels and provide improved post-operative mobility, when compared to uncemented hip hemi-arthroplasties for displaced femoral neck fractures, with no significant difference between the two techniques for mortality at any of the follow-up time points<sup>[25]</sup>.

Of the available National Guidelines: the NICE Guidelines currently recommend "the use cemented implants in (hip fracture) patients undergoing surgery with arthroplasty"<sup>[16]</sup>; and the SIGN Guidelines recommend that "cement should be used when undertaking hemiarthroplasty, unless there are cardiorespiratory complications, particularly in frail older patients"<sup>[36]</sup>. In keeping with this, data from the recent Scottish and English Hip Fracture Audits have found that 90% and 87% of all hip hemi-arthroplasties, from Scotland and England in 2017 respectively, were performed with a cemented femoral stem<sup>[1,2]</sup>.

The current evidence would suggest that while uncemented hemi-arthroplasties can allow for a shorter operative time, cemented hemi-arthroplasties are associated with lower rates of prosthesis-related complications (particularly peri-prosthetic femoral fracture) and improved post-operative results in terms of residual thigh pain and mobility. In addition, there appears to be no significant difference between the two techniques for intra-operative blood loss, medical complications and mortality (peri-operative and 1-year). In accordance with the current literature, a cemented hip hemi-

arthroplasty would appear to be the superior technique.

## TYPE OF PROSTHESIS ASSEMBLY - MONOBLOCK VS MODULAR HEMI- ARTHROPLASTY

There are two main types of prosthesis assembly that can be used in hip hemi-arthroplasty: monoblock prosthesis and modular prosthesis<sup>[35]</sup>.

A monoblock hemi-arthroplasty is produced as a single unit, with variations in prosthesis size based on the diameter of the patient's femoral head<sup>[35]</sup>. The most commonly used monoblock implant is the collared Thompson Hemi-Arthroplasty<sup>[35]</sup>. Given the pre-fabricated nature of this prosthesis, there is limited ability to adjust the prosthesis intra-operatively to accommodate for variations in femoral neck offset or leg length: thus, such implants often poorly recreate the patient's original hip geometry<sup>[35]</sup>. A modular hemi-arthroplasty is produced in individual components: stem, neck and head components<sup>[35]</sup>. On assembling these intra-operatively, the surgeon is able to alter component size, and so better recreate the patient's original hip geometry<sup>[35]</sup>. However, the theoretical benefits of modular prostheses in hip hemi-arthroplasty as treatment of femoral neck fractures remain to be confirmed<sup>[35]</sup>.

There is one recent meta-analysis<sup>[35]</sup> which compare the outcomes of monoblock to modular hip hemi-arthroplasties for treatment of femoral neck fractures.

The available meta-analysis is that by Sims *et al.*<sup>[35]</sup>. The authors performed a systematic database review, until September 2015, identifying all RCTs, well-designed case control studies, retrospective cohort studies and prospective cohort studies, which compared outcomes between Thompson hemi-arthroplasties and modular unipolar hemi-arthroplasties for femoral neck fracture<sup>[35]</sup>. Four studies were included in the review (1 RCT, 2 Retrospective Cohort Studies, 1 Swedish Joint Registry Paper), providing a synthesis cohort of 21017 patients<sup>[35]</sup>. On meta-analysis, the odds ratio favoured modular designs for both mortality (OR = 1.3; 95%CI: 0.78 to 2.46) and post-operative complications (OR = 1.1; 95%CI: 0.79 to 1.55); however no significant difference was noted for either factor, between the prosthesis types<sup>[35]</sup>. On review of the study quality of the included studies, the authors found these all to be subject to potential bias with significant heterogeneity noted in the methods and results<sup>[35]</sup>. Thus the authors concluded that there is insufficient evidence at present to accurately compare monoblock to modular hemi-arthroplasty prosthesis for patients with femoral neck fractures<sup>[35]</sup>.

To note, the same authors subsequently published a multi-centre, pragmatic RCT comparing the outcome of the Thompson monoblock cemented hemi-arthroplasty to a modular hemi-arthroplasty using a cemented Exeter femoral stem and a Unitrax hemi-arthroplasty head (The WHITE 3: Hemi Trial) (2018)<sup>[37]</sup>. The initial

recruitment cohort comprised 964 patients (monoblock group  $n = 482$ ; modular group  $n = 482$ ); however four-month follow-up data was only available for 482 patients (50%)<sup>[37]</sup>. Outcome assessment was performed using the EuroQol questionnaire (EQ-5D-5L)<sup>[37]</sup>. At four-month follow-up, the modular cohort had a marginally improved mean EQ-5D-5L (mean EQ-5D-5L for modular cohort 0.379; mean EQ-5D-5L for monoblock cohort 0.321); however, this difference did not meet the minimum required clinical difference of 0.08, nor was it statistically significant (MD = 0.037; 95%CI: -0.014 to 0.087;  $P = 0.156$ ). Other factors which failed to show significant difference between the two groups included: mortality (OR = 1.02; 95%CI: 0.72 to 1.46;  $P = 0.911$ ); post-operative walking ability (OR = 0.76; 95%CI: 0.54 to 1.06;  $P = 0.107$ ); local complications (*i.e.*, wound complications; revision procedures; structural injury; deep vein thrombosis; dislocation) (OR = 1.50; 95%CI: 0.828 to 2.741;  $P = 0.179$ ); requirement for blood transfusion (OR = 1.51; 95%CI: 0.530 to 4.316;  $P = 0.439$ ); and medical complications (OR = 0.95; 95%CI: 0.665 to 1.358;  $P = 0.779$ ). Length of hospital stay was marginally higher in the monoblock group (mean stay for monoblock group = 9.67 d; mean stay for modular group = 9 d;  $P = 0.039$ ). There was no significant difference in post-operative radiographic femoral offset between the two groups (mean neck length for monoblock group = 3.01 mm; mean neck length for modular group = 2.91 mm;  $P = 0.834$ ). The authors concluded that, accounting for the limited follow-up, there was no significant difference detected in clinical outcome between the two prosthesis types, when used as treatment for femoral neck fractures.

Of the current National Guidelines, the NICE guidelines advise to "use a proven femoral stem design (*i.e.*, those with an Orthopaedic Data Evaluation Panel rating of 10A, 10B, 10C, 7A, 7B, 5A, 5B, 3A or 3B) rather than Austin Moore or Thompson Stems for arthroplasties"<sup>[16]</sup>. However, such guidance is directed from evidence in primary total hip arthroplasty and expert opinion<sup>[35]</sup>.

Thus, despite clear recommendations from NICE, the current evidence which compares monoblock to modular hemi-arthroplasty prosthesis for femoral neck fracture remains limited and equivocal. Despite the logical bio-mechanical advantage of the modular prosthesis, further research is required in this area to confirm their clinical benefit.

## WOUND CLOSURE TECHNIQUES - SUTURES VS STAPLES

Wound closure technique remains a controversial area in hip hemi-arthroplasty surgery<sup>[38]</sup>. The two most common skin closure methods are staples and sutures<sup>[38]</sup>. Historically, it has been felt that staples were more time efficient, though associated with a higher rate of post-operative infection<sup>[38]</sup>. This belief was strengthened by a systematic review and meta-

analysis on the topic, from 2010, which reported that the rate of post-operative infection following orthopaedic surgery, was over three times greater for staple wound closure compared to suture wound closure<sup>[39]</sup>. However, the recent evidence provides a more balanced perspective<sup>[38]</sup>.

There is one recent meta-analysis comparing the outcomes of skin closure techniques (sutures vs staples) in orthopaedic surgery, with a sub-group analysis on hip surgery procedures<sup>[38]</sup>.

This meta-analysis is that by Krishnan *et al*<sup>[38]</sup>. The authors performed a systematic database review, until January 2015, identifying all RCTs and observational studies which compared the outcome of suture to staple wound closure technique following orthopaedic surgery<sup>[38]</sup>. The rate of post-operative wound infection was the primary outcome measure, with secondary outcome measures comprising time of closure, wound dehiscence, inflammation, post-operative pain, length of hospital stay, necrosis, abscess formation, discharge, allergic reaction<sup>[38]</sup>. Thirteen studies were included meta-analysis (ten RCTs, three observational studies), with a combined cohort of 1255 patients (suture group = 563 patients, staple group = 692 patients)<sup>[38]</sup>. Six of the studies comprised patients undergoing hip surgery (suture group = 164 patients, staple group = 245 patients)<sup>[38]</sup>. On meta-analysis, no significant difference was found in post-operative infection rates between sutures and staples (RR = 1.06; 95%CI: 0.46 to 2.44;  $P = 0.89$ )<sup>[38]</sup>. On sub-group analysis, for the patients who underwent hip surgery, no significant difference was also found in post-operative infection rates between sutures and staples (RR = 0.48; 95%CI: 0.10 to 2.45;  $P = 0.38$ )<sup>[38]</sup>. On further meta-analysis of the total cohort, closure time was found to be quicker for staples compared to sutures (MD = 5.84; 95%CI: 4.52 to 7.15;  $P < 0.001$ )<sup>[38]</sup>. However, there was no significant difference between the two techniques for all other outcome measures: wound dehiscence (RR = 0.96; 95%CI: 0.32 to 2.84;  $P = 0.94$ ), inflammation (RR = 0.22; 95%CI: 0.00 to 12.07;  $P = 0.46$ ), discharge (RR = 0.66; 95%CI: 0.14 to 3.23;  $P = 0.61$ ), necrosis (RR = 0.51; 95%CI: 0.07 to 3.88;  $P = 0.52$ ), allergic reaction (RR = 1.37; 95%CI: 0.22 to 8.60;  $P = 0.74$ ), abscess formation (RR = 1.86; 95%CI: 0.22 to 15.71;  $P = 0.57$ )<sup>[38]</sup>. The authors concluded that, apart from time of closure, no significant difference was found between suture and staple wound closure techniques<sup>[38]</sup>.

The current orthopaedic literature, particularly with regards to hip-related procedures, provides an equivocal conclusion on the optimal wound closure technique. From the available evidence, either suture or staple wound closure techniques appear equally appropriate for hip hemi-arthroplasty procedures.

is a cemented modular bipolar hemi-arthroplasty, through an antero-lateral approach. The wound closure technique varies, as per the preference of the responsible surgeon, with either skin clips or sub-cuticular sutures used. At present, there is a randomised controlled trial being run in this unit between cemented modular bipolar hemi-arthroplasty prostheses and cemented modular UH prostheses: the result from this may influence the future choice of prosthesis head component selection in the institution.

The second author manages this fracture with a cemented, monoblock hemiarthroplasty through an antero-lateral approach, using a triple wound closure technique, which comprises monocryl, staples and glue.

## CONCLUSIONS

From the current evidence on Hip Hemi-Arthroplasty, the following conclusions can be drawn: (1) posterior approaches are associated with: a higher rate of dislocation compared to lateral and anterior approaches; and a higher rate of re-operation compared to lateral approaches. Thus for fracture-related hip hemi-arthroplasty, posterior approaches should be avoided; (2) while UH can be associated with increased rates of acetabular erosion at short-term follow-up (up to 1 year), there is no significant difference between unipolar and bipolar hemi-arthroplasty for surgical outcome, complication profile, functional outcome and acetabular erosion rates at longer-term follow-up (2 to 4 years). Thus, with bipolar hemi-arthroplasty being the more expensive prosthesis, UH is the recommended option; (3) while cemented hip hemi-arthroplasties are associated with a longer operative time compared to uncemented hip hemi-arthroplasties, cemented prostheses have lower rates of implant-related complications (particularly peri-prosthetic femoral fracture) and improved post-operative outcome regarding residual thigh pain and mobility. No other significant difference has been found between the two techniques, regarding medical complications and mortality. As such, cemented hip hemi-arthroplasty appear to be the superior technique; (4) there is insufficient evidence at present to accurately compare the outcome of modular to monoblock hemi-arthroplasty prostheses for femoral neck fractures. However, based on evidence from total hip arthroplasty and expert opinion, current recommendations advocate for "a proven femoral stem design" with a modular prosthesis, as opposed to a monoblock prosthesis; and (5) while staples can result in a quicker closure time, there is no significant difference in post-operative infection rates or wound healing outcomes when comparing staples to sutures. Thus, either suture or staple wound closure techniques appear equally appropriate for hip hemi-arthroplasty procedures.

## AUTHORS' CURRENT PRACTICE

Within the affiliated institution of the first author, the default choice for fracture-related hip hemi-arthroplasty

## REFERENCES

- 1 Royal College of Physicians. National Hip Fracture Database

- (NHFD) annual report 2017. London: Royal College of Physicians, 2017
- 2 **National Health Service Scotland.** Scottish Hip Fracture Audit: Hip Fracture Care Pathway Report 2017. Edinburgh: NHS National Services Scotland, 2017
  - 3 **Burge R,** Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. *J Bone Miner Res* 2007; **22:** 465-475 [PMID: 17144789 DOI: 10.1359/jbmr.061113]
  - 4 **Michael Lewiecki E,** Wright NC, Curtis JR, Siris E, Gagel RF, Saag KG, Singer AJ, Steven PM, Adler RA. Hip fracture trends in the United States, 2002 to 2015. *Osteoporos Int* 2018; **29:** 717-722 [PMID: 29282482 DOI: 10.1007/s00198-017-4345-0]
  - 5 **Leslie WD,** O'Donnell S, Jean S, Lagacé C, Walsh P, Bancej C, Morin S, Hanley DA, Papaioannou A; Osteoporosis Surveillance Expert Working Group. Trends in hip fracture rates in Canada. *JAMA* 2009; **302:** 883-889 [PMID: 19706862 DOI: 10.1001/jama.2009.1231]
  - 6 **Lee YK,** Ha YC, Park C, Koo KH. Trends of surgical treatment in femoral neck fracture: a nationwide study based on claim registry. *J Arthroplasty* 2013; **28:** 1839-1841 [PMID: 23523212 DOI: 10.1016/j.arth.2013.01.015]
  - 7 **Cooper C,** Campion G, Melton LJ 3rd. Hip fractures in the elderly: a world-wide projection. *Osteoporos Int* 1992; **2:** 285-289 [PMID: 1421796 DOI: 10.1007/BF01623184]
  - 8 **Court-Brown C,** McQueen MM, Tornetta P III, Einhorn TA, editors. Trauma. Philadelphia: Lippincott Williams & Wilkins, 2006
  - 9 **Thorngren KG,** Hommel A, Norrman PO, Thorngren J, Wingstrand H. Epidemiology of femoral neck fractures. *Injury* 2002; **33** Suppl 3: C1-C7 [PMID: 12423584 DOI: 10.1016/S0020-1383(02)00324-8]
  - 10 **Parker MJ,** Gurusamy K. Internal fixation versus arthroplasty for intracapsular proximal femoral fractures in adults. *Cochrane Database Syst Rev* 2006; CD001708 [PMID: 17054139 DOI: 10.1002/14651858.CD001708.pub2]
  - 11 **Rogmark C,** Johnell O. Primary arthroplasty is better than internal fixation of displaced femoral neck fractures: a meta-analysis of 14 randomized studies with 2,289 patients. *Acta Orthop* 2006; **77:** 359-367 [PMID: 16819672 DOI: 10.1080/17453670610046262]
  - 12 **Heetveld MJ,** Rogmark C, Frihagen F, Keating J. Internal fixation versus arthroplasty for displaced femoral neck fractures: what is the evidence? *J Orthop Trauma* 2009; **23:** 395-402 [PMID: 19550224 DOI: 10.1097/BOT.0b013e318176147d]
  - 13 **Jiang J,** Yang CH, Lin Q, Yun XD, Xia YY. Does Arthroplasty Provide Better Outcomes Than Internal Fixation At Mid- and Long-term Followup? A Meta-analysis. *Clin Orthop Relat Res* 2015; **473:** 2672-2679 [PMID: 25981713 DOI: 10.1007/s11999-015-4345-3]
  - 14 **Dai Z,** Li Y, Jiang D. Meta-analysis comparing arthroplasty with internal fixation for displaced femoral neck fracture in the elderly. *J Surg Res* 2011; **165:** 68-74 [PMID: 19552922 DOI: 10.1016/j.jss.2009.03.029]
  - 15 **Miyamoto RG,** Kaplan KM, Levine BR, Egol KA, Zuckerman JD. Surgical management of hip fractures: an evidence-based review of the literature. I: femoral neck fractures. *J Am Acad Orthop Surg* 2008; **16:** 596-607 [PMID: 18832603 DOI: 10.5435/00124635-200810000-00005]
  - 16 **National Institute for Health and Care Excellence.** Hip fracture: management 2011. London: National Institute for Health and Care Excellence, 2011
  - 17 **Hopley C,** Stengel D, Ekkernkamp A, Wich M. Primary total hip arthroplasty versus hemiarthroplasty for displaced intracapsular hip fractures in older patients: systematic review. *BMJ* 2010; **340:** c2332 [PMID: 20543010 DOI: 10.1136/bmj.c2332]
  - 18 **Wang F,** Zhang H, Zhang Z, Ma C, Feng X. Comparison of bipolar hemiarthroplasty and total hip arthroplasty for displaced femoral neck fractures in the healthy elderly: a meta-analysis. *BMC Musculoskelet Disord* 2015; **16:** 229 [PMID: 26316274 DOI: 10.1186/s12891-015-0696-x]
  - 19 **Carroll C,** Stevenson M, Scope A, Evans P, Buckley S. Hemiarthroplasty and total hip arthroplasty for treating primary intracapsular fracture of the hip: a systematic review and cost-effectiveness analysis. *Health Technol Assess* 2011; **15:** 1-74 [PMID: 21978400 DOI: 10.3310/hta15360]
  - 20 **Burgers PT,** Van Geene AR, Van den Bekerom MP, Van Lieshout EM, Blom B, Aleem IS, Bhandari M, Poolman RW. Total hip arthroplasty versus hemiarthroplasty for displaced femoral neck fractures in the healthy elderly: a meta-analysis and systematic review of randomized trials. *Int Orthop* 2012; **36:** 1549-1560 [PMID: 22623062 DOI: 10.1007/s00264-012-1569-7]
  - 21 **Goh SK,** Samuel M, Su DH, Chan ES, Yeo SJ. Meta-analysis comparing total hip arthroplasty with hemiarthroplasty in the treatment of displaced neck of femur fracture. *J Arthroplasty* 2009; **24:** 400-406 [PMID: 18701252 DOI: 10.1016/j.arth.2007.12.009]
  - 22 **Zhao Y,** Fu D, Chen K, Li G, Cai Z, Shi Y, Yin X. Outcome of hemiarthroplasty and total hip replacement for active elderly patients with displaced femoral neck fractures: a meta-analysis of 8 randomized clinical trials. *PLoS One* 2014; **9:** e98071 [PMID: 24854195 DOI: 10.1371/journal.pone.0098071]
  - 23 **Jameson SS,** Lees D, James P, Johnson A, Nachtsheim C, McVie JL, Rangan A, Muller SD, Reed MR. Cemented hemiarthroplasty or hip replacement for intracapsular neck of femur fracture? A comparison of 7732 matched patients using national data. *Injury* 2013; **44:** 1940-1944 [PMID: 23618782 DOI: 10.1016/j.injury.2013.03.021]
  - 24 **Leighton RK,** Schmidt AH, Collier P, Trask K. Advances in the treatment of intracapsular hip fractures in the elderly. *Injury* 2007; **38** Suppl 3: S24-S34 [PMID: 17723789 DOI: 10.1016/j.injury.2007.08.008]
  - 25 **Parker MJ,** Gurusamy KS, Azegami S. Arthroplasties (with and without bone cement) for proximal femoral fractures in adults. *Cochrane Database Syst Rev* 2010; CD001706 [PMID: 20556753 DOI: 10.1002/14651858.CD001706.pub4]
  - 26 **Parker MJ,** Pervez H. Surgical approaches for inserting hemiarthroplasty of the hip. *Cochrane Database Syst Rev* 2002; CD001707 [PMID: 12137630 DOI: 10.1002/14651858.CD001707]
  - 27 **van der Sijp MPL,** van Delft D, Krijnen P, Niggebrugge AHP, Schipper IB. Surgical Approaches and Hemiarthroplasty Outcomes for Femoral Neck Fractures: A Meta-Analysis. *J Arthroplasty* 2018; **33:** 1617-1627.e9 [PMID: 29398259 DOI: 10.1016/j.arth.2017.12.029]
  - 28 **Kunkel ST,** Sabatino MJ, Kang R, Jevsevar DS, Moschetti WE. A systematic review and meta-analysis of the direct anterior approach for hemiarthroplasty for femoral neck fracture. *Eur J Orthop Surg Traumatol* 2018; **28:** 217-232 [PMID: 28852880 DOI: 10.1007/s00590-017-2033-6]
  - 29 **Zhou Z,** Yan F, Sha W, Wang L, Zhang X. Unipolar Versus Bipolar Hemiarthroplasty for Displaced Femoral Neck Fractures in Elderly Patients. *Orthopedics* 2015; **38:** 697-702 [PMID: 26558663 DOI: 10.3928/01477447-20151016-08]
  - 30 **Jia Z,** Ding F, Wu Y, Li W, Li H, Wang D, He Q, Ruan D. Unipolar versus bipolar hemiarthroplasty for displaced femoral neck fractures: a systematic review and meta-analysis of randomized controlled trials. *J Orthop Surg Res* 2015; **10:** 8 [PMID: 25616914 DOI: 10.1186/s13018-015-0165-0]
  - 31 **Yang B,** Lin X, Yin XM, Wen XZ. Bipolar versus unipolar hemiarthroplasty for displaced femoral neck fractures in the elder patient: a systematic review and meta-analysis of randomized trials. *Eur J Orthop Surg Traumatol* 2015; **25:** 425-433 [PMID: 25476243 DOI: 10.1007/s00590-014-1565-2]
  - 32 **Veldman HD,** Heyligers IC, Grimm B, Boymans TA. Cemented versus cementless hemiarthroplasty for a displaced fracture of the femoral neck: a systematic review and meta-analysis of current generation hip stems. *Bone Joint J* 2017; **99-B:** 421-431 [PMID: 28385929 DOI: 10.1302/0301-620X.99B4.BJJ-2016-0758.R1]
  - 33 **Ning GZ,** Li YL, Wu Q, Feng SQ, Li Y, Wu QL. Cemented versus uncemented hemiarthroplasty for displaced femoral neck fractures: an updated meta-analysis. *Eur J Orthop Surg Traumatol* 2014; **24:** 7-14 [PMID: 23412274 DOI: 10.1007/s00590-012-1151-4]
  - 34 **Luo X,** He S, Li Z, Huang D. Systematic review of cemented versus uncemented hemiarthroplasty for displaced femoral neck

- fractures in older patients. *Arch Orthop Trauma Surg* 2012; **132**: 455-463 [PMID: 22160512 DOI: 10.1007/s00402-011-1436-9]
- 35 **Sims AL**, Farrier AJ, Reed MR, Sheldon TA. Thompson hemiarthroplasty versus modular unipolar implants for patients requiring hemiarthroplasty of the hip: A systematic review of the evidence. *Bone Joint Res* 2017; **6**: 506-513 [PMID: 28851695 DOI: 10.1302/2046-3758.68.BJR-2016-0256.R1]
- 36 **Scottish Intercollegiate Guidelines Network**. Management of hip fracture in older people - A national clinical guideline. Edinburgh: NHS National Services Scotland, 2009
- 37 **Sims AL**, Parsons N, Achten J, Griffin XL, Costa ML, Reed MR; CORNET trainee collaborative. A randomized controlled trial comparing the Thompson hemiarthroplasty with the Exeter polished tapered stem and Unitrax modular head in the treatment of displaced intracapsular fractures of the hip. *Bone Joint J* 2018; **100-B**: 352-360 [PMID: 29589786 DOI: 10.1302/0301-620X.100B3.BJJ-2017-0872.R2]
- 38 **Krishnan R**, MacNeil SD, Malvankar-Mehta MS. Comparing sutures versus staples for skin closure after orthopaedic surgery: systematic review and meta-analysis. *BMJ Open* 2016; **6**: e009257 [PMID: 26792213 DOI: 10.1136/bmjopen-2015-009257]
- 39 **Smith TO**, Sexton D, Mann C, Donell S. Sutures versus staples for skin closure in orthopaedic surgery: meta-analysis. *BMJ* 2010; **340**: c1199 [PMID: 20234041 DOI: 10.1136/bmj.c1199]

**P- Reviewer:** Drampalos E, Elgafy H, Fanter NJ **S- Editor:** Wang JL  
**L- Editor:** A **E- Editor:** Wu YXJ



## Biomechanics of posterior shoulder instability - current knowledge and literature review

Henrik Constantin Bäcker, Samuel E Galle, Mauro Maniglio, Melvin Paul Rosenwasser

Henrik Constantin Bäcker, Samuel E Galle, Melvin Paul Rosenwasser, Department of Orthopedic Surgery, New York Presbyterian/Columbia University Medical Center, New York, NY 10032, United States

Mauro Maniglio, Department of Orthopedics, HFR Cantonal Hospital of Fribourg, Fribourg 1752, Switzerland

ORCID number: Henrik Constantin Bäcker (0000-0002-4265-477X); Samuel E Galle (0000-0002-1740-9959); Mauro Maniglio (0000-0001-7748-0389); Melvin Paul Rosenwasser (0000-0002-0516-3824).

**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.

**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:** Henrik Constantin Bäcker, MD, Academic Fellow, Research Fellow, Senior Postdoctoral Fellow, Surgeon, Department of Orthopedic Surgery, Columbia University Medical Center - Presbyterian Hospital, 622 West, 168th Street, 11th floor, Apartment 64, New York, NY 10032, United States. [hb2573@cumc.columbia.edu](mailto:hb2573@cumc.columbia.edu)  
Telephone: +1-212-3053912  
Fax: +1-212-3421749

Received: July 12, 2018

Peer-review started: July 12, 2018

First decision: August 2, 2018

Revised: August 7, 2018

Accepted: October 10, 2018

Article in press: October 10, 2018

Published online: November 18, 2018

### Abstract

Posterior instability of the shoulder is a rare condition and represents about 10% of shoulder instability. It has become more frequently recognized in the last year, even though it is more difficult to diagnose than anterior shoulder instability. As this form of shoulder pathology is somewhat rare, biomechanical knowledge is limited. The purpose of our study was to perform an extensive literature search, including PubMed and Medline, and to give an overview of the current knowledge on the biomechanics of posterior shoulder instability. The PubMed/Medline databases were utilized, and all articles related to posterior shoulder instability and biomechanics were included to form a comprehensive compilation of current knowledge. A total of 93 articles were deemed relevant according to our inclusion and exclusion criteria. As expected with any newly acknowledged pathology, biomechanical studies on posterior shoulder instability remain limited in the literature. Current biomechanical models are performed in a static manner, which limits their translation for explaining a dynamic pathology. Newer models should incorporate dynamic stabilization of both the rotator cuff and scapulothoracic joint. There is a current lack of knowledge with regards to the pathomechanism of posterior shoulder instability, with no consensus on appropriate treatment regimens. Further investigation is therefore required at both basic science and clinical levels.

**Key words:** Posterior shoulder instability; Anatomy; Shoulder complex; Scapula; Humerus; Glenohumeral

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Posterior shoulder instability is an infrequent

type of injury, and there is limited discussion of this topic within the literature. Other authors have acknowledged the current paucity of papers on this topic. To our knowledge, no comparable literature review has been performed showing the interactions of the individual shoulder parts, including the osseous structures, capsule, labrum, ligaments and muscles<sup>[1]</sup>. This article aspires to help develop new protocols to investigate shoulder instability and inform clinicians about the importance of this topic in daily practice.

Bäcker HC, Galle SE, Maniglio M, Rosenwasser MP. Biomechanics of posterior shoulder instability - current knowledge and literature review. *World J Orthop* 2018; 9(11): 245-254 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i11/245.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i11.245>

## INTRODUCTION

The shoulder joint is the least congruent joint in the human body and thus has a tremendous potential range of motion with daily activities. These movements are a well-balanced and complex interplay between the osseous structures (scapula, humeral head and clavicle) and the surrounding soft tissue, consisting of shoulder capsule, ligamentous, labral and muscular stabilizers. Dysfunction of one or more of these components through injury, degeneration or congenital abnormalities may lead to shoulder instability with concomitant pain and dysfunction. Anterior laxity or dislocation occurs more commonly than the posterior equivalent and is thus more discussed in the literature. However, posterior instability is an equally important cause of patients pain and loss of shoulder function.

The first reported case of posterior shoulder instability was published by White *et al* in 1741<sup>[2]</sup>, followed by a case study in 1839<sup>[3]</sup> and a clinical case series in 1855<sup>[4]</sup>. A variety of pathologies have been described regarding posterior shoulder instability, such as atraumatic lesions in ligamentous laxity, repetitive microtrauma (especially in overhead-throwing athletes or the active duty military population) and traumatic posterior luxation<sup>[5,6]</sup>. In repetitive microtrauma, shearing forces may cause a loss of chondrolabral containment (e.g., frank labral tear)<sup>[7,8]</sup>.

Classifications for recurrent posterior subluxation have been established according to its anatomical and biomechanical properties. It can be distinguished between volitional (ability to subluxate the shoulder using abnormal patterns of muscular activity), dysplastic (due to glenoid retroversion or humeral head retrotorsion) and acquired posterior shoulder dislocation (caused by soft tissue deficiency, bony deficiency or scapulothoracic dysfunction)<sup>[5,9]</sup>.

## LITERATURE SEARCH

A comprehensive literature search was conducted using PubMed/MEDLINE databases (US National Library of

Medicine, National Institutes of Health) for shoulder instability and biomechanics/anatomy of the shoulder between 1957 and 2017. The search terms were intentionally broad to maximize capture of the relevant literature. The following keywords were used: "posterior shoulder instability" ( $n = 1026$ ), "shoulder biomechanics" ( $n = 1389$ ) and "posterior shoulder instability anatomy" ( $n = 295$ ). Articles in English, German and French were included. All papers that both evaluated the biomechanics on posterior shoulder instability as well as described the anatomy in patients who suffered from posterior shoulder instability were included. Exclusion criteria included duplicate results, non-relevant articles that did not involve posterior shoulder instability or biomechanical studies, and letters to the editors or comments.

In total, 2710 abstracts were reviewed, of which 40 articles were duplicates and further 2542 did not investigate shoulder instability or the biomechanics of the shoulder complex. One hundred-twenty-eight full text articles were reviewed, of which 35 studies were excluded as these ones did not meet inclusion criteria. Finally, leaving 93 studies for our review. These included papers describing the biomechanics of anterior and posterior shoulder instability, the anatomy of the shoulder complex, as well as the clinical aspects.

## CLINICAL PRESENTATION OF POSTERIOR SHOULDER INSTABILITY

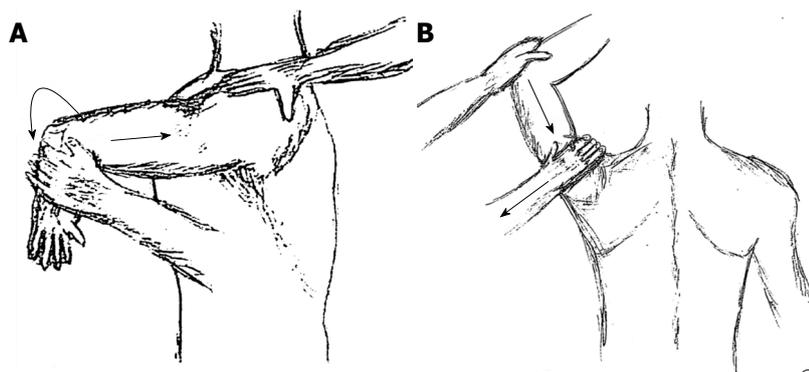
### Incidence

The incidence of posterior shoulder instability is between 2%-5% of all shoulder dislocations<sup>[10]</sup>. According to the literature, it may be under- or mis-diagnosed due to the lack of both awareness and experience of treating physicians. A significant proportion (62.5%) of patients who failed surgery and suffered from ongoing instability were diagnosed with unidirectional, posterior shoulder instability. Those patients demonstrated signs of inferior or multi-directional instability prior to revision surgery, which may be related to the capsular laxity. This appears to be an underestimation - 75% of these patients did not show labral tear, yet would have required more aggressive stabilization<sup>[11]</sup>.

### Current knowledge of biomechanics

In the beginning of the investigation, the mechanism was simply believed to be the counterpart to anterior shoulder instability<sup>[12-14]</sup>. Later on, this paradigm was questioned by several researchers, who described the posterior shoulder instability as a unique injury condition<sup>[15-17]</sup>.

Generally, posterior shoulder dislocation has been described in the setting of 90° forward elevation, adduction and internal rotation of the humerus<sup>[17-19]</sup>. Assumingly, the humerus then dislocates either posteriorly through rupture of the posterior band of the inferior glenohumeral ligament (IGHL) or posterior inferiorly through rupture of the whole posteriorIGHL<sup>[20]</sup>. Unfortunately, the exact biomechanical mechanism of posterior shoulder instability is not well



©2018 Henrik Constantin Bäcker all rights reserved

**Figure 1 Jerk test and Kim test.** A: Jerk test: The patient is sitting, their arm is flexed to 90° and internally rotated. An axial loading and horizontal adduction is applied; B: Kim test: The patient is sitting and the arm is abducted to 90° at the beginning. The examiner elevates the arm approximately 45° while applying postero-inferior force to the upper arm and axial load to the elbow. In a positive test, a subluxation of the glenohumeral joint can be observed.

understood or described to date.

### Clinical presentation

Posterior shoulder dislocation patients present with generalized symptoms about the shoulder and commonly include an intense discomfort with inability to mobilize the shoulder joint. This may be related to excessive stretching of the muscles or the joint capsule during the dislocation itself<sup>[21]</sup>. For clinical examination, the Kim test shows the highest sensitivity of 80% and specificity of 90%. Further examinations like the Jerk test, posterior apprehension test and stress test are useful to estimate the stability and dislocation tendency. The Jerk test is the most reliable diagnostic examination, however may only be pathologic in 4 of 50 patients suffering from posterior shoulder instability<sup>[22]</sup>. When performing the anterior apprehension test, patients may feel inconvenienced with a slight anterior subluxation. However, this test is neither sensitive nor specific<sup>[23]</sup>. The Kim test and Jerk test are illustrated in Figure 1.

### Radiographic signs

**X-ray and computed tomography:** To exclude any osseous lesions and diagnose posterior shoulder dislocation, an anteroposterior, lateral and axillary radiograph should be performed. Furthermore, computed tomography (CT) may help identify injuries of the shoulder complex, such as reverse Bankart lesions or, when performing with intraarticular contrast, labral lesions. Displacement of the humeral head in relation to the glenoid, reverse Hill Sachs lesions or posterior Bankart/glenoid lesions may be pathognomonic for posterior shoulder instability but not necessarily present in all cases.

**Magnetic resonance imaging:** Magnetic resonance imaging (MRI) is an invaluable tool to assess soft tissue lesions about the shoulder. In patients who have suffered a posterior shoulder dislocation, a labral tear of the posterior wall or edema in the posterior humeral head is typically present. Furthermore, other patholo-

gical conditions can be excluded, such as superior, anterior posterior labral lesions or rotator cuff tears masquerading as posterior instability (Figure 2 provided by Dr. Charles M. Jobin). When comparing conventional MRI with MR arthrography, MR arthrography is superior to assess glenohumeral pathology, Perthes lesions and labral tears<sup>[24]</sup>.

The rigor of MRI and CT arthrograms in posterior shoulder instability is summarized in Table 1.

## SHOULDER JOINT COMPLEX IN POSTERIOR SHOULDER DISLOCATION

The glenohumeral, scapulothoracic, acromioclavicular and sternoclavicular joints can be summarized as the shoulder complex. A full range of motion, including protraction/retraction, elevation/depression, anterior/posterior tilt, internal/external and upward/downward rotation can only be achieved in combination with each individual joint<sup>[25]</sup>. The complex can be divided into osseous and soft tissue structures, enabling stability and facilitating anatomic motion.

### Osseous

**Scapula:** The scapula lies on ribs two through seven and has a triangular shape<sup>[26,27]</sup>. It is solely stabilized by soft tissue restraints through a series of bursal and muscular planes. Its position is obliquely in between the frontal and sagittal planes. Besides a slight abduction by 3°, it is located 30°-45° anterior to the coronal plane, with a slight anterior tilt between 9°-20° in the sagittal plane in relation to the vertical line of the spine<sup>[25]</sup>.

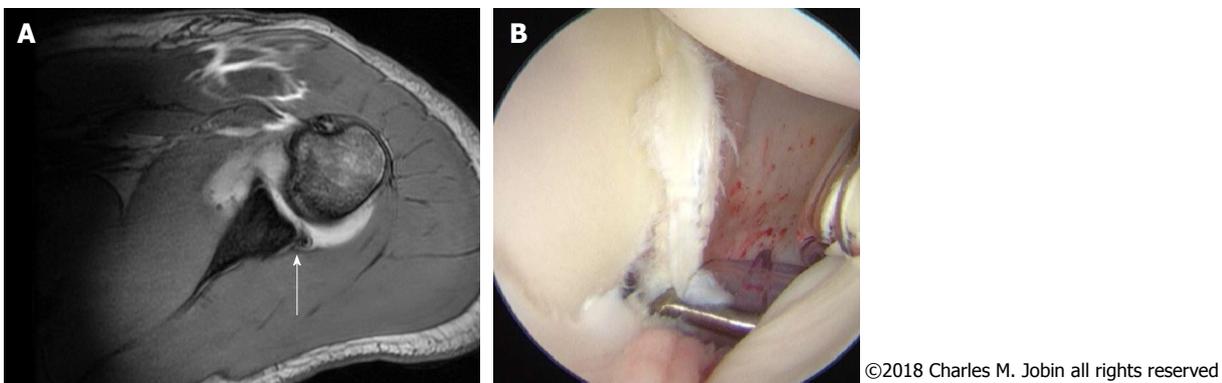
Multiaxial articulation can be enabled by the scapulothoracic joint between the humerus and the thorax. When elevating the humerus above 90° in the coronal plane, the scapular mainly rotates laterally in the coronal plane with less protraction in all three planes. At 30° and 40° of humeral elevation, a significant backward tilt occurs in the sagittal plane.

The glenoid cavity, which forms the articular surface of the glenohumeral joint, is concave in shape and

**Table 1** The role of computed tomography scans, magnetic resonance imaging arthrograms and diagnostic rigor

	CT arthrography	MRI arthrography
Sensitivity	82%-100% <sup>[75]</sup>	48%-89% <sup>[76,77]</sup>
Specificity	96%-100% <sup>[75]</sup>	93% <sup>[77]</sup>
Advantage	Identifying bony lesions, severity of fractures, assessing humeral and glenoid version <sup>[78]</sup>	Identifying the soft tissue from labrum to the rotator cuff <sup>[80]</sup> , good for preoperative classification of labroligamentous injuries <sup>[81]</sup>
Disadvantage	lower inter-examiner reliability <sup>[79]</sup>	
	Radiation	Limited in elderly patients <sup>[80]</sup>
Pathologies	Small soft tissue lesions <sup>[82]</sup> Bony lesions/ fractures (Bankart fragments, Hill-Sachs Lesion) <sup>[82,83]</sup> Accurate in labroligamentous, cartilaginous lesions <sup>[75]</sup>	Avulsion of posterior periosteum <sup>[82]</sup> Medial displacement of the labrum (posterior labro-scapular sleeve avulsion) <sup>[84]</sup> Kim lesion - incomplete and concealed superficial tear in the posterior glenoid labrum Glenoid rim articular divot lesion <sup>[7]</sup> Chondral loose bodies <sup>[85]</sup>

CT: Computed tomography scans; MRI: Magnetic resonance imaging.



**Figure 2** Posterior labral tear. A: Posterior labral tear in magnetic resonance arthrography; B: Intraoperative finding of a posterior labral tear and posterior SLAP tear.

slightly retroverted 6.2°<sup>[28]</sup>. An abnormal glenoid shape, such as higher retroversion or smaller cavities, leads to a higher glenohumeral index (the relationship between the humeral head and glenoid). This may predispose posterior shoulder instability<sup>[29-31]</sup>, although some authors were unable to reproduce this finding<sup>[32]</sup>.

The most important osseous feature of the scapula is the coracoid process, which is tilted approximately 120°-160° anterolaterally<sup>[33]</sup>. It has several attachments, which have major impact on posterior instability: the coracobrachial muscle, the short head of the biceps brachii muscle, the pectoralis minor muscle, the coracohumeral ligament (although in a few cases they insert in the pectoralis minor muscle<sup>[34]</sup>), the coracoacromial ligament, as well as the coracoclavicular ligament. The individual function and mechanism of stabilization are discussed in full detail below.

The most frequent osseous lesion of the scapula involved during a posterior shoulder dislocation is the reverse Bankart lesion. It is located mainly in the posterior-inferior quarter of the glenoid (86%), and leads to an 86% increase in posterior translation and 31% increase in inferior translation of the humerus in the sulcus position. In patients with posterior capsular tears or posterior Bankart lesions, a bidirectional instability must be suspected<sup>[35]</sup>.

In large glenoid defects, a posterior bone block

transfer can be performed to extend the glenoid surface rather than reconstruct the glenoid anatomically. Additional indications for posterior bone block transfer include glenoid erosions, failure of primary capsular plication or congenital abnormalities. This procedure can be considered the counterpart to the Latarjet procedure, and was first described by Hindenach in 1947<sup>[36]</sup>.

Overall, the posterior bone block transfer procedure shows poor results, with a high rate of osteoarthritis in long-term follow-up, although three of 11 patients were pleased with it<sup>[36]</sup>.

In patients who suffer from higher glenoid retroversion (more than 15°-20°) with intact soft tissue, an open wedge osteotomy may be the treatment of choice. DeLong *et al.*<sup>[37]</sup> performed a systematic literature review, stating that posterior glenoid osteotomy does not show any good results in terms of return to pre-injury athletic level<sup>[22,38]</sup>.

**Humeral head:** The humeral head presents anatomically with a retroversion of 25°-35° (related to the condyles of the elbow) and an inclination of about 130° related to the shaft<sup>[39,40]</sup>. It consists of hyaline cartilage (thickest in the center) and forms a true sphere<sup>[41,42]</sup>. Tendinous and ligamentous attachments form a ring to tighten and centralize the humeral head, placing it in the middle of the glenoid cavity<sup>[43,44]</sup>. Even though no

data exist, it is likely that retroversion of  $> 35^\circ$  in the humeral head may predispose posterior luxation, similar to retroversion of the glenoid.

**Glenohumeral joint:** The glenohumeral joint permits movement with many degrees of freedom, including flexion-extension, abduction-adduction, circumduction and medial-lateral rotation. Humeral motion is possible in the frontal, coronal/sagittal and scapular planes<sup>[25,45]</sup>.

Damage of articular cartilage and reverse Hill Sachs lesions, also called Malgaigne fractures, are rather infrequent complications of posterior shoulder instability. In high traumatic injuries, Malgaigne fractures may lead to painful clicking or catching in movements, which may worsen the damage and lead to further injuries.

Surgical correction of a reverse Hill Sachs lesion includes the McLaughlin procedure, where the subscapularis tendon is transferred into the bony defect. Other procedures include implantation of bone allograft or humeral osteotomy when the retroversion may be suspected to predispose the instability. Rotational osteotomies have shown fair results, and one paper demonstrated a 50% return to a pre-injury level of activity<sup>[46]</sup>.

**Clavicle:** The clavicle is less important than the scapula for posterior shoulder instability. Nevertheless, the S-shape bone does provide some elasticity, some component of shock absorption and forms a strut holding the glenohumeral joint in the parasagittal plane. At rest, it is tilted slightly superior by  $10^\circ$ - $12^\circ$ <sup>[25]</sup>. Major impact on the rotation in the coronal plane could be observed which increases from  $3^\circ$ - $20^\circ$  to  $21^\circ$ - $150^\circ$  of humeral elevation. Clavicle posterior rotation was increased by elevation in the sagittal plane between  $20^\circ$  at  $90^\circ$  to  $27^\circ$  at  $150^\circ$  of elevation as well as protraction from  $-17^\circ$  to  $-45^\circ$ <sup>[47]</sup>.

The acromioclavicular joint is a synovial joint allowing anterior/posterior and internal/external rotation over the lateral end of the clavicle<sup>[48]</sup>. The sternoclavicular joint enables elevation and depression of the clavicle as well as protraction and retraction<sup>[48,49]</sup>.

In an intact clavicle, the degree of freedoms are external rotation, upward rotation and posterior tilting, which are greatest in the sagittal plane, thus enabling more stabilization and support in glenohumeral joint motion<sup>[50]</sup>.

According to Poppen *et al.*<sup>[45]</sup>, the relation between the glenohumeral and scapulothoracic movement has a ratio of 4.3:1, with an upward translation of 3 mm. When abducting the humerus, a counterclockwise rotation of the scapula in the frontal plane is accompanied. Hereby, a rotation of the clavicle can be noted up to a taut costoclavicular ligament. After initial abduction by  $30^\circ$ , the glenohumeral and scapulothoracic joint movements occur simultaneously and facilitate elevation. Approximately  $40^\circ$  of abduction is enabled by the sternoclavicular joint, and  $20^\circ$  by the acromioclavicular joint<sup>[25,51]</sup>.

### Soft tissue

With regards to the pathology of posterior shoulder instability, resistance to injury is provided substantially by the soft tissue. Most important are the subscapularis muscle, the coracohumeral ligament in neutral rotation, the coracohumeral ligament and the posterior band of the IGHL in internal rotation<sup>[20]</sup>.

**Shoulder capsule:** It is believed that posterior instability is initiated by insufficiency of the capsule, which secondarily leads to laxity of the joint. Various angles of humerus abduction have been investigated, and emphasize the importance of the posterior capsule and the IGHL as significant stabilizers<sup>[52,53]</sup>. About 90% of patients show a rupture of the posterior capsule mainly on the scapular side after posterior shoulder dislocation. Ovesen *et al.*<sup>[17,54]</sup> noted that between  $40^\circ$ - $90^\circ$  of abduction of the major stability is conferred by the entire posterior capsule. When sectioning posterior structures such as the teres minor, infraspinatus muscles and proximal half of the posterior capsule, there was a significant increase in posterior displacement.

Tears of the lower and proximal half of the posterior capsule have only little impact on stability in internal rotation (mainly above  $40^\circ$  of abduction). An entire rupture of the posterior capsule increases displacement in the last part of abduction, though not significantly. In cases of posterior structure trauma, an increase in anterior instability can also be seen<sup>[54]</sup>.

On the other hand, lesions of the anterior capsule show even more impact on the posterior stability. The anterior capsule strengthens the glenohumeral ligaments by close adherence of the coracohumeral ligaments (superiorly), as well as the teres minor and infraspinatus tendons (posteriorly), and tightens in various positions. When sectioning the entire anterior capsule, posterior displacement significantly increases in abduction between  $0^\circ$ - $90^\circ$ <sup>[17]</sup>.

**Labrum:** The labrum is a circumferential soft tissue extension of the bony glenoid rim, which is loosely attached to the surrounding capsule. It allows compressing forces, called "concavity compression", for stabilization and enables centralization of the humeral head<sup>[55]</sup>. In 52%-66%, a posterior labrum defect (also called posterior/reverse Bankart lesion) can be found after traumatic posterior shoulder dislocation<sup>[56]</sup>. No consensus exists on the association between posterior capsular laxity and reverse Bankart lesions<sup>[53,57]</sup>.

**Ligaments:** There are several ligaments that provide passive glenohumeral stabilization and help control the external forces on glenohumeral articulation.

The coracohumeral ligament is divided into a superficial and deep layer. The deep layer inserts into the rotator interval. It consists of fibers originating from the coracoid process and crisscrossing the supraspinatus and subscapularis muscles. These fibers form the pulley

system that stabilizes the long head of the biceps at the entrance into the sulcus bicipitalis<sup>[57,58]</sup>. It allows external rotation and resists inferior and posterior translation in the suspended shoulder, which enables resistance to posterior subluxation in the neutral position<sup>[20,58]</sup>.

Three main strands build the glenohumeral ligament: the superior, middle and IGHL. The influence of the IGHL on shoulder stability is well-described. It is a thickening of the capsule with a prominent anterior band (between 2-4 o'clock)<sup>[59]</sup> and a less prominent posterior branch. Typically, the posterior band or IGHL ruptures (posterior inferior part) in posterior dislocation (23 Blasler 1997), which can be provoked by elevation to 90° and abduction of internal rotation.

Today, most stabilization procedures are performed arthroscopically and target the capsulolabral complex. Surgical techniques can be divided into those inclusive or exclusive of suture anchor capsulolabral repair.

Bradley *et al.*<sup>[60]</sup> suggests using suture-anchor capsulolabral repair in completely- or partially-detached labral injury patterns. He stated a success rate of 92% and 68%, respectively, returning to baseline sport when using suture anchors; otherwise, 84% and 48%, respectively, without suture anchors. The overall satisfaction is stated to be 94%, as measured using the American Shoulder and Elbow Surgeons Shoulder (ASES) score<sup>[60]</sup>. Savoie *et al.*<sup>[53]</sup> published a study stating that the success rate was 97% based on the Neer Foster rating scale in 92 patients after arthroscopically capsulolabral repair. The overall satisfaction in those patients who returned to sport at a pre-injury level was approximately 63.5%, and the mean ASES score improved from 45.9 to 85.1<sup>[53,60]</sup>. Unfortunately, arthroscopic methods are somewhat limited, as the technique is not able to address severe erosions of the glenoid bone or retroversion of the glenoid exceeding 15°-20°, nor volitional instability<sup>[30,61]</sup>.

A rather infrequent method is capsulorrhaphy, which shows good to excellent results in 73.3%; however 3 patients experienced recurrent instability according to Bisson *et al.*<sup>[62]</sup>. It should be noted that surgical indications in this study were very closely controlled, as only patients with isolated posterior instability without labral detachment underwent this technique.

**Muscles:** There are 17 muscles with origins or insertions at the scapula, and these can be classified according to their function and location. Three main groups exist: Scapular stabilizers ( $n = 6$ ), Rotator cuff ( $n = 4$ ) and Scapulohumeral muscles ( $n = 6$ ). The omohyoid muscle is not included in this simple classification, as it originates from the superior border of the scapula yet functionally depresses the larynx and hyoid. All tendons of the rotator cuff interact intricately with the fibrous capsule, which allows dynamic stabilization and movement of the glenohumeral joint. This group includes the infraspinatus, subscapularis, supraspinatus and teres minor. After posterior shoulder dislocation, a rupture of the teres minor and infraspinatus tendon is

present in most of the cases (90% partial, 10% total rupture)<sup>[25]</sup>.

Biomechanical investigations after teres minor tenotomy demonstrate an increase of internal rotation by 7° at 30°-40° of humeral abduction compared to an intact glenohumeral joint. Similarly, infraspinatus tenotomies show a significant increase in internal rotation between 0° and 30°-50° of abduction<sup>[32,54,63]</sup>.

The scapular stabilizers include the levator scapulae (elevates and rotates the scapula), the pectoralis minor (protracts, rotates downwards and depresses the scapula), the major and minor rhomboid muscles (retract and elevate the scapula to depress the glenoid cavity, the serratus anterior (performs protraction and upward scapular rotation) and the trapezius muscle (a passive and dynamic scapular stabilizer, active elevator of the lateral scapular angle, scapular retractor and rotator). The pectoralis major, which does not attach the scapula, potentiates the scapulothoracic stabilization of the latissimus dorsi and deltoid muscle. This leads to a space in scapulothoracic articulation between the surface of the posterior thoracic cage and the subscapular fossa<sup>[25,58]</sup>, thus facilitating gliding movement.

The last group includes the scapulohumeral muscles, which are responsible for stabilizing the humeral head. The biceps brachii muscle attaches with both heads to the scapula, the long and short head which work as elbow flexors and forearm supinators. Its antagonist muscle is the triceps brachii muscle long head, which extends the elbow as well as acts as an adductor of the elbow and of the humerus. Flexion and adduction of the humerus is performed by the coracobrachial muscle, and the prime mover of the glenohumeral abduction, flexion, extension and adduction of the humerus is the deltoid muscle. The latissimus dorsi and teres major muscles perform adduction, internal rotation of the humerus, rotation of the trunk (latissimus dorsi) and extension of the humerus (teres major)<sup>[44,64]</sup>.

### Treatment

In the literature, several different treatment algorithms have been developed based on bony defects, osteoarthritis and the physical state of patients<sup>[65-68]</sup>. In athletes, authors tend to be a bit more aggressive in terms of surgical procedures. Guehring *et al.*<sup>[69]</sup> additionally considers the time interval between trauma and surgery. Conservative therapy is a reasonable initial treatment, as one study demonstrated a subjective improvement after 6 mo in 70%-89% of patients. To avoid repetitive dislocation, certain exercises (internal rotation and horizontal adduction) and activities should be avoided for life<sup>[70-72]</sup>.

Directly after trauma, the shoulder should be kept in slight external or neutral rotation to avoid any stress to the posterior capsule. In physical therapy, a general strengthening of the dynamic muscular stabilizers is essential. This includes the rotator cuff (with focus on external rotation), infraspinatus muscle, teres minor,

**Table 2** Different therapeutic options and considerations of posterior shoulder instability

Procedure	Consideration	Success rate
Conservative	Leads to loss of rotation and deformity of the shoulder, mainly performed in elderly patients	68%-77%, however only in isolated posterior shoulder instability; recurrence rate up to 96% <sup>[38,86]</sup>
Capsular-labral repair ( <i>i.e.</i> , post. - inf. capsular shift) or reverse Bankart repair	In isolated unidirectional posterior instability	96% in post. - inf. capsular shift <sup>[73]</sup> 91% in posterior capsulorrhaphy in isolated post. instability <sup>[5]</sup> Posterior Bankart repair – 93% <sup>[87]</sup>
Other procedures not/or rarely performed:		
Thermal capsulorrhaphy	High recurrence rate	57%, capsular insufficiency 33% <sup>[88,89]</sup>
Posterior bone block or posterior wedge osteotomy	After failed capsular plication, or congenital formations	Posterior glenoid transfer: 53%; 41% complication rate <sup>[22,90]</sup> Posterior bone block: 45%; 36% osteoarthritis <sup>[36]</sup>
McLaughlin's procedure	In patients with locked posterior shoulder dislocation from reverse Hill-Sachs lesions	improvement in average constant scoring system from 16 preoperatively to 72 postoperatively <sup>[91]</sup>
Humeral head allograft	Alternative option to McLaughlin's procedure	Complication rate between 25%-50% <sup>[92,93]</sup>

periscapular muscles (for scapulohumeral rhythm) and posterior deltoid muscle<sup>[73]</sup>. The aim of physiotherapeutic exercises is to compensate for the injured static structures of bone and tissue<sup>[68,74]</sup>.

For postoperative care, various protocols have been described. The shoulder is immobilized with an orthosis in 30° of abduction and 0° of rotation to prevent internal rotation. Cryotherapy is recommended and active elevation should be avoided for at least 4 wk. In the following weeks, passive and active assisted movements are recommended, followed by full passive and active range of motion 2 to 3 mo after. When the muscle strength is at least 80% of the contralateral side, a sport-specific rehabilitation program can be pursued, which is generally 6 mo post-operatively<sup>[36,60,74]</sup>.

As there are only a few evidence-based studies regarding treatment protocols and techniques, it is difficult to develop a uniform algorithm. The different treatment options, such as conservative and operative treatment, and success rates are summarized in Table 2.

## CONCLUSION

Posterior shoulder instability seems to be underdiagnosed due to its complexity and limited diagnostic examinations in general practice. So far, no real consensus on classification of posterior shoulder instability exists. Moreover, the correct mechanism of injury is not well understood, which has led to a lack of consensus regarding treatment regimens and general awareness by physicians.

Posterior shoulder instability can be provoked according to the Kim/Jerk test in forward flexion, adduction and internal rotation. A variety of reasons for posterior shoulder instability have been described. The most important ones are capsular lesions, especially anterior ones as well as ruptures of the IGHL. Patients who suffered from posterior shoulder dislocation mostly suffer from a rupture of the posterior capsule, loosening of the posterior labrum, and a rupture of the teres minor and/or infraspinatus tendon. This increases the risk of recurrent posterior shoulder instability, especially in abduction between 0°-90°. Further predisposing conditions, which

have not yet been well investigated, include retroversion of the glenoid or humeral head.

Current treatment options vary in outcome in long-term follow-up. Currently, the best results have been observed using arthroscopic capsulolabral repair in conjunction with a careful postoperative management, with a delay in return to sport of about 4-6 mo.

With regards to the current biomechanical literature describing posterior shoulder dislocations, the predominant form of experimentation has used a static glenohumeral model. To our knowledge, no dynamic model yet exists to investigate the entire shoulder complex, including the scapulothoracic joint.

## ACKNOWLEDGEMENTS

The authors would like to thank Dr. Charles M Jobin for his assistance and for providing the MR arthrography and intraoperative imaging, as well as Lee Ann Finno for her administrative support.

## REFERENCES

- Xu W, Huang LX, Guo JJ, Jiang DH, Zhang Y, Yang HL. Neglected posterior dislocation of the shoulder: A systematic literature review. *J Orthop Translat* 2015; 3: 89-94 [PMID: 30035045 DOI: 10.1016/j.jot.2015.02.004]
- Loebenberg MI, Cuomo F. The treatment of chronic anterior and posterior dislocations of the glenohumeral joint and associated articular surface defects. *Orthop Clin North Am* 2000; 31: 23-34 [PMID: 10629330 DOI: 10.1016/S0030-5898(05)70125-5]
- Cooper A. On the dislocations of the os humeri upon the dorsum scapulae and upon fractures near the shoulder joint. *A Guys Hosp Rep* 1839; 4: 265-284
- Malgaigne JF. *Traité des fractures et des luxations*. Paris: JB Bailliere; 1855
- Fronek J, Warren RF, Bowen M. Posterior subluxation of the glenohumeral joint. *J Bone Joint Surg Am* 1989; 71: 205-216 [PMID: 2918005 DOI: 10.2106/00004623-198971020-00006]
- Nho SJ, Frank RM, Van Thiel GS, Wang FC, Wang VM, Provencher MT, Verma NN. A biomechanical analysis of shoulder stabilization: posteroinferior glenohumeral capsular plication. *Am J Sports Med* 2010; 38: 1413-1419 [PMID: 20522831 DOI: 10.1177/0363546510363460]
- Kim SH, Ha KI, Yoo JC, Noh KC. Kim's lesion: an incomplete and concealed avulsion of the posteroinferior labrum in posterior

- or multidirectional posteroinferior instability of the shoulder. *Arthroscopy* 2004; **20**: 712-720 [PMID: 15346113 DOI: 10.1016/j.arthro.2004.06.012]
- 8 **Provencher MT**, King S, Solomon DJ, Bell SJ, Mologne TS. Recurrent Posterior Shoulder Instability: Diagnosis and Management. *Oper Tech Sports Med* 2005; **13**: 196-205 [DOI: 10.1053/j.otsm.2006.01.004]
  - 9 **Lamar DS**, Williams GR, Iannotti JP, Ramsey ML. Posterior Instability of the Glenohumeral Joint: Diagnosis and Management. *The University of Pennsylvania Orthopaedic Journal* 2001; **14**: 5-14
  - 10 **Steinmann SP**. Posterior shoulder instability. *Arthroscopy* 2003; **19** Suppl 1: 102-105 [PMID: 14673426 DOI: 10.1016/j.arthro.2003.09.033]
  - 11 **Bradley JP**, Baker CL 3rd, Kline AJ, Armfield DR, Chhabra A. Arthroscopic capsulolabral reconstruction for posterior instability of the shoulder: a prospective study of 100 shoulders. *Am J Sports Med* 2006; **34**: 1061-1071 [PMID: 16567458 DOI: 10.1177/0363546505285585]
  - 12 **Harryman DT 2nd**, Sidles JA, Clark JM, McQuade KJ, Gibb TD, Matsen FA 3rd. Translation of the humeral head on the glenoid with passive glenohumeral motion. *J Bone Joint Surg Am* 1990; **72**: 1334-1343 [PMID: 2229109 DOI: 10.2106/00004623-199072090-00009]
  - 13 **Lippitt SB**, Vanderhooft JE, Harris SL, Sidles JA, Harryman DT 2nd, Matsen FA 3rd. Glenohumeral stability from concavity-compression: A quantitative analysis. *J Shoulder Elbow Surg* 1993; **2**: 27-35 [PMID: 22959294 DOI: 10.1016/S1058-2746(09)80134-1]
  - 14 **Wuelker N**, Brews F, Sperveslage C. Passive glenohumeral joint stabilization: A biomechanical study. *J Shoulder Elbow Surg* 1994; **3**: 129-134 [PMID: 22959688 DOI: 10.1016/S1058-2746(09)80091-8]
  - 15 **Harryman DT 2nd**, Sidles JA, Harris SL, Matsen FA 3rd. The role of the rotator interval capsule in passive motion and stability of the shoulder. *J Bone Joint Surg Am* 1992; **74**: 53-66 [PMID: 1734014 DOI: 10.2106/00004623-199274010-00008]
  - 16 **Helmg P**, Søjbjerg JO, Sneppen O, Loehr JF, Ostgaard SE, Suder P. Glenohumeral movement patterns after puncture of the joint capsule: An experimental study. *J Shoulder Elbow Surg* 1993; **2**: 209-215 [PMID: 22971736 DOI: 10.1016/1058-2746(93)90064-N]
  - 17 **Ovesen J**, Nielsen S. Anterior and posterior shoulder instability. A cadaver study. *Acta Orthop Scand* 1986; **57**: 324-327 [PMID: 3788495 DOI: 10.3109/17453678608994402]
  - 18 **Michaelis LS**. Internal rotation dislocation of the shoulder; report of a case. *J Bone Joint Surg Br* 1950; **32-B**: 223-225 [PMID: 15422021 DOI: 10.1302/0301-620X.32B2.223]
  - 19 **Rockwood CA**. Posterior dislocation of the shoulder. Philadelphia: JB Lippincott: Rockwood, C.A., Green, D.P., 1984
  - 20 **Blasier RB**, Soslowsky LJ, Malicky DM, Palmer ML. Posterior glenohumeral subluxation: active and passive stabilization in a biomechanical model. *J Bone Joint Surg Am* 1997; **79**: 433-440 [PMID: 9070535 DOI: 10.2106/00004623-199703000-00018]
  - 21 **Hawkins RJ**, McCormack RG. Posterior shoulder instability. *Orthopedics* 1988; **11**: 101-107 [PMID: 3281149]
  - 22 **Hawkins RJ**, Koppert G, Johnston G. Recurrent posterior instability (subluxation) of the shoulder. *J Bone Joint Surg Am* 1984; **66**: 169-174 [PMID: 6693442 DOI: 10.2106/00004623-198466020-00002]
  - 23 **Schwartz E**, Warren RF, O'Brien SJ, Fronek J. Posterior shoulder instability. *Orthop Clin North Am* 1987; **18**: 409-419 [PMID: 3327030]
  - 24 **Pavic R**, Margetic P, Bencic M, Brnadic RL. Diagnostic value of US, MR and MR arthrography in shoulder instability. *Injury* 2013; **44** Suppl 3: S26-S32 [PMID: 24060014 DOI: 10.1016/S0020-1383(13)70194-3]
  - 25 **Peat M**. Functional anatomy of the shoulder complex. *Phys Ther* 1986; **66**: 1855-1865 [PMID: 3786416 DOI: 10.1093/ptj/66.12.1855]
  - 26 **Terry GC**, Chopp TM. Functional anatomy of the shoulder. *J Athl Train* 2000; **35**: 248-255 [PMID: 16558636]
  - 27 **Steindler A**. *Kinesiology of the Human Body under Normal and Pathological Conditions*. Springfield, IL: Charles C Thomas 1955
  - 28 **Fuchs B**, Jost B, Gerber C. Posterior-inferior capsular shift for the treatment of recurrent, voluntary posterior subluxation of the shoulder. *J Bone Joint Surg Am* 2000; **82**: 16-25 [PMID: 10653080 DOI: 10.2106/00004623-200001000-00003]
  - 29 **Inui H**, Sugamoto K, Miyamoto T, Yoshikawa H, Machida A, Hashimoto J, Nobuhara K. Glenoid shape in atraumatic posterior instability of the shoulder. *Clin Orthop Relat Res* 2002; : 87-92 [PMID: 12360012 DOI: 10.1097/00003086-200210000-00014]
  - 30 **Brewer BJ**, Wubben RC, Carrera GF. Excessive retroversion of the glenoid cavity. A cause of non-traumatic posterior instability of the shoulder. *J Bone Joint Surg Am* 1986; **68**: 724-731 [PMID: 3722229 DOI: 10.2106/00004623-198668050-00013]
  - 31 **Saha AK**. Dynamic stability of the glenohumeral joint. *Acta Orthop Scand* 1971; **42**: 491-505 [PMID: 5144199 DOI: 10.3109/17453677108989066]
  - 32 **Weber SC**, Caspari RB. A biomechanical evaluation of the restraints to posterior shoulder dislocation. *Arthroscopy* 1989; **5**: 115-121 [PMID: 2736007 DOI: 10.1016/0749-8063(89)90006-6]
  - 33 **Aggarwal A**, Wahee P, Harjeet, Aggarwal AK, Sahni D. Variable osseous anatomy of costal surface of scapula and its implications in relation to snapping scapula syndrome. *Surg Radiol Anat* 2011; **33**: 135-140 [PMID: 20809245 DOI: 10.1007/s00276-010-0723-4]
  - 34 **Yang HF**, Tang KL, Chen W, Dong SW, Jin T, Gong JC, Li JQ, Wang HQ, Wang J, Xu JZ. An anatomic and histologic study of the coracohumeral ligament. *J Shoulder Elbow Surg* 2009; **18**: 305-310 [PMID: 19095467 DOI: 10.1016/j.jse.2008.07.012]
  - 35 **Wellmann M**, Blasig H, Bobrowitsch E, Kobbe P, Windhagen H, Petersen W, Bohnsack M. The biomechanical effect of specific labral and capsular lesions on posterior shoulder instability. *Arch Orthop Trauma Surg* 2011; **131**: 421-427 [PMID: 21165630 DOI: 10.1007/s00402-010-1232-y]
  - 36 **Meuffels DE**, Schuit H, van Biezen FC, Reijman M, Verhaar JA. The posterior bone block procedure in posterior shoulder instability: a long-term follow-up study. *J Bone Joint Surg Br* 2010; **92**: 651-655 [PMID: 20436001 DOI: 10.1302/0301-620X.92B5.23529]
  - 37 **DeLong JM**, Bradley JP. Posterior shoulder instability in the athletic population: Variations in assessment, clinical outcomes, and return to sport. *World J Orthop* 2015; **6**: 927-934 [PMID: 26716088 DOI: 10.5312/wjo.v6.i11.927]
  - 38 **Hurley JA**, Anderson TE, Dear W, Andrish JT, Bergfeld JA, Weiker GG. Posterior shoulder instability. Surgical versus conservative results with evaluation of glenoid version. *Am J Sports Med* 1992; **20**: 396-400 [PMID: 1415880 DOI: 10.1177/036354659202000405]
  - 39 **Cyprien JM**, Vasey HM, Burdet A, Bonvin JC, Kritsikis N, Vuagnat P. Humeral retrotorsion and glenohumeral relationship in the normal shoulder and in recurrent anterior dislocation (scapulometry). *Clin Orthop Relat Res* 1983: 8-17 [PMID: 6839612 DOI: 10.1097/00003086-198305000-00002]
  - 40 **Iannotti JP**, Gabriel JP, Schneck SL, Evans BG, Misra S. The normal glenohumeral relationships. An anatomical study of one hundred and forty shoulders. *J Bone Joint Surg Am* 1992; **74**: 491-500 [PMID: 1583043 DOI: 10.2106/00004623-199274040-0004]
  - 41 **O'Brien SJ**, Allen AA, Fealy S. Developmental anatomy of the shoulder and anatomy of the glenohumeral joint. In: Rockwood CA Jr, Matsen FA 111. *The Shoulder Philadelphia*. WB Saunders, 1998
  - 42 **Turkel SJ**, Panio MW, Marshall JL, Girgis FG. Stabilizing mechanisms preventing anterior dislocation of the glenohumeral joint. *J Bone Joint Surg Am* 1981; **63**: 1208-1217 [PMID: 7287791 DOI: 10.2106/00004623-198163080-00002]
  - 43 **Jobe CM**. Gross anatomy of the shoulder. In: Rockwood CA Jr, Matsen FA 111. *The Shoulder Philadelphia*. WB Saunders, 1998
  - 44 **Halder AM**, Itoi E, An KN. Anatomy and biomechanics of the shoulder. *Orthop Clin North Am* 2000; **31**: 159-176 [PMID: 10736387 DOI: 10.1016/S0030-5898(05)70138-3]
  - 45 **Poppen NK**, Walker PS. Normal and abnormal motion of the shoulder. *J Bone Joint Surg Am* 1976; **58**: 195-201 [PMID: 1254624 DOI: 10.2106/00004623-197658020-00006]
  - 46 **Surin V**, Blåder S, Markhede G, Sundholm K. Rotational

- osteotomy of the humerus for posterior instability of the shoulder. *J Bone Joint Surg Am* 1990; **72**: 181-186 [PMID: 2303504 DOI: 10.2106/00004623-199072020-00004]
- 47 **Fung M**, Kato S, Barrance PJ, Elias JJ, McFarland EG, Nobuhara K, Chao EY. Scapular and clavicular kinematics during humeral elevation: a study with cadavers. *J Shoulder Elbow Surg* 2001; **10**: 278-285 [PMID: 11408912 DOI: 10.1067/mse.2001.114496]
- 48 **Moseley HF**. The clavicle: its anatomy and function. *Clin Orthop Relat Res* 1968; **58**: 17-27 [PMID: 5666861 DOI: 10.1097/00003086-196805000-00005]
- 49 **Frankel VH**, Nordin M. Basic Biomechanics of the Skeletal System. Philadelphia, PA, Lea Febiger 1980
- 50 **Matsumura N**, Nakamichi N, Ikegami H, Nagura T, Imanishi N, Aiso S, Toyama Y. The function of the clavicle on scapular motion: a cadaveric study. *J Shoulder Elbow Surg* 2013; **22**: 333-339 [PMID: 22608930 DOI: 10.1016/j.jse.2012.02.006]
- 51 **Inman VT**, Saunders JB, Abbott LC. Observations of the function of the shoulder joint. 1944. *Clin Orthop Relat Res* 1996; 3-12 [PMID: 8804269 DOI: 10.1097/00003086-199609000-00002]
- 52 **Itoi E**, Hsu HC, An KN. Biomechanical investigation of the glenohumeral joint. *J Shoulder Elbow Surg* 1996; **5**: 407-424 [PMID: 8933465 DOI: 10.1016/S1058-2746(96)80074-7]
- 53 **Savoie FH 3rd**, Holt MS, Field LD, Ramsey JR. Arthroscopic management of posterior instability: evolution of technique and results. *Arthroscopy* 2008; **24**: 389-396 [PMID: 18375269 DOI: 10.1016/j.arthro.2007.11.004]
- 54 **Ovesen J**, Nielsen S. Posterior instability of the shoulder. A cadaver study. *Acta Orthop Scand* 1986; **57**: 436-439 [PMID: 3811890 DOI: 10.3109/17453678609014766]
- 55 **Bahk M**, Keyurapan E, Tasaki A, Sauers EL, McFarland EG. Laxity testing of the shoulder: a review. *Am J Sports Med* 2007; **35**: 131-144 [PMID: 17130247 DOI: 10.1177/0363546506294570]
- 56 **Saupe N**, White LM, Bleakney R, Schweitzer ME, Recht MP, Jost B, Zanetti M. Acute traumatic posterior shoulder dislocation: MR findings. *Radiology* 2008; **248**: 185-193 [PMID: 18458243 DOI: 10.1148/radiol.2481071003]
- 57 **Mair SD**, Zarzour RH, Speer KP. Posterior labral injury in contact athletes. *Am J Sports Med* 1998; **26**: 753-758 [PMID: 9850774 DOI: 10.1177/03635465980260060301]
- 58 **Lugo R**, Kung P, Ma CB. Shoulder biomechanics. *Eur J Radiol* 2008; **68**: 16-24 [PMID: 18511227 DOI: 10.1016/j.ejrad.2008.02.051]
- 59 **O'Brien SJ**, Neves MC, Arnoczky SP, Rozbruch SR, Dicarolo EF, Warren RF, Schwartz R, Wickiewicz TL. The anatomy and histology of the inferior glenohumeral ligament complex of the shoulder. *Am J Sports Med* 1990; **18**: 449-456 [PMID: 2252083 DOI: 10.1177/036354659001800501]
- 60 **Bradley JP**, McClincy MP, Arner JW, Tejwani SG. Arthroscopic capsulolabral reconstruction for posterior instability of the shoulder: a prospective study of 200 shoulders. *Am J Sports Med* 2013; **41**: 2005-2014 [PMID: 23804588 DOI: 10.1177/0363546513493599]
- 61 **Yanke AB**, G.S. VT, LeClere LE, Solomon DJ, Bach BR, Provencher MT. Diagnosis and Arthroscopic Management of Posterior Shoulder Instability. American Academy of Orthopaedic Surgeons. Available from: Orthopaedic Knowledge Online 2011; 9: [http://orthopaedialaas.org/oko/article.aspx?article=OKO\\_SHO043](http://orthopaedialaas.org/oko/article.aspx?article=OKO_SHO043).
- 62 **Bisson LJ**. Thermal capsulorrhaphy for isolated posterior instability of the glenohumeral joint without labral detachment. *Am J Sports Med* 2005; **33**: 1898-1904 [PMID: 16157851 DOI: 10.1177/0363546505278258]
- 63 **Ovesen J**, Søjbjerg JO. Posterior shoulder dislocation. Muscle and capsular lesions in cadaver experiments. *Acta Orthop Scand* 1986; **57**: 535-536 [PMID: 3577724 DOI: 10.3109/17453678609014787]
- 64 **Frank RM**, Ramirez J, Chalmers PN, McCormick FM, Romeo AA. Scapulothoracic anatomy and snapping scapula syndrome. *Anat Res Int* 2013; **2013**: 635628 [PMID: 24369502 DOI: 10.1155/2013/635628]
- 65 **Paul J**, Buchmann S, Beitzel K, Solovyova O, Imhoff AB. Posterior shoulder dislocation: systematic review and treatment algorithm. *Arthroscopy* 2011; **27**: 1562-1572 [PMID: 21889868 DOI: 10.1016/j.arthro.2011.06.015]
- 66 **Habermeyer P**, Lichtenberg S. [Diagnosis and treatment of anterior and posterior shoulder dislocation. II. Treatment]. *Chirurg* 2003; **74**: 1178-1194 [PMID: 14756134 DOI: 10.1007/s00104-003-0771-y]
- 67 **Cunningham G**, Hoffmeyer P. [Posterior dislocation of the shoulder, challenges in diagnosis and management]. *Rev Med Suisse* 2011; **7**: 2489-2493 [PMID: 22288288]
- 68 **Tannenbaum E**, Sekiya JK. Evaluation and management of posterior shoulder instability. *Sports Health* 2011; **3**: 253-263 [PMID: 23016015 DOI: 10.1177/1941738111400562]
- 69 **Guehring M**, Lambert S, Stoeckle U, Ziegler P. Posterior shoulder dislocation with associated reverse Hill-Sachs lesion: treatment options and functional outcome after a 5-year follow up. *BMC Musculoskelet Disord* 2017; **18**: 442 [PMID: 29132328 DOI: 10.1186/s12891-017-1808-6]
- 70 **Tibone JE**, Bradley JP. The treatment of posterior subluxation in athletes. *Clin Orthop Relat Res* 1993; 124-137 [PMID: 8504591 DOI: 10.1097/00003086-199306000-00014]
- 71 **Burkhead WZ Jr**, Rockwood CA Jr. Treatment of instability of the shoulder with an exercise program. *J Bone Joint Surg Am* 1992; **74**: 890-896 [PMID: 1634579 DOI: 10.2106/00004623-199274060-00010]
- 72 **Engle RP**, Canner GC. Posterior shoulder instability: approach to rehabilitation. *J Orthop Sports Phys Ther* 1989; **10**: 1-494 [PMID: 18796935 DOI: 10.2519/jospt.1989.10.12.488]
- 73 **Pollock RG**, Bigliani LU. Recurrent posterior shoulder instability. Diagnosis and treatment. *Clin Orthop Relat Res* 1993; 85-96 [PMID: 8504618]
- 74 **Seppel G**, Braun S, Imhoff AB. Surgical Management of Posterior Shoulder Instability. ISAKOS: Brockmeier SF, 2013
- 75 **Acid S**, Le Corroller T, Aswad R, Pauly V, Champsaur P. Preoperative imaging of anterior shoulder instability: diagnostic effectiveness of MDCT arthrography and comparison with MR arthrography and arthroscopy. *AJR Am J Roentgenol* 2012; **198**: 661-667 [PMID: 22358006 DOI: 10.2214/AJR.11.7251]
- 76 **Cvitanić O**, Tirman PF, Feller JF, Bost FW, Minter J, Carroll KW. Using abduction and external rotation of the shoulder to increase the sensitivity of MR arthrography in revealing tears of the anterior glenoid labrum. *AJR Am J Roentgenol* 1997; **169**: 837-844 [PMID: 9275908 DOI: 10.2214/ajr.169.3.9275908]
- 77 **Smith TO**, Drew BT, Toms AP. A meta-analysis of the diagnostic test accuracy of MRI and MRI for the detection of glenoid labral injury. *Arch Orthop Trauma Surg* 2012; **132**: 905-919 [PMID: 22395821 DOI: 10.1007/s00402-012-1493-8]
- 78 **van de Bunt F**, Pearl ML, Lee EK, Peng L, Didomenico P. Glenoid version by CT scan: an analysis of clinical measurement error and introduction of a protocol to reduce variability. *Skeletal Radiol* 2015; **44**: 1627-1635 [PMID: 26201674 DOI: 10.1007/s00256-015-2207-4]
- 79 **Kodali P**, Jones MH, Polster J, Miniaci A, Fening SD. Accuracy of measurement of Hill-Sachs lesions with computed tomography. *J Shoulder Elbow Surg* 2011; **20**: 1328-1334 [PMID: 21493104 DOI: 10.1016/j.jse.2011.01.030]
- 80 **Rowan KR**, Keogh C, Andrews G, Cheong Y, Forster BB. Essentials of shoulder MR arthrography: a practical guide for the general radiologist. *Clin Radiol* 2004; **59**: 327-334 [PMID: 15041451 DOI: 10.1016/j.crad.2003.10.011]
- 81 **Castagna A**, Nordenson U, Garofalo R, Karlsson J. Minor shoulder instability. *Arthroscopy* 2007; **23**: 211-215 [PMID: 17276230 DOI: 10.1016/j.arthro.2006.11.025]
- 82 **Shah N**, Tung GA. Imaging signs of posterior glenohumeral instability. *AJR Am J Roentgenol* 2009; **192**: 730-735 [PMID: 19234271 DOI: 10.2214/AJR.07.3849]
- 83 **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]
- 84 **Yu JS**, Ashman CJ, Jones G. The POLPSA lesion: MR imaging findings with arthroscopic correlation in patients with posterior

- instability. *Skeletal Radiol* 2002; **31**: 396-399 [PMID: 12107572 DOI: 10.1007/s00256-002-0513-0]
- 85 **Ruiz Santiago F**, Martínez Martínez A, Tomás Muñoz P, Pozo Sánchez J, Zarza Pérez A. Imaging of shoulder instability. *Quant Imaging Med Surg* 2017; **7**: 422-433 [PMID: 28932699 DOI: 10.21037/qims.2017.08.05]
- 86 **Kirkley A**, Griffin S, Richards C, Miniaci A, Mohtadi N. Prospective randomized clinical trial comparing the effectiveness of immediate arthroscopic stabilization versus immobilization and rehabilitation in first traumatic anterior dislocations of the shoulder. *Arthroscopy* 1999; **15**: 507-514 [PMID: 10424554 DOI: 10.1053/ar.1999.v15.015050]
- 87 **Garcia JC Jr**, Maia LR, Fonseca JR, Zabeu JL, Garcia JP. Evaluation of arthroscopic treatment of posterior shoulder instability. *Acta Ortop Bras* 2015; **23**: 134-137 [PMID: 26207089 DOI: 10.1590/1413-7852.2015230300540]
- 88 **Hawkins RJ**, Krishnan SG, Karas SG, Noonan TJ, Horan MP. Electrothermal arthroscopic shoulder capsulorrhaphy: a minimum 2-year follow-up. *Am J Sports Med* 2007; **35**: 1484-1488 [PMID: 17456642 DOI: 10.1177/0363546507301082]
- 89 **Wong KL**, Williams GR. Complications of thermal capsulorrhaphy of the shoulder. *J Bone Joint Surg Am* 2001; **83-A** Suppl 2 Pt 2: 151-155 [PMID: 11712836 DOI: 10.2106/00004623-200100022-00013]
- 90 **Norwood LA**, Terry GC. Shoulder posterior subluxation. *Am J Sports Med* 1984; **12**: 25-30 [PMID: 6703179 DOI: 10.1177/036354658401200104]
- 91 **Delcogliano A**, Caporaso A, Chiossi S, Menghi A, Cillo M, Delcogliano M. Surgical management of chronic, unreduced posterior dislocation of the shoulder. *Knee Surg Sports Traumatol Arthrosc* 2005; **13**: 151-155 [PMID: 15756620 DOI: 10.1007/s00167-004-0524-6]
- 92 **Gerber C**, Lambert SM. Allograft reconstruction of segmental defects of the humeral head for the treatment of chronic locked posterior dislocation of the shoulder. *J Bone Joint Surg Am* 1996; **78**: 376-382 [PMID: 8613444 DOI: 10.2106/00004623-199603000-00008]
- 93 **Martinez AA**, Navarro E, Iglesias D, Domingo J, Calvo A, Carbonel I. Long-term follow-up of allograft reconstruction of segmental defects of the humeral head associated with posterior dislocation of the shoulder. *Injury* 2013; **44**: 488-491 [PMID: 23195206 DOI: 10.1016/j.injury.2012.10.027]

**P- Reviewer:** Guerado E; Malik H; Emara KM **S- Editor:** Dou Y  
**L- Editor:** Filipodia **E- Editor:** Wu YXJ



## Recently highlighted nutraceuticals for preventive management of osteoarthritis

Silvia Ravalli, Marta Anna Szychlinska, Rosalia Maria Leonardi, Giuseppe Musumeci

Silvia Ravalli, Marta Anna Szychlinska, Giuseppe Musumeci, Department of Biomedical and Biotechnological Sciences, Human Anatomy and Histology Section, School of Medicine, University of Catania, Catania 95123, Italy

Rosalia Maria Leonardi, Department of Orthodontics, Policlinico Universitario "Vittorio Emanuele", University of Catania, Catania 95124, Italy

ORCID number: Silvia Ravalli (0000-0003-3358-1086); Marta Anna Szychlinska (0000-0001-5281-1516); Rosalia Maria Leonardi (0000-0002-9433-9528); Giuseppe Musumeci (0000-0002-8260-8890).

**Author contributions:** Ravalli S generated the figures and wrote the manuscript; Szychlinska MA contributed to the writing of the manuscript; Leonardi RM contributed to manuscript revision; Musumeci G designed the aim of the review and supervised the manuscript writing.

**Conflict-of-interest statement:** All authors have no competing interests to declare.

**Open-Access:** This 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:** Giuseppe Musumeci, BSc, MSc, PhD, Associate Professor, Department of Biomedical and Biotechnological Sciences, Human Anatomy and Histology Section, School of Medicine, University of Catania, Via S. Sofia 87, Catania 95123, Italy. [g.musumeci@unict.it](mailto:g.musumeci@unict.it)  
Telephone: +39-95-3782043  
Fax: +39-95-3782034

Received: August 28, 2018

Peer-review started: August 28, 2018

First decision: October 5, 2018

Revised: October 11, 2018

Accepted: October 17, 2018

Article in press: October 18, 2018

Published online: November 18, 2018

### Abstract

Osteoarthritis (OA) is a chronic degenerative disease of articular cartilage with limited treatment options. This reality encourages clinicians to suggest preventive measures to delay and contain the outbreak of the pathological conditions. Articular cartilage and synovium suffering from OA are characterised by an inflammatory state and by significant oxidative stress, responsible for pain, swelling and loss of mobility in the advanced stages. This review will focus on the ability of olive oil to exert positive effects on the entire joint to reduce pro-inflammatory cytokine release and increase lubricin synthesis, olive leaf extract, since it maintains lubrication by stimulating high molecular weight hyaluronan synthesis in synovial cells, curcumin, which delays the start of pathological cartilage breakdown, sanguinarine, which downregulates catabolic proteases, vitamin D for its capacity to influence the oxidative and pro-inflammatory environment, and carnosic acid as an inducer of heme oxygenase-1, which helps preserve cartilage degeneration. These molecules, considered as natural dietary supplements, appear like a cutting-edge answer to this tough health problem, playing a major role in controlling homeostatic balance loss and slowing down the pathology progression. Natural or food-derived molecules that are able to exert potential therapeutic effects are known as "nutraceutical", resulting from the combination of the words "nutrition" and "pharmaceutical". These compounds have gained popularity due to their easy availability, which represents a huge advantage for food and pharmaceutical industries. In addition, the chronic nature of OA implies the use of pharmacological compounds with proven long-term safety, especially because current treatments like nonsteroidal anti-inflammatory drugs and analgesics

improve pain relief but have no effect on degenerative progression and can also cause serious side effects.

**Key words:** Osteoarthritis; Nutraceuticals; Prevention; Diet; Inflammation; Oxidative stress

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Osteoarthritis involves the significant expression of inflammatory cytokines, matrix proteins and proteolytic enzymes. For this reason, anti-inflammatory molecules play a major role in controlling the adverse effects of cartilage homeostatic balance loss. Olive oil, olive leaf extract, curcumin and sanguinarine have been studied as supplements with anti-inflammatory properties. Moreover, chondrocytes undergo senescence and cell death in the presence of oxidative stress. Potential targets involved in this mechanism are counteracted by anti-oxidant molecules like vitamin D and carnosic acid.

Ravalli S, Szychlińska MA, Leonardi RM, Musumeci G. Recently highlighted nutraceuticals for preventive management of osteoarthritis. *World J Orthop* 2018; 9(11): 255-261 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i11/255.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i11.255>

## INTRODUCTION

Osteoarthritis (OA) is a very complex and multifactorial disease of articular cartilage, which represents a leading cause of joint pain and disability worldwide<sup>[1]</sup>. The entire synovial joint is affected by the progression of this pathology, including the underlying bone, synovium, meniscus, ligaments/tendons, and cartilage<sup>[2,3]</sup>. OA is characterized by the degradation of the articular cartilage, which can be used as hallmark of pathological advancement beyond changes in subchondral bone, osteophyte formation, joint space narrowing and chronic synovial inflammation<sup>[4]</sup>. In normal joints, cartilage covers and cushions the ends of bones, reducing friction and absorbing shocks. Its destruction progress leads to stiffness, pain, mobility limitations and compromised overall quality of life<sup>[5,6]</sup>. Some of the most important risk factors include aging, inflammatory state, muscle atrophy, injury and metabolic disorders<sup>[7]</sup>.

The management of OA focuses on alleviating its secondary effects since there is currently no resolutive cure. Nonsteroidal anti-inflammatory drugs and analgesics are generally prescribed to patients to reduce pain and improve joint function, but they fail in modifying disease progression in terms of prevention and chondroprotection<sup>[8]</sup>. The chronic nature of OA forces the use of pharmacological approaches that can be considered safe for long term use and, at the same time, might be able to slow its progression. The basis

of articular damage relies on impaired balance between anabolic and catabolic mechanisms, which can be influenced by dietary compounds like nutraceuticals<sup>[9]</sup>. Due to their minimal side effects, especially in the long term, their easy extraction and low costs of production, they may represent a valid preventive management of OA.

Forty-seven percent of people who suffer from OA use complementary medications including nutraceuticals due to their anti-inflammatory and antioxidant activities<sup>[10]</sup>. Herbal and natural products have been used since ancient times. A 5000-year-old Sumerian clay tablet is the first proof of plants use as medication, especially to treat pain and inflammation<sup>[11]</sup>.

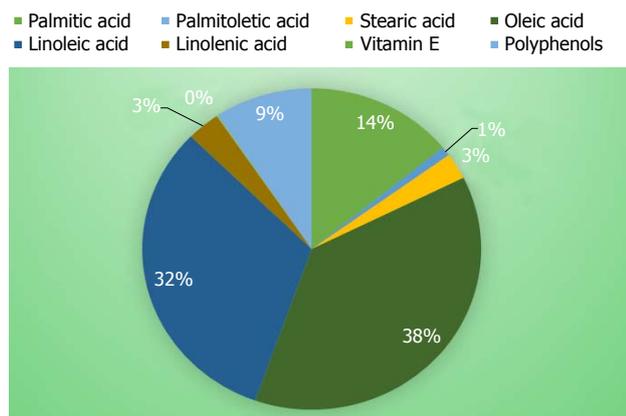
During the 19<sup>th</sup> century, improvement in chemical technologies allowed for the extraction of active substances from medicinal plants such as alkaloids, tannins, saponosides, etheric oils, vitamins and glycosides, isolated in pure form<sup>[12]</sup>. The term "nutraceutical", resulting from the combination of the words "nutrition" and "pharmaceutical", is used to define any natural or food-derived molecule able to exert a potential therapeutic effect that could be integrated into a daily diet<sup>[13]</sup>.

Statutory law of these type of medicaments differ by country. For example, in the United States, they are considered dietary supplements by the Dietary Supplement Health and Education Act of 1994<sup>[14]</sup>. The Food and Drug Administration is in charge of reviewing and approving any health claims about these products. In some countries of the European Union, nutraceuticals may require registration whereas in others, they could be easily sold as food preparations<sup>[15]</sup>.

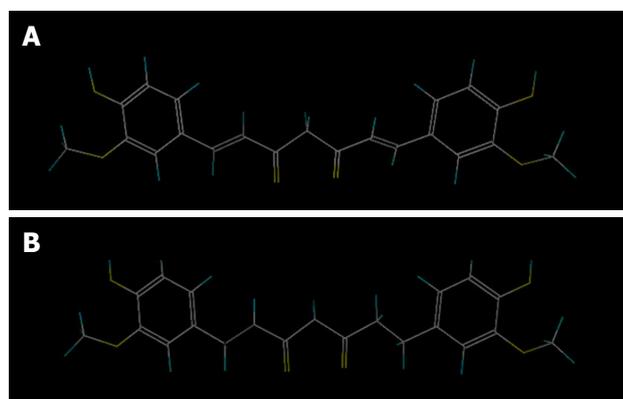
This review will summarize natural-based approaches for chondroprotection, highlighting the peculiarity of some molecules whose positive effect in preserving cartilage health has recently been discovered. This approach may be useful both to prevent OA onset and to slow down its progression.

## ANTI-INFLAMMATORY APPROACH

The involvement of an inflammatory component, marked by joint pain, swelling and stiffness, is now well recognized in the pathogenesis of OA. Indeed, chondrocytes undergo a loss of homeostatic balance, which includes expression of inflammatory cytokines, matrix proteins such as collagen and lubricin and proteolytic enzymes<sup>[16]</sup>. The most important pro-inflammatory cytokines involved are interleukin (IL)-1 $\beta$  and tumour necrosis factor (TNF)- $\alpha$ <sup>[17]</sup>. Some of the consequences of the development of an inflammatory scenario are as follows: downregulation of structural components, including type II collagen and proteoglycans<sup>[18-21]</sup>, upregulation of proteolytic enzymes, such as matrix metalloproteinases (MMPs)-1, -3, -13, and a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS)<sup>[22-24]</sup> and stimulation of inflammatory mediators like prostaglandin E2 (PGE2), cyclooxygenase-2 (COX-2), and Reactive oxygen species (ROS)<sup>[25,26]</sup>.



**Figure 1** Composition of fatty acids, vitamin E and polyphenols in a Sicilian extra virgin olive oil-supplemented diet. Palmitic acid (16:0) (mg/kg) 9002; palmitoleic acid (16:1) (mg/kg) 579; stearic acid (18:0) (mg/kg) 1689; oleic acid (18:1) (mg/kg) 24047; linoleic acid (18:2) (mg/kg) 20352; linolenic acid (18:3) (mg/kg) 2018; vitamin E (mg/kg) 72.167; polyphenols (mg/kg) 5.960.



**Figure 2** Chemical structure of curcumin and tetrahydrocurcumin. A: Curcumin,  $C_{21}H_{20}O_6$ ; B: Tetrahydrocurcumin,  $C_{21}H_{24}O_6$ .

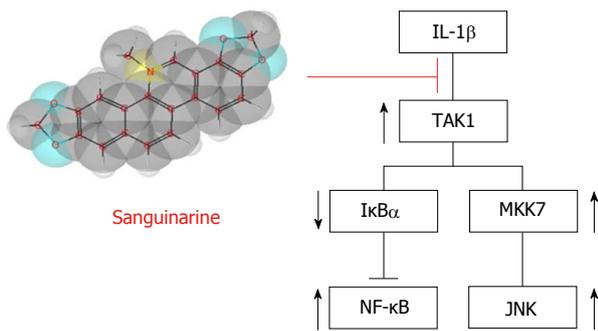
Recently, our lab carried out studies to determine the chondroprotective role of phytoactive molecules [e.g., polyphenols and monounsaturated fatty acids naturally present in olive tree-derived products, olive oil (-OO-) and olive leaf extract (-OLE-)] able to preserve the articular cartilage and skeletal muscle condition, in the context of early development of OA because of their antioxidant and anti-inflammatory properties<sup>[7]</sup>. In addition, the study examined differences between three types of oils in term of origin and polyphenol contents: Sicilian extra virgin olive oil (S-EVOO), Tunisian extra virgin olive oil (T-EVOO) and Tunisian extra virgin olive oil and leaves extract (T-enriched-EVOO), concluding that the first variety of oil (S-EVOO) is the best in exerting positive effects on the entire joint, remarkably reducing IL-6 release and increasing lubricin synthesis, compared to the other diet protocols (Figure 1). The effects of physical activity were also analysed in combination with the diet<sup>[27]</sup>. The studies demonstrated that an olive oil supplemented diet plus physical activity improved cartilage recovery after anterior cruciate ligament transection by lowering IL-6 and IL-1 expression and

by increasing lubricin expression, suggestive of chondroprotective activity. Lubricin is a glycoprotein released by type B synoviocytes and chondrocytes from the superficial layer of articular cartilage, and its functions are to lubricate and nourish articular cartilage<sup>[28]</sup>.

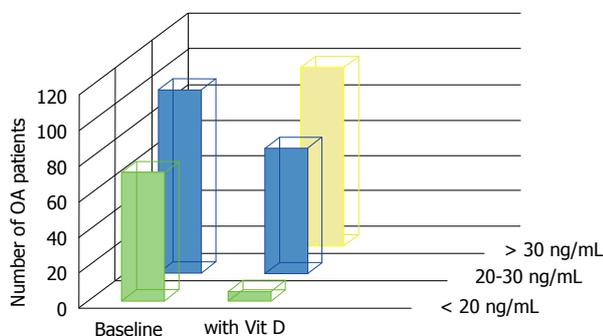
Another recent study that confirms the healthy effect of OLE was presented by Maruyama *et al.*<sup>[29]</sup>, which addressed the main activity of hydroxytyrosol [4-(2-hydroxyethyl)-1, 2-benzenediol] (HT), an OLE polyphenol. STR/ort mice were used as a model for knee OA, and 100 mg/kg OLE was orally administered every day for 8 wk. The chondroprotective effect of the extract was proven by Mankin scores of the non-OA control group, OA control group and OLE-treated group, which were 3.50, 11.13 and 7.20, respectively. Moreover, the study suggests that these natural molecules were able to impair cartilage damage and, consequently, the pathology progression, since they stimulated the synthesis of high molecular weight hyaluronan in synovial cells *in vitro*. High molecular weight hyaluronan is involved in maintaining joint moisture and lubrication<sup>[30]</sup>. The authors suggested that OLE administration can effectively help suppress OA progression.

Traditionally used as an anti-inflammatory treatment in Chinese and Ayurvedic medicine, *Curcuma longa* is a plant rich in phytochemicals, which are responsible for its most impressive and wide-ranging health benefits. Some of its active components, curcumin and tetrahydrocurcumin (THC), a major metabolite of curcumin, have been studied because of their anti-inflammatory, antioxidant, chemopreventive, anti-aging and anti-bacterial activities<sup>[31,32]</sup>. Park *et al.*<sup>[33]</sup> analysed the effects of long-term THC administration and curcumin in OA progression in rats with oestrogen deficiency. Ovariectomized obese rats underwent monoiodoacetate injections into the knee to simulate OA conditions, and then curcumin and THC were fed to prevent postmenopausal and OA symptoms. One of the most significant findings of the study was the differences between the two molecules. The chemical structures of curcumin involved in exerting the main activities are methoxy, hydroxyl,  $\alpha,\beta$ -unsaturated carbonyl, and diketone groups, whereas its metabolite lacks the presence of the  $\alpha,\beta$ -unsaturated carbonyl group, changing its functionality and efficacy (Figure 2). Park *et al.*<sup>[33]</sup> found that both natural products showed similar abilities to decrease expression of TNF- $\alpha$ , IL-1 $\beta$ , IL-6 and MMP3 and MMP13, but only THC could enhance glucose tolerance, allowing it to decrease advanced glycation end products in articular cartilage, delaying the start of the pathological process of cartilage breakdown.

Furthermore, Ma *et al.*<sup>[34]</sup> demonstrated for the first time the anti-inflammatory effect of sanguinarine (SA), a benzophenanthridine alkaloid isolated from the roots of *Sanguinaria canadensis*, on the pathogenesis of OA, *in vitro*, *ex vivo* and *in vivo*. Evaluation of the potential cytotoxicity of SA revealed that this compound does not affect cell viability at concentrations lower than 1.25  $\mu\text{mol/L}$ . As stimulation of IL-1 $\beta$  increased the mRNA expression of MMP1a, MMP3, MMP13, and ADAMTS-5,



**Figure 3 Anti-inflammatory effect of sanguinarine.** Sanguinarine acts as suppressor of IL-1 $\beta$ , targeting the pathways involved in JNK activation and the degradation of I $\kappa$ B $\alpha$ , an inhibitory subunit of NF- $\kappa$ B. IL: Interleukin; I $\kappa$ B $\alpha$ : Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha; NF- $\kappa$ B: Nuclear factor kappa B; JNK: c-Jun N-terminal kinases; MKK7: Dual specificity mitogen-activated protein kinase kinase 7.



**Figure 4 Vitamin D levels in osteoarthritis patients at baseline and after vitamin D2 supplementation.** At baseline, 72 participants had vitamin D deficiency (< 20 ng/mL) and 103 patients had vitamin D insufficiency (20-30 ng/mL). After 40000 IU of vitamin D2 supplementation per week for 6 mo, 100 knee OA participants achieved concentration above 30 ng/mL, 70 knee OA participants had vitamin D insufficiency, and only 5 patients had vitamin D deficiency. Vit D: Vitamin D; OA: Osteoarthritis.

SA downregulated these catabolic proteases through a dose-dependent manner indicative of IL-1 $\beta$  activity. More specifically, the anti-inflammatory molecule acts as suppressor of phosphorylation of the c-Jun N-terminal kinases (JNK) and nuclear factor kappa B (NF- $\kappa$ B) (Figure 3). These *in vitro* analyses were followed by *ex vivo* evaluation of SA's effects on cartilage matrix degradation, which were consistent with the previous results. Intra-articular administration of different SA concentrations was used to determine whether the molecule could slow down the progression of ACLT-induced OA in mice. The hypothesis was finally and positively confirmed by immunochemistry results, evaluation of protease mRNA levels and Osteoarthritis Research Society International scoring.

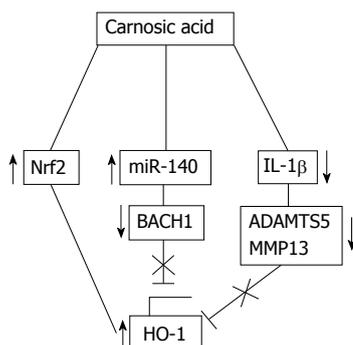
## ANTIOXIDANT APPROACH

It is well established that oxidative stress-induced ROS production (commonly experienced because of post-traumatic events or aging) is a crucial mediator

of OA disease progression<sup>[35]</sup>. As a consequence, chondrocytes experience more significant senescence and cell death<sup>[36,37]</sup>. In addition, cartilage and joint fluid are not able to counteract this scenario because superoxide dismutase antioxidant levels are consistently decreased in OA<sup>[38]</sup>. This is the reason why an effective preventive approach to this pathology should consider boosting antioxidant shields to enhance the potency of constitutive defences such as the antioxidants catalase, superoxide dismutase, glutathione peroxidase and glutathione reductase.

A study about dietary supplementation in OA by Manoy *et al.*<sup>[39]</sup> highlighted the role of the commonly used antioxidant vitamin D. Even though the correlation between this vitamin and musculoskeletal diseases is still not clear, low levels of 25-hydroxyvitamin D [25(OH)D] have been observed in OA patient serum. In fact, evidence suggests that vitamin D deficiency is a co-factor for OA pathogenesis<sup>[40]</sup>. The study involved 175 primary knee OA patients who received 40000 IU vitamin D (ergocalciferol) per week. Six months after the first administration, the patients experienced ameliorated grip strength, physical performance and improved quality of life (Figure 4). Moreover, to confirm its anti-oxidant activity, analysis of protein carbonyl levels was performed to obtain information about oxidative damage. The results confirmed that vitamin D supplementation remarkably decreased carbonyl levels, and as a consequence, stress and the pro-inflammatory environment that can affect protein function and DNA. The underlying mechanism for this vitamin D activity may be explained by evidences for the downregulation of nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase), IL-6, TNF- $\alpha$ , NF- $\kappa$ B and p38<sup>[41,42]</sup>.

Heme oxygenase-1 (HO-1) is another potential target that can be used in an anti-oxidant strategy against OA. Constitutive expression of HO-1 in chondrocytes and the meniscus in mice has been linked to preserve cartilage degeneration<sup>[43]</sup>. For this reason, Hiroyuki *et al.*<sup>[44]</sup> explored the effect of carnolic acid (CA) as an inducer of HO-1 upregulation in preventing OA progress. This molecule is a natural diterpene commonly found in rosemary and common sage, and it has demonstrated protective qualities in pathologies like cancer, diabetes and neurodegenerative disease<sup>[45]</sup>. Immunoblotting assays were used to test whether CA affected HO-1 expression in articular chondrocytes. The results showed that CA increased enzyme levels in a dose-dependent manner. More specifically, the best treatment seemed to require 10 to 50  $\mu$ mol/L of CA. In addition, it was able to restore HO-1 levels under IL-1 $\beta$  treatment, which specifically inhibits the anti-oxidant effects of the enzyme. According to this study, the mechanisms by which this natural compound acts rely on downregulation of MMP-13 and ADAMTS-5, activation of nuclear factor erythroid 2-related factor 2 (Nrf2), regulation of the Kelch-like ECH-associated protein 1/nuclear factor erythroid 2-related factor 2 (KEAP1/NRF2) transcriptional pathway and an increase in



**Figure 5 Mechanisms of heme oxygenase-1 upregulation by carnosic acid.** CA induces the expression of HO-1 by: Activation of the Nrf2 transcription factor, downregulation of Bach1 via miR-140 and downregulation of the IL-1 $\beta$ -induced expression of extracellular matrix degrading enzymes such as MMP-13 and ADAMTS-5. CA: Carnosic acid; HO-1: Heme oxygenase-1; Nrf2: Nuclear factor erythroid 2-related factor 2; IL: Interleukin; MMP: Matrix metalloproteinase; ADAMTS: A disintegrin and metalloproteinase with thrombospondin motifs; miR-140: MicroRNA 140.

microRNA 140 (miR-140) binding to the 3'UTR of Bach1 (an HO-1 repressor) in articular chondrocytes (Figure 5).

Furthermore, our lab examined the relationship between oxidative stress and physical activity or a sedentary lifestyle, suggesting therapeutic solutions that involve natural dietary supplements. One study analysed the effects of oleic acid on ROS production induced by exhaustive physical activity in rat skeletal muscle<sup>[46]</sup>. The results highlight the importance of extra-virgin olive oil as a protective agent against oxidative stress following physical efforts. The group of rats subjected to exhaustive exercise but fed with a diet rich in oleic acid experienced a decrease in hydroperoxides and thiobarbituric acid reactive substances and an increase in antioxidant defences, rated as non-enzymatic antioxidant capacity and levels of 70 kDa heat shock proteins (Hsp70). OA cannot be completely prevented, but some precautions can help delay the progression of the pathology and manage the risk of its progression<sup>[47]</sup>. Since sarcopenia and sedentary life are possibly associated with knee OA<sup>[48]</sup>, another study is worth citing because it evaluated whether different dietary profiles, containing or not containing vitamin D, could exert some effects on muscle fibres<sup>[49]</sup>. The study found that muscle fibres of rats fed with high-fat extra-virgin olive oil-based diets were hypertrophic compared to those of the regular diet group. These data confirmed that this natural supplement does not impair muscle fibre metabolism, unlike high-fat butter-based diets. In addition, Vitamin D exerted a trophic action on muscle fibres both in rats fed regular diets and in those fed a diet enriched with extra-virgin olive oil, suggesting that insulin-like growth factor-1 (IGF-1) and dickkopf-1 (DKK-1) may be involved in this mechanism.

## CONCLUSION

When physical activity and a healthy lifestyle are not enough, anti-inflammatory drugs and painkillers are

commonly used to alleviate pain, but sometimes rehabilitation and surgical intervention are unavoidable. For these reasons, trying to preserve the cartilage joint is imperative.

The use of natural approaches is a cutting-edge strategy. Nutraceuticals offer a wide range of molecules able to exert positive effects at different joint structures with several mechanisms of actions. In particular, this review focused on the anti-inflammatory and antioxidant properties of compounds that ameliorate cartilage conditions, suggesting that they should be integrated into a framework of prevention.

The presented studies offer thorough evaluations of olive oil, demonstrating that it reduces IL-6 release and increases lubricin synthesis, of olive leaf extract, as a stimulator of high molecular weight hyaluronan synthesis in synovial cells, of curcumin, addressing its ability to decrease TNF- $\alpha$ , IL-1 $\beta$ , IL-6 and MMP3 and MMP13 expression, of SA, as a downregulator of catabolic proteases through interaction with IL-1 $\beta$ , of vitamin D, since it influences the oxidative and pro-inflammatory environment and of CA, as an inducer of HO-1, preserving cartilage degeneration even under IL-1 $\beta$  treatment.

From a general analysis, it is worth noting that a common positive element of all these molecules is their availability in nature, which represents a huge advantage for food and pharmaceutical industries, and their low side effects, allowing for a broad range of safe uses for the derived products.

## REFERENCES

- 1 **Suri P**, Morgenroth DC, Hunter DJ. Epidemiology of osteoarthritis and associated comorbidities. *PMR* 2012; **4**: S10-S19 [PMID: 22632687 DOI: 10.1016/j.pmrj.2012.01.007]
- 2 **Loeser RF**, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. *Arthritis Rheum* 2012; **64**: 1697-1707 [PMID: 22392533 DOI: 10.1002/art.34453]
- 3 **Burr DB**, Gallant MA. Bone remodelling in osteoarthritis. *Nat Rev Rheumatol* 2012; **8**: 665-673 [PMID: 22868925 DOI: 10.1038/nrrheum.2012.130]
- 4 **Castañeda S**, Roman-Blas JA, Largo R, Herrero-Beaumont G. Subchondral bone as a key target for osteoarthritis treatment. *Biochem Pharmacol* 2012; **83**: 315-323 [PMID: 21964345 DOI: 10.1016/j.bcp.2011.09.018]
- 5 **Sun HB**. Mechanical loading, cartilage degradation, and arthritis. *Ann N Y Acad Sci* 2010; **1211**: 37-50 [PMID: 21062294 DOI: 10.1111/j.1749-6632.2010.05808.x]
- 6 **Musumeci G**, Castrogiovanni P, Mazzone V, Szychlinska MA, Castorina S, Loreto C. Histochemistry as a unique approach for investigating normal and osteoarthritic cartilage. *Eur J Histochem* 2014; **58**: 2371 [PMID: 24998926 DOI: 10.4081/ejh.2014.2371]
- 7 **Szychlinska MA**, Castrogiovanni P, Trovato FM, Nsir H, Zarrouk M, Lo Furno D, Di Rosa M, Imbesi R, Musumeci G. Physical activity and Mediterranean diet based on olive tree phenolic compounds from two different geographical areas have protective effects on early osteoarthritis, muscle atrophy and hepatic steatosis. *Eur J Nutr* 2018; [PMID: 29450729 DOI: 10.1007/s00394-018-1632-2]
- 8 **Cheng DS**, Visco CJ. Pharmaceutical therapy for osteoarthritis. *PM R* 2012; **4**: S82-S88 [PMID: 22632707 DOI: 10.1016/j.pmrj.2012.02.009]
- 9 **Musumeci G**, Mobasheri A, Trovato FM, Szychlinska MA, Imbesi R, Castrogiovanni P. Post-operative rehabilitation and nutrition

- in osteoarthritis. *F1000Res* 2014; **3**: 116 [PMID: 26962431 DOI: 10.12688/f1000research.4178.3]
- 10 **Akhtar N**, Haqqi TM. Current nutraceuticals in the management of osteoarthritis: a review. *Ther Adv Musculoskelet Dis* 2012; **4**: 181-207 [PMID: 22850529 DOI: 10.1177/1759720X11436238]
  - 11 **Petrovska BB**. Historical review of medicinal plants' usage. *Pharmacogn Rev* 2012; **6**: 1-5 [PMID: 22654398 DOI: 10.4103/0973-7847.95849]
  - 12 **Dervendzi V**. Contemporary treatment with medicinal plants. Skopje: Tabernakul 1992; 5-43.
  - 13 **Castrogiovanni P**, Trovato FM, Loreto C, Nsir H, Szychlińska MA, Musumeci G. Nutraceutical Supplements in the Management and Prevention of Osteoarthritis. *Int J Mol Sci* 2016; **17**: [PMID: 27929434 DOI: 10.3390/ijms17122042]
  - 14 **Finley JW**, Finley JW, Ellwood K, Hoadley J. Launching a new food product or dietary supplement in the United States: industrial, regulatory, and nutritional considerations. *Annu Rev Nutr* 2014; **34**: 421-447 [PMID: 24850389 DOI: 10.1146/annurev-nutr-071813-105817]
  - 15 **Gulati OP**, Berry Ottaway P. Legislation relating to nutraceuticals in the European Union with a particular focus on botanical-sourced products. *Toxicology* 2006; **221**: 75-87 [PMID: 16487647 DOI: 10.1016/j.tox.2006.01.014]
  - 16 **Musumeci G**, Mobasher A, Trovato FM, Szychlińska MA, Graziano AC, Lo Furno D, Avola R, Mangano S, Giuffrida R, Cardile V. Biosynthesis of collagen I, II, RUNX2 and lubricin at different time points of chondrogenic differentiation in a 3D in vitro model of human mesenchymal stem cells derived from adipose tissue. *Acta Histochem* 2014; **116**: 1407-1417 [PMID: 25307495 DOI: 10.1016/j.acthis.2014.09.008]
  - 17 **Kapoor M**, Martel-Pelletier J, Lajeunesse D, Pelletier JP, Fahmi H. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. *Nat Rev Rheumatol* 2011; **7**: 33-42 [PMID: 21119608 DOI: 10.1038/nrrheum.2010.196]
  - 18 **Chadjichristos C**, Ghayor C, Kyriotou M, Martin G, Renard E, Ala-Kokko L, Suske G, de Crombrughe B, Pujol JP, Galéra P. Sp1 and Sp3 transcription factors mediate interleukin-1 beta down-regulation of human type II collagen gene expression in articular chondrocytes. *J Biol Chem* 2003; **278**: 39762-39772 [PMID: 12888570 DOI: 10.1074/jbc.M303541200]
  - 19 **Goldring MB**, Fukuo K, Birkhead JR, Dudek E, Sandell LJ. Transcriptional suppression by interleukin-1 and interferon-gamma of type II collagen gene expression in human chondrocytes. *J Cell Biochem* 1994; **54**: 85-99 [PMID: 8126089 DOI: 10.1002/jcb.240540110]
  - 20 **Séguin CA**, Bernier SM. TNF $\alpha$  suppresses link protein and type II collagen expression in chondrocytes: Role of MEK1/2 and NF- $\kappa$ B signaling pathways. *J Cell Physiol* 2003; **197**: 356-369 [PMID: 14566965 DOI: 10.1002/jcp.10371]
  - 21 **Saklatvala J**. Tumour necrosis factor alpha stimulates resorption and inhibits synthesis of proteoglycan in cartilage. *Nature* 1986; **322**: 547-549 [PMID: 3736671 DOI: 10.1038/322547a0]
  - 22 **Mengshol JA**, Vincenti MP, Coon CI, Barchowsky A, Brinckerhoff CE. Interleukin-1 induction of collagenase 3 (matrix metalloproteinase 13) gene expression in chondrocytes requires p38, c-Jun N-terminal kinase, and nuclear factor kappaB: differential regulation of collagenase 1 and collagenase 3. *Arthritis Rheum* 2000; **43**: 801-811 [PMID: 10765924 DOI: 10.1002/1529-0131(200004)43:4<801::AID-ANR10>3.0.CO;2-4]
  - 23 **Lefebvre V**, Peeters-Joris C, Vaes G. Modulation by interleukin 1 and tumor necrosis factor alpha of production of collagenase, tissue inhibitor of metalloproteinases and collagen types in differentiated and dedifferentiated articular chondrocytes. *Biochim Biophys Acta* 1990; **1052**: 366-378 [PMID: 2162214 DOI: 10.1016/0167-4889(90)90145-4]
  - 24 **Tortorella MD**, Malfait AM, Deccico C, Arner E. The role of ADAM-TS4 (aggrecanase-1) and ADAM-TS5 (aggrecanase-2) in a model of cartilage degradation. *Osteoarthritis Cartilage* 2001; **9**: 539-552 [PMID: 11520168 DOI: 10.1053/joca.2001.0427]
  - 25 **Abramson SB**. Nitric oxide in inflammation and pain associated with osteoarthritis. *Arthritis Res Ther* 2008; **10** Suppl 2: S2 [PMID: 19007427 DOI: 10.1186/ar2463]
  - 26 **Giunta S**, Castorina A, Marzagalli R, Szychlińska MA, Pichler K, Mobasher A, Musumeci G. Ameliorative effects of PACAP against cartilage degeneration. Morphological, immunohistochemical and biochemical evidence from in vivo and in vitro models of rat osteoarthritis. *Int J Mol Sci* 2015; **16**: 5922-5944 [PMID: 25782157 DOI: 10.3390/ijms16035922]
  - 27 **Musumeci G**, Trovato FM, Pichler K, Weinberg AM, Loreto C, Castrogiovanni P. Extra-virgin olive oil diet and mild physical activity prevent cartilage degeneration in an osteoarthritis model: an in vivo and in vitro study on lubricin expression. *J Nutr Biochem* 2013; **24**: 2064-2075 [PMID: 24369033 DOI: 10.1016/j.jnutbio.2013.07.007]
  - 28 **Leonardi R**, Rusu MC, Loreto F, Loreto C, Musumeci G. Immunolocalization and expression of lubricin in the bilaminar zone of the human temporomandibular joint disc. *Acta Histochem* 2012; **114**: 1-5 [PMID: 21955422 DOI: 10.1016/j.acthis.2010.11.011]
  - 29 **Maruyama T**, Kamihama H, Watanabe M, Matsuo T, Matsuda K, Tanaka A, Matsuda H, Nomura Y. Olive leaf extract prevents cartilage degeneration in osteoarthritis of STR/ort mice. *Bioscience, Biotechnology, and Biochemistry*, 2018; **82**: 7, 1101-1106 [DOI: 10.1080/09168451.2018.1451741]
  - 30 **Elmorsy S**, Funakoshi T, Sasazawa F, Todoh M, Tadano S, Iwasaki N. Chondroprotective effects of high-molecular-weight cross-linked hyaluronic acid in a rabbit knee osteoarthritis model. *Osteoarthritis Cartilage* 2014; **22**: 121-127 [PMID: 24185110 DOI: 10.1016/j.joca.2013.10.005]
  - 31 **Muthumani M**, Miltonprabu S. Ameliorative efficacy of tetrahydrocurcumin against arsenic induced oxidative damage, dyslipidemia and hepatic mitochondrial toxicity in rats. *Chem Biol Interact* 2015; **235**: 95-105 [PMID: 25869292 DOI: 10.1016/j.cbi.2015.04.006]
  - 32 **Wu JC**, Tsai ML, Lai CS, Wang YJ, Ho CT, Pan MH. Chemopreventative effects of tetrahydrocurcumin on human diseases. *Food Funct* 2014; **5**: 12-17 [PMID: 24220621 DOI: 10.1039/c3fo60370a]
  - 33 **Park S**, Lee LR, Seo JH, Kang S. Curcumin and tetrahydrocurcumin both prevent osteoarthritis symptoms and decrease the expressions of pro-inflammatory cytokines in estrogen-deficient rats. *Genes Nutr* 2016; **11**: 2 [PMID: 27482294 DOI: 10.1186/s12263-016-0520-4]
  - 34 **Ma Y**, Sun X, Huang K, Shen S, Lin X, Xie Z, Wang J, Fan S, Ma J, Zhao X. Sanguinarine protects against osteoarthritis by suppressing the expression of catabolic proteases. *Oncotarget* 2017; **8**: 62900-62913 [PMID: 28968958 DOI: 10.18632/oncotarget.17036]
  - 35 **Loeser RF**. The effects of aging on the development of osteoarthritis. *HSS J* 2012; **8**: 18-19 [PMID: 23372520 DOI: 10.1007/s11420-011-9237-9]
  - 36 **Martin JA**, Buckwalter JA. Post-traumatic osteoarthritis: the role of stress induced chondrocyte damage. *Biorheology* 2006; **43**: 517-521 [PMID: 16912423]
  - 37 **Musumeci G**, Castrogiovanni P, Trovato FM, Weinberg AM, Al-Wasiyah MK, Alqahtani MH, Mobasher A. Biomarkers of Chondrocyte Apoptosis and Autophagy in Osteoarthritis. *Int J Mol Sci* 2015; **16**: 20560-20575 [PMID: 26334269 DOI: 10.3390/ijms160920560]
  - 38 **Scott JL**, Gabrielides C, Davidson RK, Swingle TE, Clark IM, Wallis GA, Boot-Handford RP, Kirkwood TB, Taylor RW, Young DA. Superoxide dismutase downregulation in osteoarthritis progression and end-stage disease. *Ann Rheum Dis* 2010; **69**: 1502-1510 [PMID: 20511611 DOI: 10.1136/ard.2009.119966]
  - 39 **Manoy P**, Yuktanandana P, Tanavalee A, Anomasiri W, Ngarmukos S, Tanpowpong T, Honsawek S. Vitamin D supplementation improves quality of life and physical performance in osteoarthritis patients. *Nutrients* 2017; **9**: [PMID: 28933742 DOI: 10.3390/nu9080799]
  - 40 **Mabey T**, Honsawek S. Role of vitamin D in osteoarthritis: molecular, cellular, and clinical perspectives. *Int J Endocrinol* 2015; **2015**: 383918 [PMID: 26229532 DOI: 10.1155/2015/383918]
  - 41 **Mokhtari Z**, Hekmatdoost A, Nourian M. Antioxidant efficacy of vitamin D. *J Parathyroid Dis* 2017; **5**: 11-16.
  - 42 **Pojednic RM**, Ceglia L. The emerging biomolecular role of vitamin D in skeletal muscle. *Exerc Sport Sci Rev* 2014; **42**: 76-81

- [PMID: 24508736 DOI: 10.1249/JES.000000000000013]
- 43 **Takada T**, Miyaki S, Ishitobi H, Hirai Y, Nakasa T, Igarashi K, Lotz MK, Ochi M. Bach1 deficiency reduces severity of osteoarthritis through upregulation of heme oxygenase-1. *Arthritis Res Ther* 2015; **17**: 285 [PMID: 26458773 DOI: 10.1186/s13075-015-0792-1]
- 44 **Ishitobi H**, Sanada Y, Kato Y, Ikuta Y, Shibata S, Yamasaki S, Lotz MK, Matsubara K, Miyaki S, Adachi N. Carnosic acid attenuates cartilage degeneration through induction of heme oxygenase-1 in human articular chondrocytes. *Eur J Pharmacol* 2018; **830**: 1-8 [PMID: 29678719 DOI: 10.1016/j.ejphar.2018.04.018]
- 45 **Bahri S**, Jameleddine S, Shlyonsky V. Relevance of carnosic acid to the treatment of several health disorders: Molecular targets and mechanisms. *Biomed Pharmacother* 2016; **84**: 569-582 [PMID: 27694001 DOI: 10.1016/j.biopha.2016.09.067]
- 46 **Musumeci G**, Maria Trovato F, Imbesi R, Castrogiovanni P. Effects of dietary extra-virgin olive oil on oxidative stress resulting from exhaustive exercise in rat skeletal muscle: a morphological study. *Acta Histochem* 2014; **116**: 61-69 [PMID: 23810034 DOI: 10.1016/j.acthis.2013.05.006]
- 47 **Musumeci G**, Castrogiovanni P, Trovato FM, Imbesi R, Giunta S, Szychlinska MA, Loreto C, Castorina S, Mobasher A. Physical activity ameliorates cartilage degeneration in a rat model of aging: a study on lubricin expression. *Scand J Med Sci Sports* 2015; **25**: e222-e230 [PMID: 25039883 DOI: 10.1111/sms.12290]
- 48 **Musumeci G**. Sarcopenia and Exercise “The State of the Art?”. *J Funct Morphol Kinesiol* 2017; **2**: 40 [DOI: 10.3390/jfmk2040040]
- 49 **Trovato FM**, Castrogiovanni P, Szychlinska MA, Purrello F, Musumeci G. Impact of Western and Mediterranean Diets and Vitamin D on Muscle Fibers of Sedentary Rats. *Nutrients* 2018; **10**: [PMID: 29462978 DOI: 10.3390/nu10020231]

**P- Reviewer:** Gheita TA, Yukata, K **S- Editor:** Ma RY  
**L- Editor:** Filipodia **E- Editor:** Wu YXJ



## Should antibiotics be administered before arthroscopic knee surgery? A systematic review of the literature

John Carney, Nathanael Heckmann, Erik N Mayer, Ram K Alluri, Carleton Thomas Vangsness Jr., George F Hatch III, Alexander E Weber

John Carney, Nathanael Heckmann, Erik N Mayer, Ram K Alluri, Carleton Thomas Vangsness Jr., George F Hatch III, Alexander E Weber, Department of Orthopaedic Surgery, University of Southern California, Los Angeles, CA 90033, United States

ORCID number: John Carney (0000-0002-0865-0548); Nathanael Heckmann (0000-0003-1293-1702); Erik N Mayer (0000-0003-3149-7139); Ram K Alluri (0000-0001-5919-707X); Carleton Thomas Vangsness Jr. (0000-0002-0143-0155); George F Hatch III (0000-0003-1655-4588); Alexander E Weber (0000-0002-4957-4334).

**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.

**PRISMA 2009 Checklist statement:** The guidelines of the PRISMA 2009 Statement have been adopted.

**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:** Alexander E Weber, MD, Assistant Professor, Department of Orthopaedic Surgery, University of Southern California, 1520 San Pablo Street, Suite 2000, Los Angeles, CA 90033, United States. [weberae@usc.edu](mailto:weberae@usc.edu)  
Telephone: +1-818-9497381

Received: July 2, 2018

Peer-review started: July 2, 2018

First decision: July 18, 2018

Revised: September 9, 2018

Accepted: October 23, 2018

Article in press: October 23, 2018

Published online: November 18, 2018

### Abstract

#### AIM

To explore the current evidence surrounding the administration of prophylactic antibiotics for arthroscopic knee surgery.

#### METHODS

Databases were searched from inception through May of 2018 for studies examining prophylactic antibiotic use and efficacy in knee arthroscopy. Studies with patient data were further assessed for types of arthroscopic procedures performed, number of patients in the study, use of antibiotics, and outcomes with the intention of performing a pooled analysis. Data pertaining to "deep tissue infection" or "septic arthritis" were included in our analysis. Reported data on superficial infection were not included in our data analysis. For the pooled analysis, a relative risk ratio was calculated and  $\chi^2$  tests were used to assess for statistical significance between rates of infection amongst the various patient groups. *Post hoc* power analyses were performed to compute the statistical power obtained from our sample sizes. Number needed to treat analyses were performed for statistically significant differences by dividing 1 by the difference between the infection rates of the antibiotic and no antibiotic groups. An alpha value of 0.05 was used for our analysis. Study heterogeneity was assessed by Cochrane's *Q* test as well as calculation of the  $I^2$  value.

#### RESULTS

A total of 49682 patients who underwent knee ar-

throscopy for a diverse set of procedures across 19 studies met inclusion criteria for pooled analysis. For those not undergoing graft procedures, there were 27 cases of post-operative septic arthritis in 34487 patients (0.08%) who received prophylactic antibiotics and 16 cases in 10911 (0.15%) who received none [risk ratio (RR) = 0.53, 95% confidence interval (CI): 0.29-0.99,  $P = 0.05$ ]. A sub-group analysis in which bony procedures were excluded was performed which found no significant difference in infection rates between patients that received prophylactic antibiotics and patients that did not ( $P > 0.05$ ). All anterior cruciate ligament reconstruction studies used prophylactic antibiotics, but two studies investigating the effect of soaking the graft in vancomycin in addition to standard intravenous (IV) prophylaxis were combined for analysis. There were 19 cases in 1095 patients (1.74%) who received IV antibiotics alone and no infections in 2034 patients who received IV antibiotics and had a vancomycin soaked graft (RR = 0.01, 95%CI: 0.001-0.229,  $P < 0.01$ ).

### CONCLUSION

Prophylactic antibiotics are effective in preventing septic arthritis following simple knee arthroscopy. In procedures involving graft implantation, graft soaking reduces the rate of infection.

**Key words:** Knee arthroscopy; Antibiotics; Systematic review; Vancomycin; Anterior cruciate ligament

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Our study is the first to demonstrate prophylactic antibiotics are effective in preventing septic arthritis following simple arthroscopic procedures of the knee, though given the large number needed to treat, the clinical significance of this finding is unclear. There is little to no debate that antibiotics should be used prophylactically for arthroscopic surgeries involving graft implantation. However, our findings indicate that the addition of graft soaking further reduces the rate of infection. Further study is warranted to identify patient populations and arthroscopic procedures in which the use of prophylactic antibiotics may not be necessary.

Carney J, Heckmann N, Mayer EN, Alluri RK, Vangsness Jr. CT, Hatch III GF, Weber AE. Should antibiotics be administered before arthroscopic knee surgery? A systematic review of the literature. *World J Orthop* 2018; 9(11): 262-270 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i11/262.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i11.262>

### INTRODUCTION

Antibiotics have been administered prophylactically in major orthopaedic surgeries for decades<sup>[1]</sup>. Their use has been shown to reduce rates of local and systemic

infection, which leads to better patient outcomes when used in combination with proper sterile surgical technique<sup>[2]</sup>. Failure to provide adequate infection prophylaxis prior to elective knee arthroscopy may result in septic arthritis, a devastating complication which has been shown to delay recovery time and diminish functional outcomes<sup>[3]</sup>. The most common pathogen responsible for septic arthritis is *Staphylococcus aureus*; though other pathogens have been identified as well<sup>[4,5]</sup>. It is accepted within the orthopaedic community that prophylactic antibiotics, typically cephalosporins or vancomycin, should be administered prior to major orthopaedic surgeries<sup>[6]</sup>. However, the use of routine prophylactic antibiotics prior to less invasive surgeries such as hand procedures and elective arthroscopic surgeries has not been established. The wide range of rates of antibiotic administration in the published literature, ranging from as low as 5% to as high as 80.5%, highlights the lack of understanding of the role of antibiotic prophylaxis<sup>[7-13]</sup>. The use of prophylactic antibiotics is not without risk; allergic reaction, development of resistant organisms, and side effects specific to the chosen antibiotic can be a burden to patients and health care providers alike.

There is published data that demonstrate that prophylactic antibiotics may be unnecessary for minimally invasive non-bony procedures such as carpal tunnel release<sup>[14]</sup>. As of 2009, the American Academy of Orthopedic Surgeons published guidelines on carpal tunnel release that did not mandate the use of prophylactic antibiotics, but rather stated their use was an option for physicians to consider<sup>[14]</sup>. There is evidence to suggest that, like carpal tunnel release, patients undergoing knee arthroscopy may receive little to no benefit from receiving prophylactic antibiotics. A recent study by Wyatt *et al*<sup>[8]</sup> found no significant difference in cases of deep infection between patients that received prophylactic antibiotics prior to knee arthroscopy and those who did not in a study that included 40810 patients. This study is in agreement with other studies on this topic, which similarly found no difference in infection rates if prophylactic antibiotics are used or withheld<sup>[7,12,15-17]</sup>. Although the study by Wyatt *et al*<sup>[8]</sup> contained large cohort of patients, other studies are relatively small and may be too underpowered to draw meaningful conclusions.

The purpose of this systematic review is to summarize current literature with regards to the efficacy of antibiotic prophylaxis in arthroscopic knee surgery and to pool available studies to better determine the true infection risk in knee arthroscopy. This study is the first to our knowledge that attempts to combine data from published studies to better understand the role of antibiotic prophylaxis in knee arthroscopy. We hypothesize that there is no evidence to support the routine administration of prophylactic antibiotics in arthroscopic knee surgery.

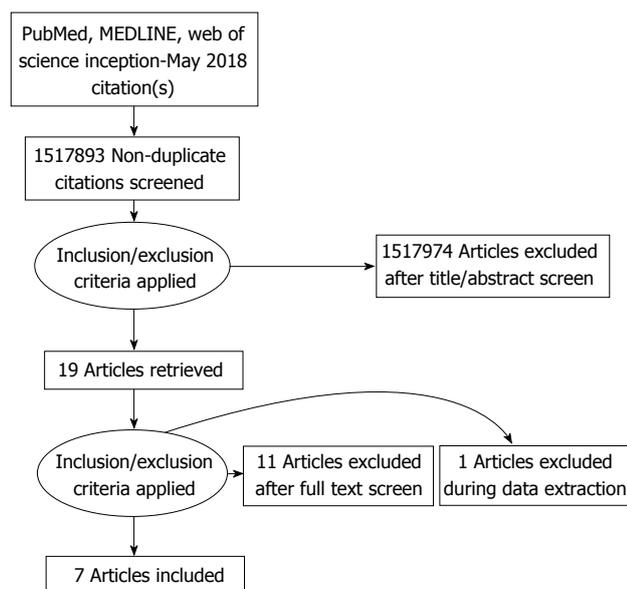


Figure 1 PRISMA flow diagram of methods for study inclusion.

## MATERIALS AND METHODS

Two reviewers completed a comprehensive search of PubMed, MEDLINE, and Web of Science to identify studies pertaining to the use of antibiotic prophylaxis in knee arthroscopy from inception to May of 2018. Search strategies were customized for each database to produce the highest yield of possible results (Appendix A). Randomized control trials, prospective and retrospective studies, case-control studies, and systematic reviews were included. Review articles and surveys discussing the use of prophylactic antibiotics in arthroscopy were excluded from use in a pooled analysis, but were included for discussion purposes. Case reports, animal studies, and cadaveric studies were also excluded. The references of each study were also assessed for eligibility for our review. Studies with patient data were further assessed for types of arthroscopic procedures performed, number of patients in the study, use of antibiotics, and outcomes with the intention of performing a pooled analysis. Data pertaining to "deep tissue infection" or "septic arthritis" were included in our analysis. Reported data on superficial infection were not included in our data analysis.

### Statistical analysis

For the pooled analysis, a relative risk ratio was calculated and  $\chi^2$  tests were used to assess for statistical significance between rates of infection amongst the various patient groups. *Post hoc* power analyses were performed to compute the statistical power obtained from our sample sizes. Number needed to treat analyses were performed for statistically significant differences by dividing 1 by the difference between the infection rates of the antibiotic and no antibiotic groups. An alpha value of 0.05 was used for our analysis. Study heterogeneity was assessed by Cochrane's *Q* test as

well as calculation of the  $I^2$  value.

## RESULTS

Our initial search yielded 1517893 studies. Nineteen studies satisfied inclusion criteria: 3 randomized control trials, 7 retrospective case control studies, 4 retrospective case series studies, 2 surveys, and 4 review articles (Table 1). These studies were further analyzed to determine if their data could be pooled for further analysis. Studies with data comparing infectious outcomes in knee arthroscopy procedures between groups that received prophylaxis and those that did not were included in our grouped analysis while studies with data not specific to the knee joint or not limited to arthroscopy were excluded.

Eight studies met inclusion criteria for pooled analysis. Upon closer review however, it was determined that two studies likely utilized the same patient database to achieve their results<sup>[18,19]</sup>. We established correspondence with one of the authors to confirm this finding. Upon confirmation the more recent and higher powered of the two was included while the other was excluded from data analysis, leaving 7 studies for pooled analysis (Figure 1). From these studies, there were a total of 49682 patients who underwent an arthroscopic procedure. Arthroscopic procedures included diagnostic arthroscopy, joint debridement, synovectomy, partial or complete meniscectomy, meniscus repair, microfracture repair, lateral retinacular release, loose body removal, and anterior cruciate ligament reconstruction.

Five of the 7 studies had similar designs that allowed us to perform a pooled analysis of prophylactic antibiotic efficacy in arthroscopic procedures that do not involve the implantation of a graft (Table 2)<sup>[7,8,12,15,17]</sup>. Out of a total of 45398 patients, 34487 received prophylactic antibiotics prior to arthroscopy while 10991 did not. All authors used a first generation cephalosporin such as cefazolin for primary prophylaxis, except in cases of known drug allergy. The antibiotic group had a total of 27 cases of septic arthritis (0.08%) while the no antibiotic group had 16 cases of septic arthritis (0.15%). The differences in infection rates was found to be significant [risk ratio (RR) = 0.53, 95% confidence interval (CI): 0.29 to 0.99,  $P = 0.05$ , *post hoc* power = 53%]. Based on these findings, the number of patients needed to treat with IV antibiotics in order to prevent 1 infection is 1463.

Regarding study heterogeneity, the Cochrane *Q* value was calculated to be 2.40 ( $P = 0.49$ ) while the  $I^2$  value was calculated to be 0% (95%CI: 0.00 to 83.11). Study heterogeneity is illustrated in Figure 2.

A subgroup analysis of this group was conducted and excluded studies that involved bony procedures (microfracture repair, procedures requiring bone tunnels, etc.), which have been demonstrated to have an increased risk of infection<sup>[20,21]</sup>. Two studies excluded bony procedures and were included in a separate

Table 1 Summary of literature review results

Study name	Study type	No. of Patients	Procedures done	Findings/results/conclusions
Wyatt <i>et al</i> <sup>[6]</sup>	Retrospective Review	40810	Diagnostic arthroscopy, joint debridement, synovectomy, partial or complete meniscectomy, meniscus repair, microfracture, and lateral retinacular release	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Bert <i>et al</i> <sup>[7]</sup>	Retrospective Review	3231	Arthroscopic meniscectomy, arthroscopic meniscal repair, loose body removal, lateral retinacular release, and arthroscopic debridement	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Qi <i>et al</i> <sup>[27]</sup>	Retrospective Review	1326	Arthroscopic diagnosis, debridement, partial or complete meniscectomy, arthroscopic shaving and microfracture, removal of loose bodies, synovectomy and lateral retinacular release	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Ghmait <i>et al</i> <sup>[15]</sup>	Randomized control trial	180	Diagnostic arthroscopy, meniscus repair	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Rose <i>et al</i> <sup>[2]</sup>	Retrospective Review	302	Meniscectomies, arthroscopic debridement, arthroscopic meniscal repair, arthroscopic shaving and microfracture, removal of loose bodies, arthroscopic synovectomy, arthroscopic lateral retinacular release and diagnostic arthroscopic	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Wieck <i>et al</i> <sup>[6]</sup>	Randomized control trial	437	Unspecified arthroscopy	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Phegan <i>et al</i> <sup>[8]</sup>	Retrospective Review	1585	ACL reconstruction with graft	Vancomycin soaked grafts have a lower infection rate than non-soaked grafts
Vertullo <i>et al</i> <sup>[9]</sup>	Retrospective Review	1135	ACL reconstruction with graft	Vancomycin soaked grafts have a lower infection rate than non-soaked grafts
Pérez-Prieto <i>et al</i> <sup>[22]</sup>	Retrospective Review	1544	ACL reconstruction with graft	Vancomycin soaked grafts have a lower infection rate than non-soaked grafts
Yazdi <i>et al</i> <sup>[31]</sup>	Randomized control trial	360	ACL reconstruction with graft	Using gentamicin in irrigating solutions during arthroscopic ACL reconstruction surgery does not statistically decrease post-operation septic arthritis
Formaini <i>et al</i> <sup>[10]</sup>	Retrospective Review	2330	Unspecified arthroscopy	No significant difference in infection rates between prophylaxis and non-prophylaxis groups
Armstrong <i>et al</i> <sup>[11]</sup>	Retrospective Review	4256	Unspecified arthroscopy	Infection following knee arthroscopy was associated with prolonged operation time and corticosteroid use, not presence or absence of prophylactic antibiotics
D'Angelo and Ogilvie-Harris <sup>[26]</sup>	Retrospective Review	9	Unspecified arthroscopy	Antibiotic prophylaxis may reduce hospital costs by reducing spending on treating septic arthritis based on a 9 case review of patients with septic arthritis following arthroscopy
Babcock <i>et al</i> <sup>[23]</sup>	Retrospective Review	27	Unspecified arthroscopy	In a case series review of septic arthritis patients, shaving and corticosteroids were found to be significant risk factors, but not antibiotics
Lubowitz <i>et al</i> <sup>[25]</sup>	Review Article	NA	NA	There is not enough evidence to conclude whether or not antibiotics should be administered prophylactically in knee arthroscopy. However, the results of articles like Bert <i>et al</i> should be further examined and studied
Kurzweil <sup>[27]</sup>	Review Article	NA	NA	There is not enough evidence to conclude whether or not antibiotics should be administered prophylactically in knee arthroscopy. However, they should still be used as a measure to reduce the risk of post procedure infection

Onyema <i>et al</i> <sup>[64]</sup>	Review Article	NA	NA	Prophylactic antibiotics should not be used for knee arthroscopy
Prokuski <sup>[6]</sup>	Review Article	NA	NA	Cephalosporins are the drug of choice for most orthopedic surgeries. However, there is a lack of evidence supporting their efficacy in arthroscopic surgery
Müller-Rath <i>et al</i> <sup>[6]</sup>	Survey	110 physicians	NA	62% of the surgeons reported the use of an antibiotic prophylaxis in every arthroscopic case, while 19% administer antibiotics only occasionally
Mini <i>et al</i> <sup>[3]</sup>	Survey	166 hospitals	NA	57.1% of orthopedic surgeons routinely use antibiotic prophylaxis for arthroscopy

ACL: Anterior cruciate ligament; NA: Not available.

analysis (Table 3)<sup>[7,15]</sup>. A study by Bert *et al*<sup>[7]</sup> examined 3231 patients undergoing various arthroscopic procedures, and analyzed meniscectomies separately, of which 933 (34%) received antibiotic prophylaxis and 1847 (66%) did not. A second study by Ghnaimat *et al*<sup>[15]</sup> randomized 180 patients undergoing either partial meniscectomy, plica excision, synovial biopsy, or diagnostic arthroscopy into two groups, of which 90 (50%) received antibiotic prophylaxis and 90 (50%) did not. From a total of 2960 patients, 1023 (35%) received antibiotics and 1937 (65%) did not. There was 1 (0.10%) case of septic arthritis in the antibiotic group and 3 (0.15%) cases of septic arthritis in the group that did not receive antibiotics, however this difference was not statistically significant (RR = 0.63, 95%CI: 0.07 to 6.06, *P* = 0.69, *post hoc* power = 5%).

Two of the 7 studies were pooled for data analysis to analyze arthroscopic anterior cruciate ligament (ACL) reconstruction (Table 4)<sup>[18,22]</sup>. Both studies investigated the role of soaking the ACL autograft in vancomycin prior to implantation. Of 3129 patients, 1095 received intravenous (IV) antibiotics alone prior to arthroscopic ACL reconstruction, while 2034 patients received IV antibiotics and had their ACL graft soaked in vancomycin. There were 19 cases of infection in the IV antibiotics alone group (1.74%) and 0 infections in the IV antibiotics with vancomycin soaked graft group (0%). The difference in rates was found to be significant (RR = 0.01, 95%CI: 0.001 to 0.229, *P* < 0.01, *post hoc* power = 99.8%). Given these infection rates, the number need to treat with vancomycin soaked grafts to prevent 1 infection is 57.0. Analysis of heterogeneity was not performed in this dataset given the rates of infection in treatment groups were equal at 0%.

## DISCUSSION

The results of our systematic review demonstrate that there is evidence supporting the use of prophylactic antibiotics in knee arthroscopic procedures to prevent postoperative infections (*P* = 0.05). The statistical significance may be attributed to knee arthroscopic procedures in which the subchondral bone is manipulated. Given the *post hoc* power analyses of our general population as well as our bone manipulation subgroup (53% and 5%, respectively), our findings should not be interpreted as a definitive answer to the question of whether antibiotic prophylaxis is appropriate in knee arthroscopy not involving a graft. However, in cases of graft implantation, particularly ACL autograft reconstruction, antibiotics appear to have a substantial protective effect particularly when antibiotics are used both locally (*i.e.*, autograft soaked in vancomycin) and systemically. Furthermore, while our findings for the pooled group were statistically significant, the clinical utility of these differences is in question as reflected by the needed to treat of approximately 1400 patients.

### Arthroscopy without graft Implantation

The findings of this systematic review are in juxtaposition with current literature on this subject. A study by Babcock *et al*<sup>[23]</sup> investigated an outbreak of septic arthritis following arthroscopy at a community hospital from 1994 to 1996. The study concluded that preoperative skin shaving and intra-articular corticosteroid injection significantly increased risk of infection, but found no link between infection and use of prophylactic antibiotics. A review of 4256 knee arthroscopies with 15% receiving prophylactic antibiotics by Armstrong *et al*<sup>[11]</sup> similarly found that antibiotic use was not linked to a lower infection rate. Rather, corticosteroid use and prolonged operation time were the two greatest risk factors.

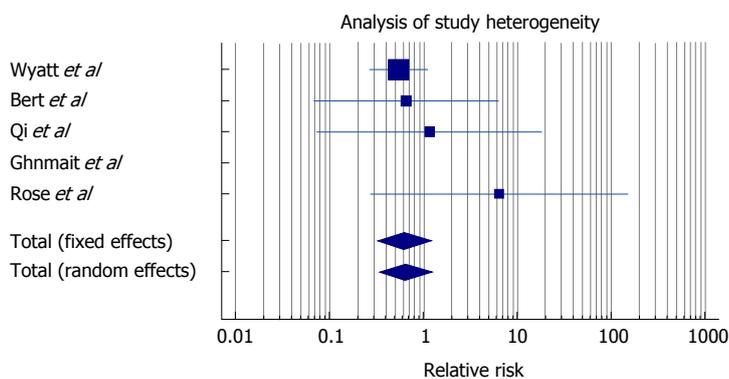
Our literature search found five studies of similar design that did not include the use of a graft and could be pooled for analysis. This pooled analysis demonstrated that

**Table 2 Comparison of infection rates in simple arthroscopy patients receiving prophylactic antibiotics**

Study name	Total patients	Patients receiving antibiotics	Patients not receiving antibiotics	No. of septic arthritis cases: Antibiotic group	No. of septic arthritis cases: No antibiotic group	Septic arthritis rate: Antibiotic group (%)	Septic arthritis rate: No antibiotic group (%)	P value
Wyatt <i>et al</i> <sup>[8]</sup>	40810	32836	7974	25	11	0.08	0.14	
Bert <i>et al</i> <sup>[7]</sup>	2780	933	1847	1	3	0.15	0.16	
Qi <i>et al</i> <sup>[17]</sup>	1326	614	712	1	1	0.16	0.14	
Ghnmait <i>et al</i> <sup>[15]</sup>	180	90	90	0	0	0	0	
Rose <i>et al</i> <sup>[12]</sup>	302	14	288	0	1	0	0.35	
Total	45398	34487	10911	27	16	0.08	0.15	0.05

**Table 3 Comparison of infection rates in simple arthroscopy patients receiving prophylactic antibiotics, excluding bony procedures**

Study name	Total patients	Patients receiving antibiotics	Patients not receiving antibiotics	No. of septic arthritis cases: Antibiotic group	No. of septic arthritis cases: No antibiotic group	Septic arthritis rate: Antibiotic group (%)	Septic arthritis rate: No antibiotic group (%)	P value
Bert <i>et al</i> <sup>[7]</sup>	2780	933	1847	1	3	0.11	0.16	
Ghnmait <i>et al</i> <sup>[15]</sup>	180	90	90	0	0	0	0	
Total	2960	1023	1937	1	3	0.1	0.15	0.69



Study name	Infection rate in no antibiotics group	Infection rate in no antibiotics group	Relative risk	95%CI	P value
Wyatt <i>et al</i> <sup>[8]</sup>	0.08	0.14	0.55	0.27-1.12	0.1
Bert <i>et al</i> <sup>[7]</sup>	0.15	0.16	0.66	0.07-6.34	0.72
Qi <i>et al</i> <sup>[17]</sup>	0.16	0.14	1.16	0.07-18.50	0.92
Ghnmait <i>et al</i> <sup>[15]</sup>	0	0	1	0.02-49.86	1
Rose <i>et al</i> <sup>[12]</sup>	0	0.35	6.42	0.27-151.12	0.25
Total	0.08	0.15	0.54	0.29-0.99	0.05
Cochrane's Q	2.4				
Significance Level	P = 0.49				
I <sup>2</sup>	0.00%				
95%CI for I <sup>2</sup>	0.00 to 83.84				

**Figure 2 Comparison of odds ratio for simple arthroscopy.**

there was a significant difference in infection rates between knee arthroscopy patients who received antibiotics and those who did not. Of these five studies, Wyatt *et al*<sup>[8]</sup> was substantially larger in size ( $n = 40810$ ) than the others, and thus our results are largely dominated by the findings of this study. Although they concluded that there was no difference in infection rate, they reported a  $P$  value that approached statistical significance ( $P = 0.10$ ). Pooling their cases with those of the other studies was able to tip the scale towards significance and show that there is a difference in infection rate between those that do and do not receive prophylactic antibiotics.

Regarding the rigour of these studies, we feel confident in the results as investigation of infection rates was the primary focus of each study. Furthermore, each study analyzed similar patient groups and used similar methods of antibiotic prophylaxis (cephalosporins) that are consistent with contemporary guidelines. Our analysis of study heterogeneity confirms that the findings amongst studies are consistent ( $I^2: 0.00\%$ ). Thus, we believe the results of this systematic review to be both accurate and applicable to current orthopaedic practice. There were other studies identified during our search that were excluded from our pooled analysis, but are worth mentioning in regards to our findings. Wieck

**Table 4 Comparison of infection rates in arthroscopic anterior cruciate ligament reconstruction with vs without vancomycin graft soaking**

Study name	Total patients	IV prophylaxis alone	IV prophylaxis + vancomycin	Number infected IV alone	Number infected IV + vancomycin	Infection rate IV alone (%)	Infection rate IV + vancomycin (%)	P value
Phegan <i>et al</i> <sup>[18]</sup>	1585	285	1300	4	0	1.4	0	
Pérez-Prieto <i>et al</i> <sup>[22]</sup>	1544	810	734	15	0	1.85	0	
Total	3129	1095	2034	19	0	1.74	0	< 0.001

*et al*<sup>[16]</sup> investigated the role of antibiotic prophylaxis in 437 patients who underwent an arthroscopic procedure, not limited to the knee, and found no cases of deep infection in either arm of their study. A retrospective study of pediatric patients undergoing minimally invasive orthopedic procedures, including arthroscopy, by Formaini *et al*<sup>[10]</sup> found no evidence to suggest that antibiotic prophylaxis reduced infection rates. Review articles by Onyema *et al*<sup>[24]</sup>, Lubowitz *et al*<sup>[25]</sup>, and Prokusi<sup>[6]</sup> all highlighted the lack of evidence with regards to prophylactic antibiotic administration in arthroscopy and noted that their use may not be necessary. Our review differs from the aforementioned articles in that we reviewed new literature as well as included our own data analysis, which provided a large enough population size to show significant differences in infection rates. Our study is the first to our knowledge to demonstrate the efficacy of prophylaxis at the alpha = 0.05 level. Thus, we emphasize the need for further study and confirmation of our findings before they can be translated into clinical practice.

There were two publications identified that recommended prophylactic antibiotics and thus are in agreement with our findings. One was a retrospective review of septic arthritis cases following arthroscopy by D'Angelo and Ogilvie-Harris<sup>[26]</sup> in which the authors recommended that prophylaxis be used to prevent deep tissue infections. However, the authors' rationale for the efficacy of antibiotic prophylaxis in arthroscopy is based on a paper on general orthopedic surgeries, not arthroscopy<sup>[11]</sup>. A 2006 opinion article by Kurzweil<sup>[27]</sup> argued that although current evidence does not demonstrate the efficacy of antibiotic prophylaxis in knee arthroscopy, there is still not enough evidence to argue for its discontinuation. Kurzweil<sup>[27]</sup> stated that although a perfectly performed arthroscopic procedure on a healthy patient may not be affected by the use of antibiotics, they may serve as a safety net for physician errors or breaks in protocol as well as both known and unknown health-related risk factors of patients. Despite our significant findings, we agree that more evidence is needed to better understand the role of antibiotic prophylaxis in arthroscopy before a strong recommendation for or against their use can be made.

#### **Arthroscopic ACL reconstruction with graft implantation**

After a review of the literature, we determined that ACL reconstruction needed to be considered separate from other arthroscopic procedures, as our search did

not yield any publications related to ACL reconstruction that did not use antibiotic prophylaxis. Rather, studies varied in the type of antibiotic prophylaxis utilized. In arthroscopic ACL reconstruction, the graft presents additional infection risk as it is inserted into the joint space from the outside environment. It has been demonstrated that the source of infection can come from direct contamination of the graft or from skin flora<sup>[28]</sup>.

A 2013 study by Torres-Claramunt *et al*<sup>[29]</sup> found an infection rate of 1.8% following ACL reconstruction with prophylactic administration of either cefazolin or vancomycin. However, three retrospective reviews found significantly reduced rates of septic arthritis when ACL grafts were soaked in vancomycin prior to insertion into the joint space<sup>[18,19,22]</sup>. Our combined analysis of two of these studies strengthens these authors' individual findings. It is particularly important to note that in all three of these studies the infection rate was reduced to 0%. This highlights the important role of local prophylactic antibiotics during ligament reconstruction, which has been demonstrated in other orthopaedic procedures<sup>[30]</sup>. An alternative method of irrigating knee joints with a solution containing gentamycin was tested in a randomized control trial by Yazdi *et al*<sup>[31]</sup>, but found to have no significant impact on infection rates.

The main weakness of this systematic review was the small number of studies that directly compared patients receiving antibiotic prophylaxis in arthroscopy to controls. Also, even in simple arthroscopic procedures without grafts, there may be many variations that affect infection risk (*e.g.*, type of meniscal repair, whether additional incisions were made as in for an inside-out approach, *etc.*). Furthermore, our findings with regards to simple arthroscopy are largely dominated by one study. Three of the four studies used in the pooled analysis were multi-surgeon retrospective cohort studies and criteria for determining which patients received prophylactic antibiotics was left to individual surgeon discretion. The controlled trial performed by Ghnaimat *et al*<sup>[16]</sup> only semi-randomized antibiotic prophylaxis by allotting according to admission number (even admission numbers received antibiotics). Additional studies are needed to better understand the role antibiotic prophylaxis plays in the development of septic arthritis. Being able to identify procedures and patient groups that do not require antibiotic prophylaxis offers the potential to reduce hospital costs, reduce the risk of allergic reaction to medication, and slow the development of drug resistant organisms. Thus, further study of this topic is

warranted.

Our study is the first to demonstrate prophylactic antibiotics are effective in preventing septic arthritis following simple arthroscopic procedures of the knee, though given the large number needed to treat, the clinical significance of this finding is unclear. Our findings regarding the addition of graft soaking indicate that further steps can be taken to reduce the rate of infection in procedures involving graft implantation. Further studies are needed to better understand when withholding prophylaxis may be appropriate.

## ARTICLE HIGHLIGHTS

### Research background

The administration of prophylactic antibiotics prior to knee arthroscopy is a common practice in the orthopaedic community.

### Research motivation

There are no studies to date that demonstrate that the use of antibiotic prophylaxis in arthroscopic surgery of the knee is effective.

### Research objectives

The purpose of this study is to analyze the literature on the effect on antibiotic prophylaxis in knee arthroscopy on rates of septic arthritis.

### Research methods

We conducted a literature review of PubMed, MEDLINE, and Web of Science from inception to May of 2018. Data from studies meeting inclusion criteria were pooled for analysis. Risk-ratios were calculated to determine the effect of antibiotic prophylaxis on rates of septic arthritis in knee arthroscopy.

### Research results

Nineteen studies met inclusion criteria for pooled analysis. For those not undergoing graft procedures, there were 27 cases of post-operative septic arthritis in 34487 patients (0.08%) who received prophylactic antibiotics and 16 cases in 10911 (0.15%) who received none [risk ratio (RR) = 0.53, 95% confidence interval (CI): 0.29-0.99,  $P = 0.05$ ]. A sub-group analysis in which bony procedures were excluded was performed which found no significant difference in infection rates between patients that received prophylactic antibiotics and patients that did not ( $P > 0.05$ ). All ACL reconstruction studies used prophylactic antibiotics, but two studies investigating the effect of soaking the graft in vancomycin in addition to standard intravenous (IV) prophylaxis were combined for analysis. There were 19 cases in 1095 patients (1.74%) who received IV antibiotics alone and no infections in 2,034 patients who received IV antibiotics and had a vancomycin soaked graft (RR = 0.01, 95%CI: 0.001-0.229,  $P < 0.01$ ).

### Research conclusions

Our study is the first to demonstrate prophylactic antibiotics are effective in preventing septic arthritis following simple arthroscopic procedures of the knee, though given the large number needed to treat, the clinical significance of this finding is unclear. Our literature search demonstrates that there is little to no debate that antibiotics should be used prophylactically for arthroscopic surgeries involving graft implantation. However, our findings indicate that the addition of graft soaking further reduces the rate of infection.

### Research perspectives

Further prospective studies on this topic will help further elucidate this conclusion.

## REFERENCES

1 Elson RA. Clean Air Operating Environment and Superficial

- Infection. In: Uthoff H.K., Stahl E (eds). *Current Concepts of Infections in Orthopedic Surgery*. Springer, Berlin, Heidelberg, 1985: 33-37 [DOI: 10.1007/978-3-642-69833-0\_6]
- 2 Bryson DJ, Morris DL, Shivji FS, Rollins KR, Snape S, Ollivere BJ. Antibiotic prophylaxis in orthopaedic surgery: difficult decisions in an era of evolving antibiotic resistance. *Bone Joint J* 2016; **98-B**: 1014-1019 [PMID: 27482011 DOI: 10.1302/0301-620X.98B8.37359]
- 3 Boström Windhamre H, Mikkelsen C, Forssblad M, Willberg L. Postoperative septic arthritis after anterior cruciate ligament reconstruction: does it affect the outcome? A retrospective controlled study. *Arthroscopy* 2014; **30**: 1100-1109 [PMID: 24836173 DOI: 10.1016/j.arthro.2014.03.019]
- 4 Helito CP, Noffs GG, Pecora JR, Gobbi RG, Tirico LE, Lima AL, de Oliveira PR, Camanho GL. Epidemiology of septic arthritis of the knee at Hospital das Clínicas, Universidade de São Paulo. *Braz J Infect Dis* 2014; **18**: 28-33 [PMID: 24029436 DOI: 10.1016/j.bjid.2013.04.010]
- 5 Lim SY, Pannikath D, Nugent K. A retrospective study of septic arthritis in a tertiary hospital in West Texas with high rates of methicillin-resistant *Staphylococcus aureus* infection. *Rheumatol Int* 2015; **35**: 1251-1256 [PMID: 25572838 DOI: 10.1007/s00296-014-3206-9]
- 6 Prokusi L. Prophylactic antibiotics in orthopaedic surgery. *J Am Acad Orthop Surg* 2008; **16**: 283-293 [PMID: 18460689 DOI: 10.5435/00124635-200805000-00007]
- 7 Bert JM, Giannini D, Nace L. Antibiotic prophylaxis for arthroscopy of the knee: is it necessary? *Arthroscopy* 2007; **23**: 4-6 [PMID: 17210420 DOI: 10.1016/j.arthro.2006.08.014]
- 8 Wyatt RWB, Maletis GB, Lyon LL, Schwalbe J, Avins AL. Efficacy of Prophylactic Antibiotics in Simple Knee Arthroscopy. *Arthroscopy* 2017; **33**: 157-162 [PMID: 27372184 DOI: 10.1016/j.arthro.2016.05.020]
- 9 Müller-Rath R, Ingenhoven E, Mumme T, Schumacher M, Miltner O. [Perioperative management in outpatient arthroscopy of the knee joint]. *Z Orthop Unfall* 2010; **148**: 282-287 [PMID: 20135619 DOI: 10.1055/s-0029-1240784]
- 10 Formaini N, Jacob P, Willis L, Kean JR. Evaluating the use of preoperative antibiotics in pediatric orthopaedic surgery. *J Pediatr Orthop* 2012; **32**: 737-740 [PMID: 22955540 DOI: 10.1097/BPO.0b013e318269543b]
- 11 Armstrong RW, Bolding F, Joseph R. Septic arthritis following arthroscopy: clinical syndromes and analysis of risk factors. *Arthroscopy* 1992; **8**: 213-223 [PMID: 1637435 DOI: 10.1016/0749-8063(92)90039-E]
- 12 Uhl GR, Liu QR, Drgon T, Johnson C, Walther D, Rose JE. Molecular genetics of nicotine dependence and abstinence: whole genome association using 520,000 SNPs. *BMC Genet* 2007; **8**: 10 [PMID: 17407593 DOI: 10.1186/1471-2156-8-10]
- 13 Mini E, Grassi F, Cherubino P, Nobili S, Periti P. Preliminary results of a survey of the use of antimicrobial agents as prophylaxis in orthopedic surgery. *J Chemother* 2001; **13** Spec No 1: 73-79 [PMID: 11936384 DOI: 10.1179/joc.2001.13.Supplement-2.73]
- 14 Keith MW, Masear V, Amadio PC, Andary M, Barth RW, Graham B, Chung K, Maupin K, Watters WC 3rd, Haralson RH 3rd, Turkelson CM, Wies JL, McGowan R. Treatment of carpal tunnel syndrome. *J Am Acad Orthop Surg* 2009; **17**: 397-405 [PMID: 19474449 DOI: 10.5435/00124635-200906000-00008]
- 15 Ghnaimat MM, Shawabkeh JS, Hijazi AM, Alturk MM, Aldweri MK. Aldweri. Is Antibiotic Prophylaxis in Knee Arthroscopy Mandatory? *J R Med Serv* 2009; **16**: 39-41
- 16 Wieck JA, Jackson JK, O'Brien TJ, Lurate RB, Russell JM, Dorchak JD. Efficacy of prophylactic antibiotics in arthroscopic surgery. *Orthopedics* 1997; **20**: 133-134 [PMID: 9048390]
- 17 Qi Y, Yang X, Pan Z, Wang H, Chen L. Value of antibiotic prophylaxis in routine knee arthroscopy : A retrospective study. *Orthopade* 2018; **47**: 246-253 [PMID: 28993891 DOI: 10.1007/s00132-017-3486-3]
- 18 Phegan M, Grayson JE, Vertullo CJ. No infections in 1300 anterior cruciate ligament reconstructions with vancomycin pre-soaking of

- hamstring grafts. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 2729-2735 [PMID: 25771788 DOI: 10.1007/s00167-015-3558-z]
- 19 **Vertullo CJ**, Quick M, Jones A, Grayson JE. A surgical technique using presoaked vancomycin hamstring grafts to decrease the risk of infection after anterior cruciate ligament reconstruction. *Arthroscopy* 2012; **28**: 337-342 [PMID: 22112612 DOI: 10.1016/j.arthro.2011.08.301]
  - 20 **Sherman OH**, Fox JM, Snyder SJ, Del Pizzo W, Friedman MJ, Ferkel RD, Lawley MJ. Arthroscopy-“no-problem surgery”. An analysis of complications in two thousand six hundred and forty cases. *J Bone Joint Surg Am* 1986; **68**: 256-265 [PMID: 3753706 DOI: 10.2106/00004623-198668020-00011]
  - 21 **Jebson PJ**, Adams BD. Wrist arthrodesis: review of current techniques. *J Am Acad Orthop Surg* 2001; **9**: 53-60 [PMID: 11174163 DOI: 10.5435/00124635-200101000-00006]
  - 22 **Pérez-Prieto D**, Torres-Claramunt R, Gelber PE, Shehata TM, Pelfort X, Monllau JC. Autograft soaking in vancomycin reduces the risk of infection after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 2724-2728 [PMID: 25416672 DOI: 10.1007/s00167-014-3438-y]
  - 23 **Babcock HM**, Carroll C, Matava M, L’ecuyer P, Fraser V. Surgical site infections after arthroscopy: Outbreak investigation and case control study. *Arthroscopy* 2003; **19**: 172-181 [PMID: 12579150 DOI: 10.1053/jars.2003.50016]
  - 24 **Onyema C**, Oragui E, White J, Khan WS. Evidence-based practice in arthroscopic knee surgery. *J Perioper Pract* 2011; **21**: 128-134 [PMID: 21560553 DOI: 10.1177/175045891102100403]
  - 25 **Lubowitz JH**, Poehling GG. Arthroscopy and antibiotics. *Arthroscopy* 2007; **23**: 1-3 [PMID: 17210418 DOI: 10.1016/j.arthro.2006.11.012]
  - 26 **D’Angelo GL**, Ogilvie-Harris DJ. Septic arthritis following arthroscopy, with cost/benefit analysis of antibiotic prophylaxis. *Arthroscopy* 1988; **4**: 10-14 [PMID: 3128307 DOI: 10.1016/S0749-8063(88)80004-5]
  - 27 **Kurzweil PR**. Antibiotic prophylaxis for arthroscopic surgery. *Arthroscopy* 2006; **22**: 452-454 [PMID: 16581459 DOI: 10.1016/j.arthro.2006.02.004]
  - 28 **Nakayama H**, Yagi M, Yoshiya S, Takesue Y. Micro-organism colonization and intraoperative contamination in patients undergoing arthroscopic anterior cruciate ligament reconstruction. *Arthroscopy* 2012; **28**: 667-671 [PMID: 22284408 DOI: 10.1016/j.arthro.2011.10.023]
  - 29 **Torres-Claramunt R**, Pelfort X, Erquicia J, Gil-González S, Gelber PE, Puig L, Monllau JC. Knee joint infection after ACL reconstruction: prevalence, management and functional outcomes. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2844-2849 [PMID: 23104168 DOI: 10.1007/s00167-012-2264-3]
  - 30 **Edelstein AI**, Weiner JA, Cook RW, Chun DS, Monroe E, Mitchell SM, Kannan A, Hsu WK, Stulberg SD, Hsu EL. Intra-Articular Vancomycin Powder Eliminates Methicillin-Resistant *S. aureus* in a Rat Model of a Contaminated Intra-Articular Implant. *J Bone Joint Surg Am* 2017; **99**: 232-238 [PMID: 28145954 DOI: 10.2106/JBJS.16.00127]
  - 31 **Yazdi H**, Moradi A, Herbolt M. The effect of gentamicin in irrigating solutions on articular infection prophylaxis during arthroscopic ACL reconstruction. *Arch Orthop Trauma Surg* 2014; **134**: 257-261 [PMID: 24323062 DOI: 10.1007/s00402-013-1910-7]

**P- Reviewer:** Elfering A, Hernandez-Sanchez S, Li JM, Robertson GAJ  
**S- Editor:** Ji FF **L- Editor:** A **E- Editor:** Wu YXJ



## Analysis of a ten step protocol to decrease postoperative spinal wound infections

Hossein Elgafy, Craig J Raberding, Megan L Mooney, Kyle A Andrews, Joan M Duggan

Hossein Elgafy, Craig J Raberding, Megan L Mooney, Kyle A Andrews, Joan M Duggan, Department of Orthopedics and Infectious Diseases, University of Toledo Medical Center, Toledo, OH 43614, United States

ORCID number: Hossein Elgafy (0000-0001-7518-9600); Craig J Raberding (0000-0001-7518-9610); Megan L Mooney (0000-0001-7518-9620); Kyle A Andrews (0000-0001-7518-9630); Joan M Duggan (0000-0001-7518-9650).

**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.

**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, FRCS (Ed), FRSC, MD, Professor, Department of Orthopedics and Infectious Diseases, University of Toledo Medical Centre, 3065 Arlington Avenue, Toledo, OH 43614, United States. [hkelgafy@aol.com](mailto:hkelgafy@aol.com)  
Telephone: +1-419-3833515  
Fax: +1-419-3833526

Received: June 25, 2018

Peer-review started: June 25, 2018

First decision: July 11, 2018

Revised: July 15, 2018

Accepted: August 26, 2018

Article in press: August 26, 2018

Published online: November 18, 2018

### Abstract

#### AIM

To define a ten-step protocol that reduced the incidence of surgical site infection in the spine surgery practice of the senior author and evaluate the support for each step based on current literature.

#### METHODS

In response to unexplained increased infection rates at our institution following spine surgery, a ten-step protocol was implemented: (1) preoperative glycemic management based on hemoglobin A1c (HbA1c); (2) skin site preoperative preparation with 2% chlorhexidine gluconate disposable cloths; (3) limit operating room traffic; (4) cut the number of personnel in the room to the minimum required; (5) absolutely no flash sterilization of equipment; (6) double-gloving with frequent changing of outer gloves; (7) local application of vancomycin powder; (8) re-dosing antibiotic every 4 h for prolonged procedures and extending postoperative coverage to 72 h for high-risk patients; (9) irrigation of subcutaneous tissue with diluted povidone-iodine solution after deep fascial closure; and (10) use of DuraPrep skin preparation at the end of a case before skin closure. Through an extensive literature review, the current data available for each of the ten steps was evaluated.

#### RESULTS

Use of vancomycin powder in surgical wounds, routine irrigation of surgical site, and frequent changing of surgical gloves are strongly supported by the literature. Preoperative skin preparation with chlorhexidine wipes is similarly supported. The majority of current literature supports control of HbA1c preoperatively to reduce risk of infection. Limiting the use of flash sterilization is supported, but has not been evaluated in spine-specific surgery. Limiting OR traffic and number of personnel in the OR are supported although without level 1 evidence. Prolonged use of antibiotics postoperatively

is not supported by the literature. Intraoperative use of DuraPrep prior to skin closure is not yet explored.

### CONCLUSION

The ten-step protocol defined herein has significantly helped in decreasing surgical site infection rate. Several of the steps have already been shown in the literature to have significant effect on infection rates. As several measures are required to prevent infection, instituting a standard protocol for all the described steps appears beneficial.

**Key words:** Wound infections; Spine; Ten step protocol; Surgical site infections

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** The rates of infection following spine surgery have been reported to range from less than 1% to 10.9% depending on the type of case. Several factors have been identified as risk for surgical site infection. In response to an increasing number of surgical site infections at the authors' institution, a new surgical protocol was initiated in an effort to reduce infection rates after an intensive epidemiological investigation failed to reveal a common source. Institution of this bundle returned surgical site infection rates to historic level of < 1%.

Elgafy H, Raberding CJ, Mooney ML, Andrews KA, Duggan JM. Analysis of a ten step protocol to decrease postoperative spinal wound infections. *World J Orthop* 2018; 9(11): 271-284 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v9/i11/271.htm> DOI: <http://dx.doi.org/10.5312/wjo.v9.i11.271>

### INTRODUCTION

Surgical site infection in spinal surgery is associated with significantly increased morbidity and costs<sup>[1]</sup>. Surgical site infections (SSIs) are the most common hospital acquired infections and are usually seen in the early postoperative period<sup>[2]</sup>. The rates of infection following spine surgery have been reported to range from less than 1% to 10.9% depending on the type of case<sup>[3]</sup>.

A variety of measures have been initiated and evaluated in the literature to reduce the occurrence of SSIs. The surgical setting is a multi-faceted environment with numerous variables and control of all risk factors associated with infection can be challenging. In addition to identifying and eliminating known factors, prophylactic treatments are available to help reduce the overall incidence of surgical site infection. Patient risk factors and prophylactic measures have often been evaluated separately, but evaluation of risk factors and interventions as a bundle may be a more appropriate approach given the dynamic environment of the surgical suite.

In response to an increasing number of SSIs at the

authors' institution, a new surgical protocol was initiated in an effort to reduce infection rates after an intensive epidemiological investigation failed to reveal a common source. In addition to standard perioperative intravenous antibiotics (within 1 h preoperative administration with continuation for 24 h) and sterile operating preparation, a new 10 step protocol was instituted after extensive review of surgical and infection control literature as well as consultation with spine, total joint surgeons in the authors' and other institutions in addition to input from division of infection disease. The postoperative SSI rate in the period preceding the implementation of the ten-step protocol climbed to 10%. Institution of this bundle returned SSI rates to historic level of < 1%. The purpose of this paper is to present this protocol with an overview and evaluation of the literature for validity of each of step.

Briefly, this "Ten Step" surgical bundle is as follow: (1) preoperative glycemic management based on hemoglobin A1c (HbA1c); (2) skin site preoperative preparation the night before surgery and in the preoperative suite with disposable cloths moistened with 2% chlorhexidine gluconate (CHG) antiseptic solution; (3) limitation of operating room traffic by closure of the front door of the room with tape once the patient is in the room and until wound closure. The door through the sterile core remains available if needed; (4) decreasing the number of personnel in the room to the minimum required; (5) absolutely no flash sterilization of equipment; (6) double-gloving with frequent changing of outer gloves for the surgeon, assistant and scrub nurse throughout the case and after any step that may contaminate the gloves; (7) vancomycin powder mixed in with bone graft and applied locally to the wound after fascial closing; (8) antibiotic re-dosing every 4 h for prolonged procedures and extending postoperative coverage to 72 h for high-risk patients; (9) irrigation of the wound with diluted povidone-iodine solution; and (10) use of DuraPrep skin preparation at the end of a case to clean the skin before skin closure.

### MATERIALS AND METHODS

A systematic computerized Medline literature search was performed using Pubmed. The electronic databases were searched from 1990 to October 2014. Searches were performed using the terms "surgical site infection" in conjunction with each of the following sets of terms; "spine," "hemoglobin A1c," "glycemic control," "skin preparation," "DuraPrep," "chlorhexidine cloths," "operating room traffic," "door opening," "flash sterilization," "double gloving," "glove exchange," "vancomycin powder," "postoperative antibiotics," and "wound irrigation." Abstracts were reviewed for content. Articles that included the use of one of the 10 aforementioned steps with associated outcomes for SSIs were included in the review. Where substantial information was available for a specific protocol step, only articles following outcomes for spine specific

surgeries were included. If no results for spine surgery were available on a topic, the available literature across surgical specialties was reviewed. Each manuscript was evaluated for level of evidence, number of patients included, outcome and, statistical significance.

## RESULTS

### **Preoperative glycemic management based on HbA1c**

Decreasing postoperative infection rates begins during the preoperative evaluation with the identification of patients at increased risk for infection. Diabetes mellitus is a well-known independent risk factor for SSIs. Approximately 25% of patients with diabetes are unaware that they have diabetes, which highlights the need for careful preoperative testing<sup>[4]</sup>. HbA1c provides a good marker of a patient overall glucose management over a 2-3 mo period. An elevation in HbA1c identifies those patients with more chronic hyperglycemia and is an important indicator of poor glucose control. If HbA1c is related to risk of infection, it may represent a modifiable factor prior to proceeding with elective surgery.

The initial reports on the effects of elevated HbA1c were in the field of urology. In 1992, Bishop *et al*<sup>[5]</sup> prospectively evaluated the influence of HbA1c on SSIs in 90 patients receiving penile implants. They found a significantly increased rate of SSI in diabetics with HbA1c greater than 11.5%. The authors recommended denying elective surgery to patients with HbA1c > 11.5% which was subsequently adopted as the standard of care. However, Wilson *et al*<sup>[6]</sup> refuted the findings in 1998 after following 389 patients with the same surgery in which they failed to find a significant increase in infection rates with elevated HbA1c.

Since that time, there has been only slight variability in the surgical literature. Although Latham *et al*<sup>[7]</sup> found no association between SSI and HbA1c, several other studies have found a significantly increased risk of SSIs with elevated preoperative HbA1c<sup>[8-13]</sup>. Still others found an increased rate of infection with high HbA1c but were unable to achieve significance. Rawlins *et al*<sup>[14]</sup> evaluated diabetics undergoing Roux-en-Y gastric bypass and Knapik *et al*<sup>[15]</sup> looked at those having coronary artery surgery. Both found elevated rates of infection with HbA1c  $\geq$  7.0% but did not reach statistical significance.

Several studies have been published in the orthopaedic literature since 2009 evaluating the effect of HbA1c on surgical outcomes (Table 1)<sup>[16-23]</sup>. Many of these studies focus on total joint arthroplasty. Marchant *et al*<sup>[16]</sup> performed the largest study by utilizing the Nationwide Inpatient Sample (NIS) database in which glycemic control and outcomes after total joint arthroplasty for over 1 million patients was evaluated. The sheer population size gave the study the power to detect small differences. Among other findings, they found a significantly increased rate of postoperative infections in diabetics with HbA1c  $\geq$  7.0% compared

to either patients without diabetes or diabetics with HbA1c < 7.0%. Iorio *et al*<sup>[17]</sup> and Jämsen *et al*<sup>[18]</sup> came to a similar conclusion using a smaller group. Myers *et al*<sup>[19]</sup> also found increased rates of infection with HbA1c > 7 in patients undergoing ankle and hindfoot fusions. Lamloom *et al*<sup>[20]</sup> retrospectively reviewed all orthopaedic procedures in their hospital and found a slightly increased infection rate without statistical significance with HbA1c  $\geq$  7.0%. Adams *et al*<sup>[21]</sup> and Harris *et al*<sup>[22]</sup> similarly evaluated HbA1c and infection rate in total joint arthroplasty and found no significant association, although Harris did find an increased overall rate of complications in patients with uncontrolled diabetes.

Specific to effects of HbA1c in spine surgery, Hikata *et al*<sup>[23]</sup> retrospectively reviewed the results of elective posterior instrumented thoracic and lumbar arthrodesis in 345 consecutive patients. Thirty-six of these patients had preexisting diabetes with preoperative HbA1c values available. In these patients, the presence of diabetes and diabetics with HbA1c  $\geq$  7.0 were both independent risk factors for surgical site infection. Although not looking specifically at infections, Takahashi *et al*<sup>[24]</sup> reviewed functional results after lumbar surgery in patients and found that patients with HbA1c  $\geq$  6.5% showed poor improvement in low back pain.

### **Preoperative skin preparation with CHG cloths**

During the preoperative clinic appointment, each patient is given a preoperative skin preparation kit and written instructions for use. The skin preparation is done with disposable cloths moistened with a rinse-free, 2% CHG antiseptic solution. The patient is instructed to shower one hour prior to prepping, then wash with the cloths. The skin is then prepped again with a second set of cloths in the preoperative holding area. The goal of the preoperative preparation is to decrease bacterial colonization.

It has been shown that preoperative cleansing the night before surgery and the morning of with CHG decreases the bacterial colonization on the skin. Murray *et al*<sup>[25]</sup> found that 66% of patients were colonized with microbes after prepping with CHG compared to 94% for those who showered alone preoperatively.

The data supporting the effectiveness of CHG preparation is based heavily on cohort studies. Johnson *et al*<sup>[26]</sup> performed a cohort study comparing infection rates in patients who performed CHG preoperative prepping the night before surgery and in the preoperative area, and those who were noncompliant with prepping. They found no infections in the compliant CHG group, and 14 (1.6%) infections in the non-compliant group. Similarly, Zywiell *et al*<sup>[27]</sup> compared compliant, partially compliant, and non-compliant patients with regard to CHG preparation. They found no infections in the group that appropriately prepared with CHG, 1 (1.5%) infections in the partial compliance group, and 21 (3%) in the noncompliant group.

**Table 1 Studies from orthopedic literature evaluating preoperative hemoglobin A1c and surgical site infections**

Ref.	Study design (level of evidence)	Surgery performed	Groups	Main outcome	Significance
Hikata <i>et al</i> <sup>[23]</sup> (2013)	Retrospective cohort (IV)	Adult elective posterior instrumented thoracic and lumbar spinal arthrodesis	Non-diabetics ( <i>n</i> = 309), Controlled diabetics (HbA1c < 7.0; <i>n</i> = 19), Uncontrolled diabetics (HbA1c ≥ 7.0; <i>n</i> = 17)	10 (3.2%) SSI in non-diabetic group, No SSI in controlled diabetic group, 6 (35.3%) SSIs in uncontrolled diabetic group	Diabetes was an independent risk factor for SSI ( <i>P</i> = 0.0005), Significantly higher rate of infection in diabetics with HbA1c ≥ 7.0 ( <i>P</i> = 0.006)
Adams <i>et al</i> <sup>[21]</sup> (2013)	Retrospective cohort (II)	Primary total knee arthroplasty	Non-diabetics ( <i>n</i> = 32924), Controlled diabetics (HbA1c < 7.0; <i>n</i> = 5042), Uncontrolled diabetics (HbA1c ≥ 7.0; <i>n</i> = 2525)	216 (0.7%) deep infections in non-diabetics, 58 (1.2%) in controlled diabetics, and 13 (0.5%) in uncontrolled diabetics	No significant association between HbA1c level and deep infection
Harris <i>et al</i> <sup>[22]</sup> (2013)	Retrospective cohort (IV)	Total joint arthroplasty	Controlled diabetics (HbA1c < 7.0; <i>n</i> = 3961), Uncontrolled diabetics (HbA1c ≥ 7.0; <i>n</i> = 2127)	Identical percentage of patients in both groups developed superficial and deep infections	Significant increase in overall complications ( <i>P</i> = 0.028), but not infections, for diabetics with HbA1c ≥ 7.0
Iorio <i>et al</i> <sup>[17]</sup> (2012)	Retrospective cohort (IV)	Primary or revision total hip or knee arthroplasty	Controlled diabetics (HbA1c < 7.0; <i>n</i> = 191), Uncontrolled diabetics (HbA1c ≥ 7.0; <i>n</i> = 85)	5 (2.6%) infections in controlled diabetics, 5 (5.9%) infections in uncontrolled diabetics	Increased rate of infections in uncontrolled diabetics without statistical significance ( <i>P</i> = 0.293)
Myers <i>et al</i> <sup>[19]</sup> (2012)	Retrospective cohort (III)	Ankle and hindfoot fusions	Non-diabetics ( <i>n</i> = 74), Controlled diabetics (HbA1c < 7.0; <i>n</i> = 30), Uncontrolled diabetics (HbA1c ≥ 7.0; <i>n</i> = 44)	1 (1.4%) SSI in non-diabetics, 2 (6.7%) SSI in controlled diabetics, 12 (27.3%) SSI in uncontrolled diabetics	Significantly higher rate of SSI in uncontrolled vs controlled diabetics ( <i>P</i> < 0.05)
Jämsen <i>et al</i> <sup>[18]</sup> (2010)	Retrospective cohort (IV)	Primary total knee arthroplasty	Patients with HbA1c < 6.5 ( <i>n</i> = 205), Patients with HbA1c ≥ 6.5 ( <i>n</i> = 176)	No infections in patients with HbA1c < 6.5, 5 infections in patients with HbA1c ≥ 6.5 (2.84%)	Significant increase in infection rate in patients with HbA1c ≥ 6.5 ( <i>P</i> = 0.015)
Lamloum <i>et al</i> <sup>[20]</sup> (2009)	Retrospective cohort (IV)	Any orthopaedic surgical procedure	Controlled diabetics (HbA1c < 7.0; <i>n</i> = 80), Uncontrolled diabetics (HbA1c ≥ 7.0; <i>n</i> = 238)	10 SSIs in controlled diabetics (12.5%), 33 SSIs in uncontrolled diabetics (13.9%)	No significant difference in SSI occurrence between the two groups ( <i>P</i> > 0.05)
Marchant <i>et al</i> <sup>[16]</sup> (2009)	Retrospective cohort (III)	Total joint arthroplasty	Non-diabetics ( <i>n</i> = 920555), Controlled diabetics (HbA1c < 7.0; <i>n</i> = 105485), Uncontrolled diabetics (HbA1c ≥ 7.0; <i>n</i> = 3973)	3807 (0.41%) non-diabetics with infection, 405 (0.38%) controlled diabetics with infection, 47 (1.18%) uncontrolled diabetics with infection	Uncontrolled diabetics had a statistically significant increased rate of infection compared to patients without or with controlled diabetes ( <i>P</i> = 0.002)

HbA1c: Hemoglobin A1C; SSI: Surgical site infections.

Veiga *et al*<sup>[28]</sup> conducted a randomized controlled trial to assess the effect of preoperative chlorhexidine showers on skin colonization and postoperative infection rates associated with plastic surgical procedures involving the trunk. Chlorhexidine showers were effective in reducing skin colonization with coagulase-negative staphylococci and yeasts, but there was no difference in postoperative infection rates. Two systematic reviews evaluated the clinical effectiveness of preoperative skin antiseptic preparations and the prevention of SSIs<sup>[29,30]</sup>. Kamel *et al*<sup>[29]</sup> reviewed 20 studies and concluded that the evidence suggests that preoperative antiseptic showers reduce bacterial colonization and may be effective at preventing SSIs. Webster and Osborne<sup>[30]</sup> additionally reviewed 3 studies that included 7791 participants comparing CHG cloth bathing vs placebo. In their systemic review, they concluded that there is no

statistically significant benefit for preoperative showering or bathing with chlorhexidine over other wash products to reduce surgical site infection.

**Limiting operative room traffic**

One of the strategies implemented in this bundle to decrease SSIs involved limiting traffic in the operating room. In order to achieve this, the front door to the operating room is taped off once the patient is in the room. Only necessary door openings were performed, all of which occurred through the sterile core rather than the main operating room door.

An operating room is an isolated environment designed to recirculate air through filtered ventilation ducts. Frequent opening of the operating room door has been shown to disrupt this airflow system<sup>[31,32]</sup>. Scaltriti *et al*<sup>[32]</sup> studied the air quality in the operating room and

compared this with multiple parameters. They found that increased door openings and personnel changes were a positive predictor of raised bacterial counts in a room. Ritter similarly found a correlation between number of operating door openings and increased colony forming unit (CFU) counts in the operating room<sup>[33]</sup>.

In addition to affecting the air quality, door openings and increased traffic have been identified as major surgical distractors. Using an observational tool to record distraction and interruption in the operating room, Healey *et al.*<sup>[34]</sup> found that interference levels significantly correlated with frequency of door openings. In addition unwanted distractions may lead to mistakes beyond just SSIs.

In response to an unexplained increase in SSIs at one institution, Lynch *et al.*<sup>[35]</sup> studied operating room foot traffic. They found that their spinal fusion cases had the highest rate of door openings at 50 per hour. Additionally, when investigating the reasons for door openings, they found the most common reason for door openings was to request information from outside the room, which could feasibly be done *via* telephone or other electronic means.

In an attempt to evaluate the risk to the patient, Young and O'Reagan<sup>[36]</sup> performed a prospective cross-sectional study in forty-six consecutive cardiac operations. An electronic door counter calculated the frequencies and rates of door openings during each surgery. Everyone was blinded to the counters except the practicing surgeons. They showed a trend toward an increased frequency of door openings per case in those patients that developed a surgical site infection vs those who had not. However, the difference did not achieve statistical significance. Additionally, there was a positive correlation between length of case and frequency of door opening.

#### **Limit number of personnel in the operative room**

Spine surgery, much like any other surgery, requires a multidisciplinary effort. In light of that fact, there is often a considerable number of people in the operating room at any given time, the attending surgeon, resident or surgical assistant, anesthesia team, surgical scrub technician, circulating nurse, radiology technician, technician for neurological monitoring, and oftentimes an equipment representative. At a teaching hospital, there is the potential for a student in the room at any of these positions as well.

Pryor *et al.*<sup>[37]</sup> attempted to find an association between surgical site infection and increased number of personnel in the operating room. Although there was an association of increased surgical site infection with the number of people in the OR, the results were not statistically significant. The increased number of people was also associated with length of the case.

In a prognostic level III evidence study, Olsen *et al.*<sup>[38]</sup> found that one of the factors that was significantly associated with an increased risk of surgical site in-

fection during spinal operations was the participation by two or more surgical residents. As suggested by the author, this was likely a proxy for the duration and complexity of the procedure rather than a direct cause for infection.

Although not yet clearly demonstrated, an increasing number of people present in the operating room may increase the risk of contamination and subsequently increased surgical site infection. With that in mind the authors have made efforts to limit the number of people in the operating room to the minimum. The minimum staff present includes the attending surgeon and assistant, surgical technician, anesthesiologist, nurse circulator, radiology technician, equipment representative, and spinal cord monitoring technician. In a teaching hospital reducing the number of the students in the room can be a challenge. However, in the authors' current protocol, no more than one student of any kind (medical, nursing, radiologist, or anesthesia) is allowed in the room. These practices require further evaluation for their effectiveness.

#### **No flash sterilization of surgical equipment**

Instrument reprocessing technique plays a vital role in maintaining a sterile surgery. Flash sterilization has often been utilized in order to turn over equipment quickly when additional sterile equipment is unavailable. As part of our policy, absolutely no flash sterilization may be used in spine surgery. An adequate number of sterile surgical trays are on the shelf prior to surgery to avoid any flash sterilization.

From the International Conference on Healthcare-Associated Infections, Lopansri *et al.*<sup>[39]</sup> demonstrated their experience with SSIs and sterilization techniques. They identified 14 cases of surgical site infection after arthroscopy over a 21 mo span. Thirteen of the infections were from an individual surgeon, representing a 2.4% infection rate, while 8 other surgeons had a total of 1 infection in the same span, representing an infection rate of 0.06%. The surgeon with the larger infection rate was the only one whose equipment underwent flash sterilization. Additionally, this same surgeon operated at a separate facility that did not use flash sterilization and experienced an infection rate of 0.3% over a 4-year span. This represented a relative risk for infection after arthroscopy of 6.7 for this individual surgeon while working at a facility that used flash sterilization as opposed to one that did not.

Tosh *et al.*<sup>[40]</sup> explored an outbreak of pseudomonas *aeruginosa* SSIs after arthroscopic procedures. In this retrospective case-control study, there were 7 patients with surgical site infection after arthroscopy with isolates that were indistinguishable from each other. On endoscopic examination of equipment that was flash sterilized during these cases, residual tissue was seen in the lumens of the arthroscopic equipment.

Although available literature on flash sterilization and the primary outcome of surgical site infection is

limited, it can be identified as a possible avoidable cause of infection. To our knowledge, there is no literature available evaluating the use of flash sterilization in spine surgery. Additional investigations as to the benefit of reducing utilization of flash sterilization may be of benefit.

### **Frequent changing of surgical gloves**

It is vital to attempt to maintain a completely sterile environment in the surgical field. An important factor in surgery, which can easily transmit bacteria, is the surgical glove. Instituting a policy of double gloving with frequent changes of the outer gloves may assist in decreasing surgical infection rates. In the authors' current protocol, the surgeon, assistant, and scrub nurse change their outer gloves after steps that may contaminate the gloves such as after draping the patient and using the surgical microscope. The policy also includes changing the outer gloves prior to instrumentation and before closure.

Ritter *et al.*<sup>[41]</sup> reported that contamination of outer gloves is common among all scrubbed personnel and occurs at a rate of 33%. It has been shown by McCue<sup>[42]</sup> in a study evaluating frequent outer glove changes in total hip arthroplasties that gloves used at draping were the most frequently contaminated. This highlighted the draping portion as an important step for glove changes.

Ward *et al.*<sup>[43]</sup> performed an experiment to determine risk of bacterial contamination associated with changing gloves with 251 prospectively randomized surgical team members in 142 cases in which all members were double gloved. Cultures were taken from the dominant palms at 1 h into the case at which time selected randomized individuals changed their outer gloves. A repeat culture was taken from the dominant palm 15 min later. They found a significant decrease in the number of positive cultures for the group exchanging their gloves ( $P = 0.0419$ ). This represented nearly 2 times greater odds of being contaminated if gloves were not exchanged. However, they did not assess subsequent infection rates.

Although several studies have been published on various double gloving techniques and rates of perforation, there is very little literature on changing of gloves and the primary outcome, SSIs. Rehman *et al.*<sup>[44]</sup> in a retrospective cohort study, compared infection rates in two groups undergoing lumbar spine fusion. The control group of 179 patients underwent surgery with the standard surgical protocol and the treatment group of 210 patients, after double gloving, the outer gloves were removed prior to instrumentation. They found a significantly decreased infection rate at 1 year postoperatively when outer gloves were removed in this manner (3.35% in control vs 0.48% in treatment;  $P = 0.0369$ ). Additional investigations to back up this data may be beneficial as this may be a simple and cost effective step in reducing surgical infections.

### **Local application of vancomycin powder**

The use of antibiotics has been very important in decreasing the rates of infection. Administration of systemic intravenous antibiotics perioperatively is standard<sup>[45]</sup>. Additionally, topical vancomycin powder has recently been evaluated in the literature. Vancomycin powder has a slow resorption rate which provides a very low rate of systemic effects and excellent local coverage against the common gram positive bacteria associated with surgical site infection, with no evidence of local or systemic toxicity<sup>[46]</sup>.

The authors' protocol for the use of vancomycin powder is two-fold. When performing a fusion surgery, 1 g of vancomycin powder is mixed in with the bone graft before placement. Additionally, after closure of the deep fascia, another 1 g of vancomycin powder is applied directly onto the surgical wound and subcutaneous tissue prior to skin closure.

Sweet *et al.*<sup>[46]</sup> first reported the benefits of using vancomycin powder during spine surgery. They performed a retrospective cohort study on a consecutive series of patients undergoing posterior instrumented thoracic and lumbar spine surgery. This study looked at a total of 1732 patients, 911 of which received 2 g of vancomycin powder, in the protocol listed dose, one gram was mixed with bone graft and 1 g was applied directly to the surgical wound. There was a statistically significant reduction in infection rate in those treated with vancomycin powder and intravenous prophylaxis as compared to intravenous antibiotic prophylaxis alone (0.2% vs 2.6%;  $P < 0.0001$ ).

Fourteen studies were identified that evaluated post-operative infection rates and the use of topical vancomycin powder intraoperatively during spine surgery (Table 2)<sup>[46-59]</sup>. Surgical site infection rates in these studies ranged from 0%-6.7%. Of these studies, 11 included a control group in which no vancomycin powder was applied. All groups in all of these studies received standard preoperative intravenous antibiotic prophylaxis. Infection rates without the use of vancomycin powder ranged from 1.2%-13%. The vast majority of these studies showed a significant decrease in overall infection rate when using vancomycin powder in addition to standard preoperative IV prophylaxis.

Kanj *et al.*<sup>[60]</sup> evaluated vancomycin prophylaxis at the surgical site in clean orthopaedic surgery. Several of the studies reviewed here were included in their analysis<sup>[46,47,49,54]</sup>. Specific to spine surgery, they calculated that a patient is 4 times more likely to develop a deep infection without vancomycin powder prophylaxis than with ( $P < 0.001$ ).

As outlined above, there is an extensive amount of literature available on the use of vancomycin powder for infection prophylaxis in surgical wounds. The majority of the evidence points toward vancomycin powder as a significant factor in reducing SSIs.

Table 2 Studies evaluating the use of vancomycin powder intraoperatively

Ref.	Study design (level of evidence)	Surgery performed	Groups	Main outcome	Significance
Chobrial <i>et al</i> <sup>[56]</sup> (2014)	Retrospective case series (IV)	Spinal procedures for degenerative disease, trauma, pain and scoliosis	Vancomycin powder (range from 1-6 g) applied to subfascial and epifascial layers but not to bone graft (n = 981)	66 infections identified (6.7%) A number of gram-negative infections were encountered	Vancomycin may increase the incidence of gram-negative or polymicrobial spinal infections
Hill <i>et al</i> <sup>[55]</sup> (2014)	Retrospective cohort (III)	Instrumented or non-instrumented posterior spine surgery in adults	Patients receiving 1-2 g vancomycin powder in surgical bed (n = 150), No vancomycin powder (n = 150)	5 superficial infections in vancomycin powder group (3.3%), 5 superficial and 6 deep infections in control group (7.3%)	Significantly fewer deep infections in patients treated with vancomycin powder (P = 0.0297)
Theologis <i>et al</i> <sup>[56]</sup> (2014)	Retrospective cohort (III)	Complex adult spinal deformity reconstruction	Patients receiving 1-2 g vancomycin powder in subfascial space (n = 151), No vancomycin powder (n = 64)	4 infections in first 90 d in treatment group (2.6%), 7 infections in first 90 d in control (10.9%)	Significantly fewer hospital readmissions within 90 d of surgery when using vancomycin powder (P = 0.01)
Caroom <i>et al</i> <sup>[48]</sup> (2013)	Retrospective comparative study of prospectively collected data (II)	Multilevel posterior decompression and instrumentation for cervical spondylitic myelopathy	1 g vancomycin powder applied subfascially along bone graft and instrumentation (n = 40), No vancomycin powder (n = 72)	Zero infections in vancomycin powder group (0%), 11 infections in control (15%)	Significant decrease in infection rate with use of vancomycin powder (P = 0.007)
Gans <i>et al</i> <sup>[58]</sup> (2013)	Therapeutic retrospective cohort (II)	Pediatric spinal deformity surgery (fusion, growing rods, vertical expandable prosthetic titanium rib)	Patients received 1g vancomycin powder in surgical wound (n = 87)	3 surgical site infections identified (3.4%) The postoperative systemic vancomycin levels remained undetectable. None of the patients experienced nephrotoxicity or red man syndrome	Local application of vancomycin powder is safe without significant changes in creatinine level or systemic vancomycin level
Kim <i>et al</i> <sup>[57]</sup> (2013)	Retrospective cohort (IV)	Instrumented spinal fusion	Patients receiving 1 g vancomycin powder in surgical wound (n = 34), No vancomycin powder (n = 40)	Zero infections in vancomycin powder group (0%), 5 infections in control (12.5%)	Significant decrease in infection rate with use of vancomycin powder (P < 0.033)
Martin <i>et al</i> <sup>[55]</sup> (2013)	Retrospective cohort (II)	Adult posterior thoracolumbar or lumbar instrumented fusion for spinal deformity	Patients receiving 2 g vancomycin powder in surgical wound (n = 156), No vancomycin powder (n = 150)	8 infections in vancomycin powder group (5.1%), 8 infections in control (5.3%)	No significant difference in infection rate with use of vancomycin powder (P = 0.944)
Pahys <i>et al</i> <sup>[50]</sup> (2013)	Therapeutic retrospective cohort (II)	Posterior cervical spine surgery	Group 1: Perioperative antibiotics alone (n = 483), Group 2: addition of alcohol foam prep and drain (n = 323), Group 3: group 2 plus vancomycin powder in wound (n = 195)	9 infections in group 1 (1.86%), 1 infection in group 2 (0.3%), No infections in group 3 (0%)	Significant decrease in infections in both group 2 (P = 0.047) and group 3 (P = 0.048) compared to group 1
Strom <i>et al</i> <sup>[48]</sup> (2013)	Retrospective cohort (IV)	Instrumented and non-instrumented posterior lumbar laminectomy and fusion	Patients receiving 1 g vancomycin powder in surgical wound (n = 156), No vancomycin powder (n = 97)	Zero infections in vancomycin powder group (0%), 11 infections in control (11%)	Significant decrease in infection rate with use of vancomycin powder (P = 0.000018)
Strom <i>et al</i> <sup>[51]</sup> (2013)	Retrospective cohort (IV)	Posterior cervical fusion	Patients receiving 1 g vancomycin powder in surgical wound (n = 79), No vancomycin powder (n = 92)	2 infections in vancomycin powder group (2.5%), 10 infections in control (10.9%)	Significant decrease in infection rate with use of vancomycin powder (P = 0.0384)
Tubaki <i>et al</i> <sup>[52]</sup> (2013)	Prospective randomized controlled trial (II)	Any primary spine surgery excluding biopsy or minimally invasive procedure	Patients receiving 1 g vancomycin powder in surgical wound (n = 433), Patients receiving 1 g vancomycin powder in surgical wound (n = 474)	7 infections in vancomycin powder group (1.61%), 8 infections in control (1.68%)	No significant difference in infection rate with use of vancomycin powder
Molinari <i>et al</i> <sup>[4]</sup> (2012)	Retrospective case series (IV)	Any spine surgery	Patients receiving 1 g vancomycin powder in surgical wound (n = 1512)	Fifteen infections identified (0.99%)	Low rate of deep spinal wound infection for both instrumented and uninstrumented cases

Sweet <i>et al.</i> <sup>[46]</sup> (2011)	Retrospective cohort (IV)	Thoracic or lumbar posterior instrumented fusion	Patients receiving 1 g vancomycin powder in bone graft and 1 g applied directly to deep and superficial wound (n = 911).	Two infections in vancomycin powder group (0.2%), Twenty-one infection in control (2.6%)	Significant decrease in infection rate with use of vancomycin powder (P < 0.0001)
O'Neill <i>et al.</i> <sup>[47]</sup> (2011)	Retrospective cohort (IV)	Instrumented posterior spine fusion for traumatic injury	No vancomycin powder (n = 821) Patients receiving 1 g vancomycin powder in surgical wound (n = 54), No vancomycin powder (n = 56)	Zero infections in vancomycin powder group (0%), Seven infections in control (13%)	Significant decrease in infection rate with use of vancomycin powder (P = 0.02)

**Re-dosing and prolonged postoperative antibiotic course**

It is standard for all of our patients undergoing surgery to receive a dose of 1-2 g of cefazolin and 1-2 g vancomycin intravenous within 1 h of incision, depending on patient weight and allergies. This is in accordance with recommendations from the North American Spine Society<sup>[45]</sup>. For short, uncomplicated cases, no additional IV antibiotics are required. In various studies, length of surgery has been associated with surgical site infection rate. For that reason, prolonged cases are re-dosed with antibiotics at 4-h intervals during surgery. Additionally, it is the authors' protocol to extend antibiotic coverage with either cefazolin or vancomycin for a full 72 h in high-risk patients. High-risk patients include diabetics, obese patients (body mass index > 30), history of previous postoperative wound infection, complex revision or deformity surgeries lasting more than 6 h.

Little data has been published on extended postoperative antibiotic prophylaxis in spine surgery. Two studies to our knowledge have explored the effects. Ohtori *et al.*<sup>[61]</sup> in a comparative cohort study evaluated two statistically similar groups undergoing lumbar spine decompression and fusion. Group 1 received 2 d of postoperative IV antibiotics, and group 2 received 9 d IV antibiotics. There was one infection in group 1 (1/70) and no infections in group 2 (0/65), but these results were not significant. The only significant findings were that longer courses of antibiotics resulted in longer hospital stays and longer time to normalize body temperature after surgery.

In a separate retrospective cohort study, Takahashi *et al.*<sup>[62]</sup> evaluated 4 different prophylaxis measures. One group had 7 d of postoperative antibiotics and no preoperative antibiotic (group 1). The remaining 3 groups all received appropriate preoperative antibiotics as well as postoperative antibiotics for 4 d (group 2), 2 d (group 3), or 1 d postoperatively (group 4). Groups 1, 2, 3 and 4 saw infection rates of 2.6% (14/539), 0.9% (5/536), 0% (0/257) and 0% (0/83) respectively. Although this showed an increase in infection rate with shorter antibiotic duration, there were significant differences among the groups with regard to age, preoperative hospitalization duration, and proportion of patients considered to be compromised hosts.

At this time, current evidence-based guidelines from the North American Spine Society only state that prolonged regimens may be considered when significant comorbidities or complex situations exist<sup>[45]</sup>. Comorbidities and complex situations considered applicable include obesity, diabetes, neurologic deficits, incontinence, preoperative serum glucose of > 125 mg/dL or a postoperative serum glucose level of > 200 mg/dL, trauma and prolonged multilevel instrumented surgery. A randomized prospective analysis of postoperative prophylactic antibiotic duration and surgical site infection rate may provide better evidence. The current recommendations additionally provide for repeated dosing of antibiotics intraoperatively at 3-4 h intervals for prolonged cases to maintain therapeutic antibiotic levels throughout the procedure. The superiority of one drug has not been demonstrated in the literature.

**Wound irrigation with diluted povidone-iodine solution**

The current infection prevention protocol involves irrigation of the surgical wound with diluted povidone-iodine solution (150 mL of saline + 5 mL of betadine aqueous solution which contains 10% povidone-iodine).

Irrigation of a surgical wound is a commonplace practice prior to closure. There is limited amount of orthopedic literature directly evaluating irrigation solutions and techniques in a clean, primary surgery. Bhandari *et al.*<sup>[63]</sup> evaluated the efficacy of various irrigating solutions in removing adherent bacteria from bone in a mice model. They found that the fewest number of residual colony-forming units were found after exposure to povidone-iodine, chlorhexidine-gluconate, and soap solutions. Normal saline was the least effective. When low-pressure pulsatile lavage was added, no growth was observed after wash with soap solution, and there was near complete removal of adherent bacteria with the povidone-iodine and chlorhexidine-gluconate solutions. As it pertains to orthopaedic clinical practice, four studies were identified in whose

**Table 3** Clinical orthopedic studies evaluating surgical wound irrigation before closure

Ref.	Study design (level of evidence)	Surgery performed	Groups	Main outcome	Significance
Yazdi <i>et al</i> <sup>[64]</sup> (2014)	Prospective randomized controlled trial ( I )	Arthroscopic ACL reconstruction	Irrigation with 0.9% normal saline and 80 mg/L gentamicin (n = 180), Irrigation with 0.9% normal saline (n = 180)	One infection in gentamicin group (0.57%), Four infections in normal saline alone group (2.2%)	Decreased rate of infection when using gentamicin in irrigating solution (P = 0.4)
Brown <i>et al</i> <sup>[65]</sup> (2012)	Retrospective cohort (IV)	Primary total hip or total knee arthroplasty	Soak wound with 500 mL 0.35% povidone-iodine followed by 1 L NS pulse lavage prior to closure (n = 688), Pulse lavage with 1 L NS only prior to closure (n = 1862)	One infection in betadine group (0.15%), Eighteen infections in saline alone group (0.97%)	Significant decrease in 90-d infection rate when soaking surgical wound with betadine solution prior to closure (P = 0.04)
Chang <i>et al</i> <sup>[66]</sup> (2006)	Prospective randomized controlled trial ( I )	Instrumented lumbosacral posterolateral fusion for degenerative spinal disorder with segmental instability	Wounds irrigated with 0.35% povidone-iodine (n = 120), Wounds irrigated with normal saline (n = 124)	No infections in povidone-iodine group, 4.8% infection rate in saline group	Overall infection rate was statistically significant when comparing betadine solution group with no betadine group (P = 0.029)
Cheng <i>et al</i> <sup>[67]</sup> (2005)	Prospective randomized controlled trial ( I )	Spinal decompression with or without fusion	Wounds irrigated with 0.35% povidone-iodine (n = 208), Wounds irrigated with normal saline (n = 206)	No infections in povidone-iodine group, 3.5% infection rate in saline group	Overall infection rate was statistically significant when comparing betadine solution group with no betadine group (P = 0.007)

ACL: Anterior cruciate ligament.

main goal was measuring outcomes of irrigating surgical wounds with antimicrobial solutions and comparing to normal saline irrigation (Table 3)<sup>[64-67]</sup>.

Most notably, as it relates to spine, Chang *et al*<sup>[66]</sup> and Cheng *et al*<sup>[67]</sup> performed prospective randomized controlled studies comparing intraoperative wound irrigation using normal saline to 0.35% povidone-iodine solutions. Both studies found a statistically significant decrease in post-operative infections with the use of povidone-iodine solution.

Yazdi *et al*<sup>[64]</sup> evaluated the effect of gentamicin in irrigating solutions during arthroscopic anterior cruciate ligament (ACL) reconstructions in a prospective randomized controlled study. Although infection rates were lower for the group receiving gentamicin as opposed to normal saline alone, statistical significance was not achieved.

Brown *et al*<sup>[65]</sup> retrospectively reviewed total knee and hip arthroplasties before and after initiating a protocol to soak the surgical wound with 0.35% povidone-iodine solution prior to closure. They found a significant decrease in 90-d postoperative infection rate when using the betadine solution.

Based on these studies, it appears that there is a significant advantage for infection prophylaxis when irrigating a surgical wound with a povidone-iodine solution.

#### **Duraprep prior to skin closure**

The final intraoperative step occurs just prior to skin closure. There is often significant handling of the skin at closure, which could potentially contaminate the surgical site. As a safeguard, prior to skin closure, DuraPrep is

used over any exposed skin as a prophylactic measure.

In a level I prospective randomized study evaluating the efficacy of both ChlorPrep (2% CHG and 70% isopropyl alcohol) and DuraPrep (0.7% iodine and 74% isopropyl alcohol) in lumbar spine surgery, Savage *et al*<sup>[68]</sup> found that both skin preparations significantly reduced bacterial flora growths after application. Cultures were taken from the skin before application, after application, and after skin closure for 100 consecutive patients randomly assigned to one of the two preparations. They found that for the ChlorPrep and DuraPrep groups, positive cultures were found, respectively, in 84% and 80% pre-preparation, 0% and 6% post-preparation, and 34% and 32% after closure. As outlined, there was a significant increase in the number of positive cultures following skin closure. It is unclear whether this is from recolonization or possibly disruption of the natural skin flora beneath the epidermis during surgery. The bio-burden on the skin at the end of a case is not the same as in the beginning. It has not been shown that this increase results in an increased rate of postoperative infection. Further studies are needed to evaluate the effectiveness of intraoperative reapplication of a skin prep solution before skin closure.

## **DISCUSSION**

Several factors have been identified as risk for surgical site infection. Although multiple reviews have addressed these risk factors and prophylactic measures individually, it is difficult to control for and evaluate all factors affecting an individual patient. In response to an increasing number of SSIs at the authors' institution,

a new surgical protocol was initiated in an effort to reduce infection rates after an intensive epidemiological investigation failed to reveal a common source. In view of the absence of a clear cause of the increased infection rate, the authors decided to implement the ten-step protocol targeting areas highlighted by the literature search. The purpose of the current study was analyzed the literature for each of the 10 steps and evaluated our own experience. As to which factor or factors affected the decreased infection rate is an area of future research.

The use of vancomycin powder has been studied extensively in the literature. We have employed the routine use of 1 g mixed in with bone graft when used and an additional 1 g spread directly over the surgical site after closure of the deep fascia. Only two of the 11 studies comparing use of vancomycin powder in spine surgery to a control failed to show a significant difference. The vast majority of the literature has found significantly lower rates of infection with routine use of vancomycin powder. Its use in spine surgery is well supported by several studies and routine use is more than acceptable.

Also strongly supported is routine irrigation of surgical wounds. Irrigation of the surgical wound has been evaluated in several surgical settings. Chang *et al.*<sup>[66]</sup> and Cheng *et al.*<sup>[67]</sup> both evaluated the use of 0.35% povidone-iodine solution irrigation in spine patients. Both studies were prospective randomized controlled studies and provided strong evidence that irrigation with 0.35% povidone-iodine significantly reduces surgical site infection in spine surgery. Also supported is the use of CHG cloths in a preoperative setting. Their use for preoperative cleansing has showed a significant reduction in skin bacterial colonization. Additionally, in a systematic review, CHG cloths have been shown to reduce the incidence of surgical site infection.

One of the measures employed in this current report is double gloving with frequent changing of outer gloves. The majority of the available literature on gloving techniques focuses on double gloving and perforation rates. It has been shown in several studies that double gloving reduces rate of perforation to the inner gloves. With respect to infection, Rehman *et al.*<sup>[44]</sup> had perhaps the most relevant study. In a retrospective study on spine fusions in which one group the surgeon removed outer gloves prior to instrumentation, there was a significant decrease in infection rates with removing outer gloves. It was also shown by Ward *et al.*<sup>[43]</sup> that changing outer gloves during a case significantly reduces contamination of gloves as seen by bacterial cultures taken from the gloves. This practice was largely adopted from reports in arthroplasty cases. Changing of the outer gloves prior to implanting total hips was shown to decrease infection rates. The routine changing of outer gloves at distinct points in a case to reduce infection is strongly supported.

HbA1c has been studied as a possible marker for increased infection risk. Although early studies identified

elevated HbA1c as a significant risk factor for infection, there has been some variation in the literature. The majority of finding point to an increased infection rate with high HbA1c, but some has found no correlation. It is possible that perioperative and intraoperative glucose levels or even absolute diabetic status are more significant. It remains to be seen if an individual's risk changes with improving their HbA1c preoperatively. The literature is lacking a level I prospective randomized study discussing the relationship between preoperative HbA1c and the risk of elective spine surgery postoperative wound infection. Ethically such a study cannot be done, as one simply cannot take a patient with poor diabetic control to an elective spine surgery. Therefore, it remains to be seen whether the postoperative spine wound infection risk changes if a diabetic is able to bring down HbA1c prior to an elective procedure. However, with the current available data, adoption of a protocol that tightly controls preoperative HbA1c to 7.0 makes sense as, in general, it improves the patient health status and may reduce the risk of postoperative wound infection.

Keeping an operating room door taped shut is an idea that has not yet been evaluated in the literature. Although Young and O'Reagan<sup>[36]</sup> showed a trend of increased infection rate in cardiac surgery with increasing numbers of door openings, the effect of limiting traffic remains to be seen. The available studies appear to support the practice limiting the number of openings of the main operating room door in order to reduce the postoperative spine wound infection especially in a long spine cases.

Similarly, there is insufficient evidence as of yet in the literature to define the risk of surgical site infection based on number of personnel in the operating room. As seen by Olsen *et al.*<sup>[38]</sup> there was a trend towards increased number of infections based on increasing personnel in the operating room. As they pointed out though, this was likely a proxy of case length and complexity. But with the thought in mind that more people means more possibilities of contamination, it is still possible that limiting the number of personnel in the operating room can be protective against surgical site infection. This practice seems to be supported but is lacking higher level evidence.

Flash sterilization, although useful if equipment needs reprocessed quickly, may present some risk to the patient. Spine surgery deals with very durable bone and soft tissue that can potentially persist on the equipment with insufficient cleaning. Tosh *et al.*<sup>[40]</sup> showed that residual tissue was commonly seen in arthroscopic equipment under endoscopic evaluation after flash sterilization. The Fifth Decennial International Conference on Healthcare-Associated Infections identified flash sterilization as a likely source of increased infection rate at one institution. Although available literature on flash sterilization and the primary outcome of surgical site infection is limited, it can be identified as a possible avoidable cause of infection. To

our knowledge, there is no literature available evaluating the use of flash sterilization in spine surgery. Additional investigations as to the benefit of reducing utilization of flash sterilization may be of benefit to support or refute the utility of restricting its use.

The use of preoperative antibiotic prophylaxis has become an important part of infection prevention. Current recommendations additionally advise on repeated dosing every 3-4 h during prolonged cases. Extending antibiotics beyond 24 h postoperatively has been evaluated, but no level 1 evidence exists. The current literature has not shown any benefit with extended antibiotics. A prospective randomized study may better help identify if there is utility in extending antibiotics in specific patients.

The final measure explored here is use of DuraPrep on exposed skin prior to wound closure. As was shown by Savage *et al.*<sup>[68]</sup> the use of DuraPrep significantly reduces the chances of obtaining a positive culture from the skin at the start of a case. However, cultures at the end of a case show a drastic increase in positive growth. Although it has not been evaluated in the literature, we have employed routine repeat cleansing of the skin prior to closure. It is thought that this theoretically reduces the bacterial load while closing. Since this is a time with significant handling of the skin, it is plausible that this may decrease contamination of the surgical wound and thus surgical site infection.

In conclusion, several details surrounding surgery have been evaluated in the literature as both patient risk factors and prophylactic measures for decreasing rates of SSIs. With the multivariable setting that is inherent in spine surgery, it is difficult to evaluate changes in all variables simultaneously. The authors attempted to control for 10 factors and found support in the literature for the majority of the 10 steps taken. This protocol resulted in a significant reduction in SSIs in the senior author's practice. Postoperative surgical site infection will remain a matter of concern for patients, surgeons and healthcare providers. Future prospective randomized studies that include some or all of the 10 steps discussed in this report are necessary to confirm whether the 10 steps adopted by the authors were in fact science or fiction in the battle for infection control.

## ARTICLE HIGHLIGHTS

### Research background

Surgical site infections (SSIs) are the most common hospital acquired infections. The rates of infection following spine surgery have been reported to range from less than 1% to 10.9%. Surgical site infection in spinal surgery is associated with significantly increased morbidity and costs

### Research motivation

In response to an increasing number of SSIs at the authors' institution, a new ten step surgical protocol was initiated in an effort to reduce infection rates after an intensive epidemiological investigation failed to reveal a common source.

### Research objectives

To define a ten-step protocol that reduced the incidence of surgical site infection

in the spine surgery practice of the senior author and evaluate the support for each step based on current literature.

### Research methods

Ten-step protocol was implemented. (1) Preoperative glycemic management based on hemoglobin A1c (HbA1c); (2) skin site preoperative preparation with 2% chlorhexidine gluconate disposable cloths; (3) Limit operating room traffic; (4) cut the number of personnel in the room to the minimum required; (5) absolutely no flash sterilization of equipment; (6) double-gloving with frequent changing of outer gloves; (7) local application of vancomycin powder; (8) re-dosing antibiotic every 4 h for prolonged procedures and extending postoperative coverage to 72 h for high-risk patients; (9) irrigation of subcutaneous tissue with diluted povidone-iodine solution after deep fascial closure; and (10) use of DuraPrep skin preparation at the end of a case before skin closure. Through an extensive literature review, the current data available for each of the ten steps was evaluated.

### Research results

Use of vancomycin powder in surgical wounds, routine irrigation of surgical site, and frequent changing of surgical gloves are strongly supported by the literature. Preoperative skin preparation with chlorhexidine wipes is similarly supported. The majority of current literature supports control of HbA1c preoperatively to reduce risk of infection. Limiting the use of flash sterilization is supported, but has not been evaluated in spine-specific surgery. Limiting OR traffic and number of personnel in the OR are supported although without level 1 evidence. Prolonged use of antibiotics postoperatively is not supported by the literature. Intraoperative use of DuraPrep prior to skin closure is not yet explored.

### Research conclusions

Several details surrounding surgery have been evaluated in the literature as both patient risk factors and prophylactic measures for decreasing rates of SSIs. The authors attempted to control for 10 factors and found support in the literature for the majority of the 10 steps taken. This protocol resulted in a significant reduction in SSIs in the senior author's practice.

### Research perspectives

In the current era of pay per performance, there is a major drive in all hospitals to reduce postoperative infection to the minimum. A variety of measures have been initiated and evaluated in the literature to reduce the occurrence of SSIs. Postoperative surgical site infection will remain a matter of concern for patients, surgeons and healthcare providers. Future prospective randomized studies that include some or all of the 10 steps discussed in this report are necessary to confirm whether the 10 steps adopted by the authors were in fact science or fiction in the battle for infection control.

## REFERENCES

- 1 **Sasso RC**, Garrido BJ. Postoperative spinal wound infections. *J Am Acad Orthop Surg* 2008; **16**: 330-337 [PMID: 18524984 DOI: 10.5435/00124635-200806000-00005]
- 2 **Horan TC**, Culver DH, Gaynes RP, Jarvis WR, Edwards JR, Reid CR. Nosocomial infections in surgical patients in the United States, January 1986-June 1992. National Nosocomial Infections Surveillance (NNIS) System. *Infect Control Hosp Epidemiol* 1993; **14**: 73-80 [PMID: 8440883 DOI: 10.2307/30147164]
- 3 **Schuster JM**, Rehtine G, Norvell DC, Dettori JR. The influence of perioperative risk factors and therapeutic interventions on infection rates after spine surgery: a systematic review. *Spine (Phila Pa 1976)* 2010; **35**: S125-S137 [PMID: 20407344 DOI: 10.1097/BRS.0b013e3181d8342c]
- 4 **American Diabetes Association**. Classification and diagnosis of diabetes. *Diabetes Care* 2015; **38** Suppl: S8-S16 [PMID: 25537714 DOI: 10.2337/dc12-s064]
- 5 **Bishop JR**, Moul JW, Sihelnik SA, Peppas DS, Gormley TS, McLeod DG. Use of glycosylated hemoglobin to identify diabetics

- at high risk for penile periprosthetic infections. *J Urol* 1992; **147**: 386-388 [PMID: 1732600 DOI: 10.1016/S0022-5347(17)37244-0]
- 6 **Wilson SK**, Carson CC, Cleves MA, Delk JR 2nd. Quantifying risk of penile prosthesis infection with elevated glycosylated hemoglobin. *J Urol* 1998; **159**: 1537-9; discussion 1539-40 [PMID: 9554349 DOI: 10.1097/00005392-199805000-00034]
  - 7 **Latham R**, Lancaster AD, Covington JF, Pirolo JS, Thomas CS Jr. The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. *Infect Control Hosp Epidemiol* 2001; **22**: 607-612 [PMID: 11776345 DOI: 10.1086/501830]
  - 8 **Endara M**, Masden D, Goldstein J, Gondek S, Steinberg J, Attinger C. The role of chronic and perioperative glucose management in high-risk surgical closures: a case for tighter glycemic control. *Plast Reconstr Surg* 2013; **132**: 996-1004 [PMID: 23783058 DOI: 10.1097/PRS.0b013e31829fe119]
  - 9 **Perna M**, Romagnuolo J, Morgan K, Byrne TK, Baker M. Preoperative hemoglobin A1c and postoperative glucose control in outcomes after gastric bypass for obesity. *Surg Obes Relat Dis* 2012; **8**: 685-690 [PMID: 21982941 DOI: 10.1016/j.soard.2011.08.002]
  - 10 **Sato H**, Carvalho G, Sato T, Lattermann R, Matsukawa T, Schricker T. The association of preoperative glycemic control, intraoperative insulin sensitivity, and outcomes after cardiac surgery. *J Clin Endocrinol Metab* 2010; **95**: 4338-4344 [PMID: 20631016 DOI: 10.1210/jc.2010-0135]
  - 11 **Alserius T**, Anderson RE, Hammar N, Nordqvist T, Ivert T. Elevated glycosylated haemoglobin (HbA1c) is a risk marker in coronary artery bypass surgery. *Scand Cardiovasc J* 2008; **42**: 392-398 [PMID: 18609043 DOI: 10.1080/14017430801942393]
  - 12 **Halkos ME**, Puskas JD, Lattouf OM, Kilgo P, Kerendi F, Song HK, Guyton RA, Thourani VH. Elevated preoperative hemoglobin A1c level is predictive of adverse events after coronary artery bypass surgery. *J Thorac Cardiovasc Surg* 2008; **136**: 631-640 [PMID: 18805264 DOI: 10.1016/j.jtcvs.2008.02.091]
  - 13 **Dronge AS**, Perkal MF, Kancir S, Concato J, Aslan M, Rosenthal RA. Long-term glycemic control and postoperative infectious complications. *Arch Surg* 2006; **141**: 375-80; discussion 380 [PMID: 16618895 DOI: 10.1001/archsurg.141.4.375]
  - 14 **Rawlins L**, Rawlins MP, Brown CC, Schumacher DL. Effect of elevated hemoglobin A1c in diabetic patients on complication rates after Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2013; **9**: 749-752 [PMID: 22884300 DOI: 10.1016/j.soard.2012.06.011]
  - 15 **Knapiak P**, Cieřla D, Filipiak K, Knapiak M, Zembala M. Prevalence and clinical significance of elevated preoperative glycosylated hemoglobin in diabetic patients scheduled for coronary artery surgery. *Eur J Cardiothorac Surg* 2011; **39**: 484-489 [PMID: 21087870 DOI: 10.1016/j.ejcts.2010.07.037]
  - 16 **Marchant MH Jr**, Viens NA, Cook C, Vail TP, Bolognesi MP. The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty. *J Bone Joint Surg Am* 2009; **91**: 1621-1629 [PMID: 19571084 DOI: 10.2106/JBJS.H.00116]
  - 17 **Iorio R**, Williams KM, Marcantonio AJ, Specht LM, Tilzey JF, Healy WL. Diabetes mellitus, hemoglobin A1C, and the incidence of total joint arthroplasty infection. *J Arthroplasty* 2012; **27**: 726-729.e1 [PMID: 22054905 DOI: 10.1016/j.arth.2011.09.013]
  - 18 **Jämsen E**, Nevalainen P, Kalliovalkama J, Moilanen T. Preoperative hyperglycemia predicts infected total knee replacement. *Eur J Intern Med* 2010; **21**: 196-201 [PMID: 20493422 DOI: 10.1016/j.ejim.2010.02.006]
  - 19 **Myers TG**, Lowery NJ, Frykberg RG, Wukich DK. Ankle and hindfoot fusions: comparison of outcomes in patients with and without diabetes. *Foot Ankle Int* 2012; **33**: 20-28 [PMID: 22381232 DOI: 10.3113/FAI.2012.0020]
  - 20 **Lamloum SM**, Mobasher LA, Karar AH, Basyon L, Abdallah TH, Al-Saleh AI, Al-Shamali NA. Relationship between postoperative infectious complications and glycemic control for diabetic patients in an orthopedic hospital in Kuwait. *Med Princ Pract* 2009; **18**: 447-452 [PMID: 19797920 DOI: 10.1159/000235893]
  - 21 **Adams AL**, Paxton EW, Wang JQ, Johnson ES, Bayliss EA, Ferrara A, Nakasato C, Bini SA, Namba RS. Surgical outcomes of total knee replacement according to diabetes status and glycemic control, 2001 to 2009. *J Bone Joint Surg Am* 2013; **95**: 481-487 [PMID: 23446446 DOI: 10.2106/JBJS.L.00109]
  - 22 **Harris AH**, Bowe TR, Gupta S, Ellerbe LS, Giori NJ. Hemoglobin A1C as a marker for surgical risk in diabetic patients undergoing total joint arthroplasty. *J Arthroplasty* 2013; **28**: 25-29 [PMID: 23910511 DOI: 10.1016/j.arth.2013.03.033]
  - 23 **Hikata T**, Iwanami A, Hosogane N, Watanabe K, Ishii K, Nakamura M, Kamata M, Toyama Y, Matsumoto M. High preoperative hemoglobin A1c is a risk factor for surgical site infection after posterior thoracic and lumbar spinal instrumentation surgery. *J Orthop Sci* 2014; **19**: 223-228 [PMID: 24368606 DOI: 10.1007/s00776-013-0518-7]
  - 24 **Takahashi S**, Suzuki A, Toyoda H, Terai H, Dohzono S, Yamada K, Matsumoto T, Yasuda H, Tsukiyama K, Shinohara Y, Ibrahim M, Nakamura H. Characteristics of diabetes associated with poor improvements in clinical outcomes after lumbar spine surgery. *Spine (Phila Pa 1976)* 2013; **38**: 516-522 [PMID: 22976346 DOI: 10.1097/BRS.0b013e318273583a]
  - 25 **Murray MR**, Saltzman MD, Gryzlo SM, Terry MA, Woodward CC, Nuber GW. Efficacy of preoperative home use of 2% chlorhexidine gluconate cloth before shoulder surgery. *J Shoulder Elbow Surg* 2011; **20**: 928-933 [PMID: 21612945 DOI: 10.1016/j.jse.2011.02.018]
  - 26 **Johnson AJ**, Daley JA, Zywił MG, Delanois RE, Mont MA. Preoperative chlorhexidine preparation and the incidence of surgical site infections after hip arthroplasty. *J Arthroplasty* 2010; **25**: 98-102 [PMID: 20570089 DOI: 10.1016/j.arth.2010.04.012]
  - 27 **Zywił MG**, Daley JA, Delanois RE, Naziri Q, Johnson AJ, Mont MA. Advance pre-operative chlorhexidine reduces the incidence of surgical site infections in knee arthroplasty. *Int Orthop* 2011; **35**: 1001-1006 [PMID: 20563806 DOI: 10.1007/s00264-010-1078-5]
  - 28 **Veiga DF**, Damasceno CA, Veiga-Filho J, Figueiras RG, Vieira RB, Garcia ES, Silva VV, Novo NF, Ferreira LM. Randomized controlled trial of the effectiveness of chlorhexidine showers before elective plastic surgical procedures. *Infect Control Hosp Epidemiol* 2009; **30**: 77-79 [PMID: 19046051 DOI: 10.1086/592980]
  - 29 **Kamel C**, McGahan L, Mierzwinski-Urban M, Embil J. Preoperative Skin Antiseptic Preparations and Application Techniques for Preventing Surgical Site Infections: A Systematic Review of the Clinical Evidence and Guidelines. 2011 [PMID: 24354038 DOI: 10.1086/665723]
  - 30 **Webster J**, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. *Cochrane Database Syst Rev* 2012; CD004985 [PMID: 22972080 DOI: 10.1002/14651858.CD004985.pub4]
  - 31 **Brohus H**, Balling KD, Jeppesen D. Influence of movements on contaminant transport in an operating room. *Indoor Air* 2006; **16**: 356-372 [PMID: 16948712 DOI: 10.1111/j.1600-0668.2006.00454.x]
  - 32 **Scaltriti S**, Cencetti S, Rovesti S, Marchesi I, Bargellini A, Borella P. Risk factors for particulate and microbial contamination of air in operating theatres. *J Hosp Infect* 2007; **66**: 320-326 [PMID: 17655973 DOI: 10.1016/j.jhin.2007.05.019]
  - 33 **Ritter MA**. Operating room environment. *Clin Orthop Relat Res* 1999; 103-109 [PMID: 10611865 DOI: 10.1097/00003086-199912000-00011]
  - 34 **Healey AN**, Sevdalis N, Vincent CA. Measuring intra-operative interference from distraction and interruption observed in the operating theatre. *Ergonomics* 2006; **49**: 589-604 [PMID: 16717011 DOI: 10.1080/00140130600568899]
  - 35 **Lynch RJ**, Englesbe MJ, Sturm L, Bitar A, Budhiraj K, Kolla S, Polyachenko Y, Duck MG, Campbell DA Jr. Measurement of foot traffic in the operating room: implications for infection control. *Am J Med Qual* 2009; **24**: 45-52 [PMID: 19139463 DOI: 10.1177/1062860608326419]
  - 36 **Young RS**, O'Regan DJ. Cardiac surgical theatre traffic: time for traffic calming measures? *Interact Cardiovasc Thorac Surg* 2010; **10**: 526-529 [PMID: 20100706 DOI: 10.1510/icvts.2009.227116]

- 37 **Pryor F**, Messmer PR. The effect of traffic patterns in the OR on surgical site infections. *AORN J* 1998; **68**: 649-660 [PMID: 9795720 DOI: 10.1016/S0001-2092(06)62570-2]
- 38 **Olsen MA**, Nepple JJ, Riew KD, Lenke LG, Bridwell KH, Mayfield J, Fraser VJ. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am* 2008; **90**: 62-69 [PMID: 18171958 DOI: 10.2106/JBJS.F.01515]
- 39 **Lopansri B**, Taylor C, Anderson V. Protracted outbreak of postarthroscopy infections associated with flash sterilization of instruments. In: Program and abstracts of the Fifth Decennial International Conference on Healthcare-Associated Infections. Atlanta: Society for Healthcare Epidemiology of America, 2010
- 40 **Tosh PK**, Disbot M, Duffy JM, Boom ML, Heseltine G, Srinivasan A, Gould CV, Berríos-Torres SI. Outbreak of *Pseudomonas aeruginosa* surgical site infections after arthroscopic procedures: Texas, 2009. *Infect Control Hosp Epidemiol* 2011; **32**: 1179-1186 [PMID: 22080656 DOI: 10.1086/662712]
- 41 **Ritter MA**, French ML, Eitzen H. Evaluation of microbial contamination of surgical gloves during actual use. *Clin Orthop Relat Res* 1976; **303**-306 [PMID: 1277681 DOI: 10.1097/00003086-197606000-00040]
- 42 **McCue SF**, Berg EW, Saunders EA. Efficacy of double-gloving as a barrier to microbial contamination during total joint arthroplasty. *J Bone Joint Surg Am* 1981; **63**: 811-813 [PMID: 7016885 DOI: 10.2106/00004623-198163050-00017]
- 43 **Ward WG Sr**, 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.0b013e3182a6f2d9]
- 44 **Rehman A**, Rehman AU, Rehman TU, Freeman C. Removing Outer Gloves as a Method to Reduce Spinal Surgery Infection. *J Spinal Disord Tech* 2015; **28**: E343-E346 [PMID: 23563341 DOI: 10.1097/BSD.0b013e31829046ca]
- 45 **Shaffer WO**, Baisden JL, Fernand R, Matz PG; North American Spine Society. An evidence-based clinical guideline for antibiotic prophylaxis in spine surgery. *Spine J* 2013; **13**: 1387-1392 [PMID: 23988461 DOI: 10.1016/j.spinee.2013.06.030]
- 46 **Sweet FA**, Roh M, Sliva C. Intraoperative application of vancomycin for prophylaxis in instrumented thoracolumbar fusions: efficacy, drug levels, and patient outcomes. *Spine (Phila Pa 1976)* 2011; **36**: 2084-2088 [PMID: 21304438 DOI: 10.1097/BRS.0b013e3181ff2cb1]
- 47 **O'Neill KR**, Smith JG, Abtahi AM, Archer KR, Spengler DM, McGirt MJ, Devin CJ. Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder. *Spine J* 2011; **11**: 641-646 [PMID: 21600853 DOI: 10.1016/j.spinee.2011.04.025]
- 48 **Strom RG**, Pacione D, Kalthorn SP, Frempong-Boadu AK. Lumbar laminectomy and fusion with routine local application of vancomycin powder: decreased infection rate in instrumented and non-instrumented cases. *Clin Neurol Neurosurg* 2013; **115**: 1766-1769 [PMID: 23622935 DOI: 10.1016/j.clineuro.2013.04.005]
- 49 **Caroom C**, Tullar JM, Benton EG Jr, Jones JR, Chaput CD. Intraoperative vancomycin powder reduces surgical site infections in posterior cervical fusion. *Spine (Phila Pa 1976)* 2013; **38**: 1183-1187 [PMID: 23474597 DOI: 10.1097/BRS.0b013e31828fcb5]
- 50 **Pahys JM**, Pahys JR, Cho SK, Kang MM, Zebala LP, Hawasli AH, Sweet FA, Lee DH, Riew KD. Methods to decrease postoperative infections following posterior cervical spine surgery. *J Bone Joint Surg Am* 2013; **95**: 549-554 [PMID: 23515990 DOI: 10.2106/JBJS.K.00756]
- 51 **Strom RG**, Pacione D, Kalthorn SP, Frempong-Boadu AK. Decreased risk of wound infection after posterior cervical fusion with routine local application of vancomycin powder. *Spine (Phila Pa 1976)* 2013; **38**: 991-994 [PMID: 23324930 DOI: 10.1097/BRS.0b013e318285b219]
- 52 **Tubaki VR**, Rajasekaran S, Shetty AP. Effects of using intravenous antibiotic only versus local intraoperative vancomycin antibiotic powder application in addition to intravenous antibiotics on postoperative infection in spine surgery in 907 patients. *Spine (Phila Pa 1976)* 2013; **38**: 2149-2155 [PMID: 24048091 DOI: 10.1097/BRS.0000000000000015]
- 53 **Martin JR**, Adogwa O, Brown CR, Bagley CA, Richardson WJ, Lad SP, Kuchibhatla M, Gottfried ON. Experience with intraoperative vancomycin powder for spinal deformity surgery. *Spine (Phila Pa 1976)* 2014; **39**: 177-184 [PMID: 24158179 DOI: 10.1097/BRS.0000000000000071]
- 54 **Molinari RW**, Khera OA, Molinari WJ 3rd. 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]
- 55 **Hill BW**, Emohare O, Song B, Davis R, Kang MM. The use of vancomycin powder reduces surgical reoperation in posterior instrumented and noninstrumented spinal surgery. *Acta Neurochir (Wien)* 2014; **156**: 749-754 [PMID: 24570187 DOI: 10.1007/s00701-014-2022-z]
- 56 **Ghobrial GM**, Thakkar V, Andrews E, Lang M, Chitale A, Oppenlander ME, Maulucci CM, Sharan AD, Heller J, Harrop JS, Jallo J, Prasad S. Intraoperative vancomycin use in spinal surgery: single institution experience and microbial trends. *Spine (Phila Pa 1976)* 2014; **39**: 550-555 [PMID: 24480966 DOI: 10.1097/BRS.0000000000000241]
- 57 **Kim HS**, Lee SG, Kim WK, Park CW, Son S. Prophylactic intraoperative application of vancomycin powder in instrumented spinal fusion surgery. *Korean J Spine* 2013; **10**: 121-125 [PMID: 24757472 DOI: 10.14245/kjs.2013.10.3.121]
- 58 **Gans I**, Dormans JP, Spiegel DA, Flynn JM, Sankar WN, Campbell RM, Baldwin KD. Adjunctive vancomycin powder in pediatric spine surgery is safe. *Spine (Phila Pa 1976)* 2013; **38**: 1703-1707 [PMID: 23759805 DOI: 10.1097/BRS.0b013e31829e05d3]
- 59 **Theologis AA**, Demirkiran G, Callahan M, Pekmezci M, Ames C, Deviren V. Local intraoperative vancomycin powder decreases the risk of surgical site infections in complex adult deformity reconstruction: a cost analysis. *Spine (Phila Pa 1976)* 2014; **39**: 1875-1880 [PMID: 25077909 DOI: 10.1097/BRS.0000000000000533]
- 60 **Kanj WW**, Flynn JM, Spiegel DA, Dormans JP, Baldwin KD. Vancomycin prophylaxis of surgical site infection in clean orthopedic surgery. *Orthopedics* 2013; **36**: 138-146 [PMID: 2379827 DOI: 10.3928/01477447-20130122-10]
- 61 **Chainuvati T**, Poovorawan Y, Luengrojankul P. The prevalence of hepatitis C virus antibody in high risk group of Thai children and adults. *Gastroenterol Jpn* 1991; **26** Suppl 3: 176-178 [PMID: 1909262 DOI: 10.1097/BRS.0b013e3181895939]
- 62 **Takahashi H**, Wada A, Iida Y, Yokoyama Y, Katori S, Hasegawa K, Shintaro T, Suguro T. Antimicrobial prophylaxis for spinal surgery. *J Orthop Sci* 2009; **14**: 40-44 [PMID: 19214686 DOI: 10.1007/s00776-008-1296-5]
- 63 **Bhandari M**, Adili A, Schemitsch EH. The efficacy of low-pressure lavage with different irrigating solutions to remove adherent bacteria from bone. *J Bone Joint Surg Am* 2001; **83-A**: 412-419 [PMID: 11263646 DOI: 10.2106/00004623-200103000-00014]
- 64 **Yazdi H**, Moradi A, Herbot M. The effect of gentamicin in irrigating solutions on articular infection prophylaxis during arthroscopic ACL reconstruction. *Arch Orthop Trauma Surg* 2014; **134**: 257-261 [PMID: 24323062 DOI: 10.1007/s00402-013-1910-7]
- 65 **Brown NM**, Cipriano CA, Moric M, Sporer SM, Della Valle CJ. Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. *J Arthroplasty* 2012; **27**: 27-30 [PMID: 21550765 DOI: 10.1016/j.arth.2011.03.034]
- 66 **Chang FY**, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Can povidone-iodine solution be used safely in a spinal surgery? *Eur Spine J* 2006; **15**: 1005-1014 [PMID: 16133077 DOI: 10.1007/s00586-005-0975-6]
- 67 **Cheng MT**, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH.

Elgafy H *et al.*. Ten step protocol to decrease postoperative spinal wound infections

Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. *Spine* (Phila Pa 1976) 2005; **30**: 1689-1693 [PMID: 16094267 DOI: 10.1097/01.brs.0000171907.60775.85]

68 **Savage JW**, Weatherford BM, Sugrue PA, Nolden MT, Liu JC, Song JK, Haak MH. Efficacy of surgical preparation solutions in lumbar spine surgery. *J Bone Joint Surg Am* 2012; **94**: 490-494 [PMID: 22437997 DOI: 10.2106/JBJS.K.00471]

**P- Reviewer:** Emara KM, Malik H, Recnik G **S- Editor:** Cui LJ  
**L- Editor:** A **E- Editor:** Wu YXJ





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



# World Journal of *Orthopedics*

*World J Orthop* 2018 December 18; 9(12): 285-303





**ORIGINAL ARTICLE**

**Retrospective Study**

- 285 Socio-demographic factors impact time to discharge following total knee arthroplasty  
*Ihekweazu UN, Sohn GH, Laughlin MS, Goytia RN, Mathews V, Stocks GW, Patel AR, Brinker MR*

**Observational Study**

- 292 Humeral retroversion and shoulder muscle changes in infants with internal rotation contractures following brachial plexus birth palsy  
*van de Bunt F, Pearl ML, van Essen T, van der Sluijs JA*

**CASE REPORT**

- 300 Metallosis following a clip breakage in a total knee arthroplasty implant: A case report  
*Saad AI, Shahban SA, Fernandes R*

**ABOUT COVER**

Editorial Board Member of *World Journal of Orthopedics*, Jian-Min Li, MD, Doctor, Professor, Surgeon, Department of Orthopedics, Qilu Hospital, Shandong University, Jinan 250012, Shandong Province, China

**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 abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), China National Knowledge Infrastructure (CNKI), and Superstar Journals Database.

**EDITORS FOR THIS ISSUE**

**Responsible Assistant Editor:** *Xiang Li*  
**Responsible Electronic Editor:** *Ying-Na Bian*  
**Proofing Editor-in-Chief:** *Lian-Sheng Ma*

**Responsible Science Editor:** *Ying Dou*  
**Proofing Editorial Office Director:** *Jin-Lei Wang*

**NAME OF JOURNAL**  
*World Journal of Orthopedics*

**ISSN**  
 ISSN 2218-5836 (online)

**LAUNCH DATE**  
 November 18, 2010

**FREQUENCY**  
 Monthly

**EDITOR-IN-CHIEF**  
**Bao-Gan Peng, MD, PhD, Professor**, Department of Spinal Surgery, General Hospital of Armed Police Force, Beijing 100039, China

**EDITORIAL BOARD MEMBERS**  
 All editorial board members resources online at <http://www.wjgnet.com/2218-5836/editorialboard.htm>

**EDITORIAL OFFICE**  
 Jin-Lei Wang, Director

*World Journal of Orthopedics*  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
 Help Desk: <http://www.f0publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLISHER**  
 Baishideng Publishing Group Inc  
 7901 Stoneridge Drive,  
 Suite 501, Pleasanton, CA 94588, USA  
 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
 Help Desk: <http://www.f0publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
 December 18, 2018

**COPYRIGHT**  
 © 2018 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.f0publishing.com>

Retrospective Study

## Socio-demographic factors impact time to discharge following total knee arthroplasty

Ugonna N Ihekweazu, Garrett H Sohn, Mitzi S Laughlin, Robin N Goytia, Vasilios Mathews, Gregory W Stocks, Anay R Patel, Mark R Brinker

Ugonna N Ihekweazu, Robin N Goytia, Vasilios Mathews, Gregory W Stocks, Anay R Patel, Mark R Brinker, Fondren Orthopedic Group, Houston, TX 77030, United States

Ugonna N Ihekweazu, Mitzi S Laughlin, Robin N Goytia, Vasilios Mathews, Gregory W Stocks, Anay R Patel, Mark R Brinker, Fondren Orthopedic Research Institute, Fondren Orthopedic Group, Houston, TX 77030, United States

Garrett H Sohn, Department of Orthopedic Surgery, Baylor College of Medicine, Houston, TX 77030, United States

ORCID number: Ugonna N Ihekweazu (0000-0002-6884-2197); Garrett H Sohn (0000-0002-3202-9671); Mitzi S Laughlin (0000-0002-6963-7144); Robin N Goytia (0000-0002-9781-7628); Vasilios Mathews (0000-0002-1862-4124); Gregory W Stocks (0000-0002-2943-5548); Anay R Patel (0000-0001-9183-4905); Mark R Brinker (0000-0001-7140-1635).

**Author contributions:** Ihekweazu UN, Goytia RN, Mathews V, Stocks GW, Patel AR and Brinker MR contributed to the study conception and design; Ihekweazu UN, Goytia RN, Mathews V, Stocks GW and Patel AR contributed to the data acquisition and data interpretation; Laughlin MS contributed the data analysis, data interpretation and preparation of the tables and figures; Ihekweazu UN, Sohn GH and Laughlin MS contributed to the literature review and the writing of the article; all authors have approved this manuscript prior to submission and believe that this manuscript represents honest work.

**Institutional review board statement:** This study was evaluated and an IRB exemption was given for this work by the Texas Orthopedic Hospital's IRB (TOH203e).

**Informed consent statement:** Patients were not required to give informed consent to the study because the analysis used anonymous clinical data and the study was given an IRB exemption.

**Conflict-of-interest statement:** All authors declare no conflicts-of-interest related to this article but the following authors have financial relationships to report in general: Robin Goytia reports personal fees from Innomed, outside the submitted work;

Gregory Stocks reports stock ownership from Nimbic Systems, Inc., outside the submitted work; Mark Brinker reports personal fees from Zimmer Biomet, outside the submitted 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/>

**Manuscript source:** Unsolicited manuscript

**Corresponding author to:** Mitzi S Laughlin, PhD, Senior Researcher, Chief Scientist, Fondren Orthopedic Research Institute, Fondren Orthopedic Group, 7401 S. Main, Houston, TX 77030, United States. [mitzi.laughlin@fondren.com](mailto:mitzi.laughlin@fondren.com)  
Telephone: +1-713-7943408

**Received:** October 4, 2018

**Peer-review started:** October 4, 2018

**First decision:** October 29, 2018

**Revised:** November 6, 2018

**Accepted:** December 10, 2018

**Article in press:** December 10, 2018

**Published online:** December 18, 2018

### Abstract

#### AIM

To determine social, logistical and demographic factors that influence time to discharge in a short stay pathway (SSP) by following total knee arthroplasty (TKA).

#### METHODS

The study included primary TKA's performed in a high-volume arthroplasty center from January 2016 through

December 2016. Potential variables associated with increased hospital length of stay (LOS) were obtained from patient medical records. These included age, gender, race, zip code, body mass index (BMI), number of pre-operative medications used, number of narcotic medications used, number of patient reported allergies (PRA), simultaneous bilateral surgery, tobacco use, marital status, living arrangements, distance traveled for surgery, employment history, surgical day of the week, procedure end time and whether the surgery was performed during a major holiday week. Multivariate step-wise regression determined the impact of social, logistical and demographic factors on LOS.

### RESULTS

Eight hundred and six consecutive primary SSP TKA's were included in this study. Patients were discharged at a median of 49 h (post-operative day two). The following factors increased LOS: Simultaneous bilateral TKA [46.1 h longer ( $P < 0.001$ )], female gender [4.3 h longer ( $P = 0.012$ )], age [3.5 h longer per ten-year increase in age ( $P < 0.001$ )], patient-reported allergies [1.1 h longer per allergy reported ( $P = 0.005$ )], later procedure end-times [0.8 h longer per hour increase in end-time ( $P = 0.004$ )] and Black or African American patients [6.1 h longer ( $P = 0.047$ )]. Decreased LOS was found in married patients [4.8 h shorter ( $P = 0.011$ )] and TKA's performed during holiday weeks [9.4 h shorter ( $P = 0.011$ )]. Non-significant factors included: BMI, median income, patient's living arrangement, smoking status, number of medications taken, use of pre-operative pain medications, distance traveled to hospital, and the day of surgery.

### CONCLUSION

The cost of TKA is dependent upon LOS, which is affected by multiple factors. The clinical care team should acknowledge socio-demographic factors to optimize LOS.

**Key words:** Total knee replacement; Total knee arthroplasty; Cost; Risk factors; Length of stay

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** In an effort to decrease post-operative length of stay (LOS), many institutions continue to develop optimal discharge pathways. Since LOS is dependent upon many variables, we sought to define which socio-demographic factors influence LOS in total knee arthroplasty (TKA). Six factors were found to increase LOS: Age, gender, Black or African American race, simultaneous bilateral TKA, later procedure end times and number of PRA. Two factors decreased LOS, patient being married and surgery during a major public holiday week. While none of the patient specific factors are modifiable by the clinician, we do have the ability to optimize surgical schedule and allocation of resources.

Ihekweazu UN, Sohn GH, Laughlin MS, Goytia RN, Mathews V, Stocks GW, Patel AR, Brinker MR. Socio-demographic factors impact time to discharge following total knee arthroplasty. *World J Orthop* 2018; 9(12): 285-291

URL: <https://www.wjgnet.com/2218-5836/full/v9/i12/285.htm>

DOI: <https://dx.doi.org/10.5312/wjo.v9.i12.285>

## INTRODUCTION

Increased utilization of total joint arthroplasty (TJA) is expected to result in a pronounced economic burden on the United States health care system<sup>[1]</sup>. Subsequently, cost reductions even at the individual case level can translate into a substantial cost savings to the overall system<sup>[2]</sup>. In-hospital length of stay (LOS) has been shown to directly influence the total cost of joint arthroplasty when patients are discharged home<sup>[3,4]</sup>. Since LOS is a modifiable cost factor, increased focus has been placed on implementing measures that aim to discharge patients from the hospital as soon as safely possible. The recent development of short stay pathways is a direct result of advancements in surgical, anesthetic and rehabilitation techniques. While there are concerns regarding the overall safety of short stay pathways (SSP) compared to conventional postoperative pathway (CPP), the literature suggests that drastic reductions in LOS can be accomplished without increasing complication rates<sup>[5]</sup>.

Factors influencing LOS such as age, gender and perioperative complications have been previously described in the literature under CPP for hip and knee arthroplasty<sup>[6,7]</sup>. At the earliest, patients in these CPP studies were discharged on the 3<sup>rd</sup> day following surgery<sup>[6-8]</sup>. Keswani *et al*<sup>[8]</sup> found that patients with later surgical start times and end of the week procedure days (Thursday and Friday) had longer LOS in a CPP. However, a separate study performed at an institution utilizing a SSP found that surgical day of the week had no correlation with LOS<sup>[9]</sup>. Another institution utilizing SSP investigated the influence of preoperative patient characteristics and perioperative surgical factors related to prolonged LOS<sup>[10,11]</sup>. Regardless there remains limited data on the factors influencing LOS following TKA in a SSP.

The primary purpose of this study was to assess the influence of social, logistical and demographic factors on time to discharge in a SSP for TKA. The findings from this study may further enhance preoperative and perioperative risk stratification models that already incorporate patient characteristics and perioperative surgical factors but neglect other potentially influential variables.

## MATERIALS AND METHODS

### Methods

A retrospective chart review was performed for a consecutive series of 806 elective primary TKA's performed at a single specialty hospital from January

2016 to December 2016. All procedures were performed by one of 3 experienced surgeons, each performing more than 250 TKAs per year. All surgeries, regardless of LOS, were performed using the hospital's SSP for each phase of care. This study was evaluated and an Institutional Review Board (IRB) exemption was given for this work by the Texas Orthopedic Hospital IRB (TOH203e).

### Short stay protocol

All patients at this institution undergo a formal pre-operative screening process to ensure they are safe for surgery and postoperative care within our specialty hospital. Active renal replacement therapy, active lung disease requiring home oxygen support, or active cardiac disease requiring a defibrillator exclude the patient from surgery at this institution. Each patient is medicated preoperatively with celecoxib 200 mg, Neurontin 100 mg, and acetaminophen 650 mg. Intra-operative anesthesia consists of a propofol infusion with no inhalation anesthetic and no muscle relaxation. During the procedure a periarticular anesthetic of weight-based ropivacaine 0.5% and morphine 5-10 mg is injected into the soft tissues prior to closure. All patients are given 1 g intravenous (IV) tranexamic acid prior to incision and 1 gram prior to closure, unless it is contraindicated, at which point it is administered topically. Post-operative medication regimen consists of a combination of hydrocodone, tramadol, methocarbamol, dexamethasone and IV ketorolac. Deep vein thrombosis prophylaxis consists of aspirin or rivaroxaban per surgeon discretion and is continued for 4 wk. Patients are mobilized approximately 2 h after surgery with physical therapists. Standing is attempted, and if tolerated, patients are allowed to walk with a walker and assistance as far as they can tolerate. Continuous passive motion devices were used during the study period per surgeon discretion. The following morning patients undergo their second session with the physical therapists. The three surgeons included in this study independently round on their patients on all days, including weekends and holidays. Patients were discharged as soon as they had adequate oral pain control, are safe to ambulate and mobilize with an assistive device and are hemodynamically stable.

### Study outcomes

Potential variables associated with increased hospital LOS were obtained from patient medical records. These included age, gender, race, zip code, body mass index (BMI), number of pre-operative medications used, number of narcotic medications used, number of patient reported allergies (PRA), simultaneous bilateral surgery, tobacco use, marital status, living arrangements, distance traveled for surgery, employment history, surgical day of the week, procedure end time and whether the surgery was performed during a major holiday week. Thanksgiving, Christmas and New Year's Eve were the major holidays included in the study. The patient's zip

code was used to obtain the median household income of the zip code from the 2016 American Community Survey performed by the United States Census Bureau<sup>[12]</sup>.

Baseline demographics, surgical factors, and social factors were summarized by mean ( $\pm$  SD) for continuous factors or by count and percentages for categorical factors in order to characterize the study population. Multivariate regression analysis was performed to determine the contribution of demographic, logistical and social factors on LOS. A stepwise model was used to determine the number of factors significantly associated with LOS. Statistical significance was defined as  $P < 0.05$  and SPSS 24 (IBM Corp., Armonk, NY, United States) was used for statistical analyses.

## RESULTS

A total of 806 primary TKA cases were included in the study. There were 491 female (60.9%) patients and the average age of the study population was 64.5 years. 76.6% of the study population were identified as White, 11.4% as other, 7.8% black/African American, 2.2% identified as Asian and 1.9% declined to state. The median LOS was 49.0 h with a range from 18-236 h. All subject characteristics that were included in the analysis are depicted in Table 1.

In our study population, the constant (or baseline regression model) for LOS was 22.7 h ( $P = 0.004$ ). Adding or subtracting beta coefficients for other factors predicts individual patient LOS. Multiple regression identified six factors that increased LOS (Table 2): Simultaneous bilateral TKA [46.1 h longer ( $P < 0.001$ )], female gender [4.3 h longer ( $P = 0.012$ )], age [3.5 h longer per ten-year increase in age ( $P < 0.001$ )], number of PRA's [1.1 h longer per each reported number of allergies ( $P = 0.005$ )], later procedure end-times [0.8 h longer per hour increase in end-time ( $P = 0.040$ )] and Black or African American patients [6.1 h longer ( $P = 0.047$ )]. Two factors were found to decrease LOS: Patients being married [4.8 h shorter ( $P = 0.011$ )] and TKAs performed during major holiday weeks [9.4 h shorter ( $P = 0.011$ )]. Non-significant factors included: BMI, median income, patient's living arrangement, smoking status, number of medications taken, use of pre-operative pain medications, distance traveled to hospital, and the day of surgery.

## DISCUSSION

LOS is a modifiable cost factor in the overall expense of TJA. Increased emphasis has been placed on both employing SSP and optimizing risk stratification models that identify those who may or may not be appropriate candidates for SSP. Our study identified simultaneous bilateral TKA, female gender, increased age, increased number of PRA, later surgery end time and race identified as Black or African American as factors that increased LOS. Two factors, patient being married and procedures

**Table 1** Baseline subject characteristics

Factor	mean $\pm$ SD or <i>n</i> (%)
Number of patients	806
Gender	
Male	315 (39.1)
Female	491 (60.9)
Age (yr)	64.5 $\pm$ 8.5
Race	
Asian	18 (2.2)
Black/African American	63 (7.8)
White	617 (76.6)
Other	94 (11.4)
Decline to state	16 (1.9)
Body mass index	33.81 $\pm$ 7.4
Employed	347 (43.1)
Median income by zip code	\$66586 $\pm$ 25562
Marital Status	
Single	105 (13.0)
Married	593 (73.6)
Widow/widower	66 (8.2)
Divorced	42 (5.2)
Patient lives alone (Y)	99 (12.3)
Smoker	
Current	68 (8.4)
Former	232 (28.8)
Never	506 (62.8)
Number of allergies	1.5 $\pm$ 2.2
Number of medications	6.1 $\pm$ 4.8
Pre-operative pain meds (Y)	108 (13.4)
Simultaneous bilateral total knee arthroplasty	37 (4.6)
Distance from hospital (miles)	61.95 $\pm$ 122.8
Day of surgery	
Monday	242 (30.0)
Tuesday	175 (21.7)
Wednesday	129 (16.0)
Thursday	194 (24.1)
Friday	61 (7.6)
Saturday	5 (0.6)
Holiday week surgery	43 (5.3)
Surgery end time (h:min)	11:05 $\pm$ 2:22

performed during major holiday weeks decreased LOS.

Increased age and female gender are factors that are known to correlate with increased LOS in SSP<sup>[11,13]</sup>. Both simultaneous bilateral TKA<sup>[14]</sup> and patient identified race as non-Caucasian<sup>[15]</sup> have been shown to increase LOS in CPP as well as SSP. Our data showed that patients identifying as Black or African American had a significantly longer LOS after TKA, while other racial groups (White and Other) showed no difference in LOS. Racial disparities in utilization, complication rates and outcomes of arthroplasty are prevalent in the literature<sup>[15-17]</sup>, however, race is often confounded with socioeconomic factors. In our study, Black patients had a longer LOS but median household income was not a significant factor influencing LOS. Further analysis showed that the median income of Black patients in our study was just over \$41000 while both White and Other patients was over \$60000 (Figure 1). According to the American Community Survey the median income for the United States in 2016 was \$55322<sup>[12]</sup>, so in our patient population Black patients were well under the United States median income while White and Other

patients were slightly above. Thus, increased LOS in Black patients may not be entirely due to race, as socioeconomic factors may also be confounded by race. Future studies will need to further define the complex relationships between race, socioeconomic status, perioperative outcomes and LOS in TJA.

To our knowledge, marital status has not previously been shown to demonstrate any influence on LOS following TKA. While limited, the literature outside of orthopedics suggests that being married may be associated with better treatment outcomes<sup>[18,19]</sup>. However, marital status has been shown to affect outcomes following TKA as patients that are married have better overall outcomes following TKA<sup>[20]</sup>. In our study, married patients had a decreased postoperative LOS. Our findings corroborate the general trend in the literature, with a positive association between being married and improved treatment outcomes. Notably, marital status has recently been identified as a key variable that should be investigated in future research on outcomes of knee and hip surgery<sup>[21]</sup>.

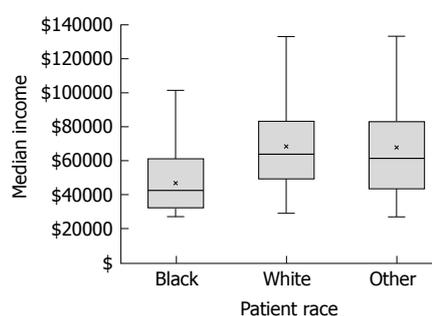
Prior studies indicate that increasing amounts of PRA's is associated with worse outcomes following total hip and knee arthroplasty<sup>[22-24]</sup>. Interestingly, the patient reported "allergy" is often a misnomer as only 15% of PRA's studied in a community hospital setting represented a true IgE mediate hypersensitivity reaction<sup>[25]</sup>. In a study utilizing data from the Canadian Community Health registry, an association between mood and anxiety disorders and PRA reporting was demonstrated<sup>[26]</sup>. As the relationship between PRA and psychiatric disorders is further elucidated, their impact on all aspects of TJA is becoming more apparent. In a prospective study of 446 patients undergoing primary hip and knee arthroplasty, Otero *et al*<sup>[22]</sup> found that patients reporting at least 1 allergy had significantly lower postoperative SF-36 physical component score compared to those reporting no allergies. In a retrospective review, McLawhorn *et al*<sup>[23]</sup> demonstrated that increasing number of PRA's was associated with both worse satisfaction and Western Ontario and McMaster Universities Arthritis Index scores, in addition to increased LOS following TKA in a CPP. The median LOS of the patients included in their TKA cohort was 4.0 d. Our study found that for each reported allergy, LOS increased by 0.8 h. While this may seem to be an insignificant amount of time, it is not uncommon to encounter patients with many PRA's in practice; in our study, one patient reported twenty-three. In an SSP, increasing the LOS by just a few hours may represent the difference in an additional day spent in the hospital.

The relationship between surgical day of the week and LOS has previously been studied in both CPP and SSP. In separate retrospective reviews, both Muppavarapu *et al*<sup>[27]</sup> and Keswani *et al*<sup>[8]</sup> found that patients who underwent TJA or total hip arthroplasty (THA) respectively, on Thursday or Friday had significantly longer hospital LOS compared to patients undergoing those procedures earlier in the week. These two studies represented a CPP as the LOS of the patients included these studies was

**Table 2** Significant factors predicting length of stay

Factor	Beta coefficient (h) <sup>1</sup>	Std. error	P value
Constant	22.7	7.8	0.004
Simultaneous bilateral total knee arthroplasty	46.1	4.1	< 0.001
Gender (female)	4.3	1.7	0.012
Age (per 10 yr)	3.5	1.0	< 0.001
Patient is married	-4.8	1.9	0.011
Number of allergies	1.1	0.4	0.005
Holiday week surgery	-9.4	3.6	0.011
Surgery end time	0.8	0.4	0.040
Black/African American	6.1	3.0	0.047

<sup>1</sup>In our study population, the constant for length of stay (LOS) was 22.7 h. Adding or subtracting beta coefficients for other factors predicts individual patient LOS.



**Figure 1** Median income level by race with the bold horizontal line representing the median, the box shows the 25% to 75% range, the x is the mean and the whiskers represent the entire range of the data.

greater than 3 d. A comprehensive PubMed search found only one study that investigates the effect of surgical day of the week on LOS in an SSP for total joint arthroplasty. In a cohort of patients with an average LOS of < 2 d, Edwards *et al*<sup>[9]</sup> found that surgical day of the week did not influence time to discharge. Our results were similar as surgical day of the week did not influence LOS in our SSP. These findings suggest that as LOS decreases the overall impact of performing a procedure towards the end of the week may diminish.

The influence of surgical start time on LOS has been investigated across several surgical subspecialties with the evidence suggesting that as cases begin later in the day, LOS increases<sup>[28,29]</sup>. Earnest *et al*<sup>[28]</sup> suspected that initial post-operative care is delayed for patients admitted in the afternoon because clinical workup and management usually occurs in the morning. Only one study has investigated the influence of surgical timing on LOS in total joint arthroplasty. In a cohort of THA patients receiving conventional postoperative care pathways, Keswani *et al*<sup>[8]</sup> found that procedures starting after 2 PM were associated with longer LOS compared to procedures starting prior to 2 PM. We found that LOS was slightly shorter for every hour later the procedure ended. In our institution's SSP, post-operative protocols do not depend on the time of day as staffing is consistent between shifts. Patients are encouraged to work with a physical therapist just a few hours after surgery when clinically feasible. Our findings suggest that unlike CPP, in SSP the

surgical start time of the procedure is less critical.

The relationship between public holidays and LOS across all medical fields has never been reported, a few studies have sought to understand the influence of holidays on clinical outcomes and readmission<sup>[30-32]</sup>. In our study, patients undergoing TKA during major public holiday weeks were found to have decreased LOS as compared to patients having surgery during a normal week. Several factors likely influence these findings including patient, surgeon and staff related variables. As our study included three surgeons, the most senior surgeon performed fewer procedures during holiday weeks and also had a slightly higher LOS average, possibly confounding the lower LOS holiday week results. While these results do leave room for speculation, the present study could not delineate any additional conclusions from these findings; therefore this is an area that future studies should consider investigating further.

Our study had several limitations. First, the data used was retrospectively collected and therefore susceptible to inherent bias in its analysis. Secondly, race identification was limited to what was reported in the chart and the 'other' classification likely encompassed a variety of distinct ethnicities that could not be further discerned. Third, there was potential for type II statistical error as certain variables approached but did not reach significance in this study. As it pertains to LOS, several variables that were originally thought to be relevant factors were not. In particular, distance traveled and pre-operative narcotic use did not reach significance in our cohort.

In an effort to decrease post-operative LOS, many institutions continue to develop optimal discharge pathways following TKA. Since LOS is dependent upon many variables, we sought to define which social, logistical and demographic factors influence LOS in TKA. Six factors were found to increase LOS in a SSP: Age, gender, Black or African American race, simultaneous bilateral TKA, later procedure end times and number of PRA's. Two factors decreased LOS in an SSP, patient being married and surgery during a major public holiday week. While none of the patient specific factors (*e.g.*, age, race, gender, marital status, socioeconomic status,

and PRA's) are modifiable by the clinician, we do have the ability to optimize surgical schedule and allocation of resources. When refining predictive models for LOS, in addition to considering known clinical factors, the care team should also appreciate the extent that social, demographic and logistical factors influence LOS. Furthermore, the influence of these factors may depend on whether a CPP or an SSP model is being employed.

## ARTICLE HIGHLIGHTS

### Research background

Time to discharge or in-hospital length of stay (LOS) has been shown to directly influence the total cost of joint arthroplasty when patients are discharged home. Since LOS is a modifiable cost factor, increased focus has been placed on implementing measures that aim to discharge patients from the hospital as soon as safely possible. The recent development of short stay pathways is a direct result of advancements in surgical, anesthetic and rehabilitation techniques. Traditional factors such as age, gender, comorbidities and perioperative complications have been studied extensively and influence LOS. Patient social, logistical and demographic factors are non-modifiable factors but potentially influence LOS.

### Research motivation

The motivation behind this research was to further improve short stay pathways by evaluating non-traditional factors that potentially could influence LOS. Our hypothesis was that social, logistical and demographic factors influence LOS following total knee arthroplasty (TKA) in a short stay pathway.

### Research objectives

The primary purpose of this study was to assess the influence of social, logistical and demographic factors on time to discharge in a short stay pathway following TKA. The findings from this study may further enhance preoperative and perioperative risk stratification models that already incorporate patient characteristics and perioperative surgical factors but neglect other potentially influential variables.

### Research methods

A retrospective chart review was performed for a consecutive series of 806 elective primary TKA's performed at a single specialty hospital from January 2016 to December 2016. Potential variables associated with increased hospital LOS were obtained from patient medical records. These included age, gender, race, zip code, body mass index (BMI), number of pre-operative medications used, number of narcotic medications used, number of patient reported allergies (PRA), simultaneous bilateral surgery, tobacco use, marital status, living arrangements, distance traveled for surgery, employment history, surgical day of the week, procedure end time and whether the surgery was performed during a major holiday week. Thanksgiving, Christmas and New Year's Eve were the major holidays included in the study. Baseline demographics, surgical factors, and social factors were summarized by mean ( $\pm$  SD) for continuous factors or by count and percentages for categorical factors in order to characterize the study population. Multivariate regression analysis was performed to determine the contribution of demographic, logistical and social factors on LOS.

### Research results

Patients were discharged at a median of 49 h (post-operative day two). Six factors increased LOS: Simultaneous bilateral TKA, female gender, age, patient-reported allergies, later procedure end-times, and Black or African American patients. Decreased LOS was found in married patients and TKA's performed during holiday weeks. Non-significant factors included: BMI, median income, patient's living arrangement, smoking status, number of medications taken, use of pre-operative pain medications, distance traveled to hospital, and the day of surgery.

### Research conclusions

The cost of TKA is dependent upon LOS, which is affected by multiple factors.

The clinical care team should acknowledge socio-demographic factors to further optimize short stay pathways and decrease LOS.

### Research perspectives

In an effort to decrease post-operative LOS, many institutions continue to develop optimal discharge pathways following TKA. Since LOS is dependent upon many variables, we sought to define which social, logistical and demographic factors influence LOS in TKA. Six factors were found to increase LOS in a short stay pathway: Age, gender, Black or African American race, simultaneous bilateral TKA, later procedure end times and number of PRA's. Two factors decreased LOS: Patient being married and surgery during a major public holiday week. While none of the patient specific factors (*e.g.*, age, race, gender, marital status, socioeconomic status, and PRA's) are modifiable by the clinician, we do have the ability to optimize surgical schedule and allocation of resources. When refining predictive models for LOS, in addition to considering known clinical factors, the care team should also appreciate the extent that social, demographic and logistical factors influence LOS.

## 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 **Teeny SM**, York SC, Benson C, Perdue ST. Does shortened length of hospital stay affect total knee arthroplasty rehabilitation outcomes? *J Arthroplasty* 2005; **20**: 39-45 [PMID: 16214001 DOI: 10.1016/j.arth.2005.04.025]
- 3 **Cram P**, Lu X, Kates SL, Singh JA, Li Y, Wolf BR. Total knee arthroplasty volume, utilization, and outcomes among Medicare beneficiaries, 1991-2010. *JAMA* 2012; **308**: 1227-1236 [PMID: 23011713 DOI: 10.1001/2012.jama.11153]
- 4 **Meyers SJ**, Reuben JD, Cox DD, Watson M. Inpatient cost of primary total joint arthroplasty. *J Arthroplasty* 1996; **11**: 281-285 [PMID: 8713907 DOI: 10.1016/S0883-5403(96)80079-9]
- 5 **Stambough JB**, Nunley RM, Curry MC, Steger-May K, Clohisy JC. Rapid recovery protocols for primary total hip arthroplasty can safely reduce length of stay without increasing readmissions. *J Arthroplasty* 2015; **30**: 521-526 [PMID: 25683296 DOI: 10.1016/j.arth.2015.01.023]
- 6 **Rissanen P**, Aro S, Paavolainen P. Hospital- and patient-related characteristics determining length of hospital stay for hip and knee replacements. *Int J Technol Assess Health Care* 1996; **12**: 325-335 [PMID: 8707504 DOI: 10.1017/S0266462300009661]
- 7 **Forrest G**, Fuchs M, Gutierrez A, Girardy J. Factors affecting length of stay and need for rehabilitation after hip and knee arthroplasty. *J Arthroplasty* 1998; **13**: 186-190 [PMID: 9526212 DOI: 10.1016/S0883-5403(98)90097-3]
- 8 **Keswani A**, Beck C, Meier KM, Fields A, Bronson MJ, Moucha CS. Day of Surgery and Surgical Start Time Affect Hospital Length of Stay After Total Hip Arthroplasty. *J Arthroplasty* 2016; **31**: 2426-2431 [PMID: 27491449 DOI: 10.1016/j.arth.2016.04.013]
- 9 **Edwards PK**, Hadden KB, Connelly JO, Barnes CL. Effect of Total Joint Arthroplasty Surgical Day of the Week on Length of Stay and Readmissions: A Clinical Pathway Approach. *J Arthroplasty* 2016; **31**: 2726-2729 [PMID: 27378632 DOI: 10.1016/j.arth.2016.05.057]
- 10 **Sibia US**, King PJ, MacDonald JH. Who Is Not a Candidate for a 1-Day Hospital-Based Total Knee Arthroplasty? *J Arthroplasty* 2017; **32**: 16-19 [PMID: 27491443 DOI: 10.1016/j.arth.2016.06.055]
- 11 **Sibia US**, MacDonald JH, King PJ. Predictors of Hospital Length of Stay in an Enhanced Recovery After Surgery Program for Primary Total Hip Arthroplasty. *J Arthroplasty* 2016; **31**: 2119-2123 [PMID: 27067175 DOI: 10.1016/j.arth.2016.02.060]
- 12 **U.S. Census Bureau**. American Community Survey, 2016 [cited 20 April 2018]. Detailed tables [Internet]. Available from: URL: [https://factfinder.census.gov/faces/nav/jsf/pages/community\\_facts.xhtml](https://factfinder.census.gov/faces/nav/jsf/pages/community_facts.xhtml)
- 13 **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]
- 14 **Suleiman LI**, Edelstein AI, Thompson RM, Alvi HM, Kwasny MJ, Manning DW. Perioperative Outcomes Following Unilateral Versus Bilateral Total Knee Arthroplasty. *J Arthroplasty* 2015; **30**: 1927-1930 [PMID: 26072300 DOI: 10.1016/j.arth.2015.05.039]
  - 15 **Inneh IA**. The Combined Influence of Sociodemographic, Preoperative Comorbid and Intraoperative Factors on Longer Length of Stay After Elective Primary Total Knee Arthroplasty. *J Arthroplasty* 2015; **30**: 1883-1886 [PMID: 26044998 DOI: 10.1016/j.arth.2015.05.032]
  - 16 **Martsof GR**, Barrett ML, Weiss AJ, Kandrack R, Washington R, Steiner CA, Mehrotra A, SooHoo NF, Coffey R. Impact of Race/Ethnicity and Socioeconomic Status on Risk-Adjusted Hospital Readmission Rates Following Hip and Knee Arthroplasty. *J Bone Joint Surg Am* 2016; **98**: 1385-1391 [PMID: 27535441 DOI: 10.2106/JBJS.15.00884]
  - 17 **Singh JA**, Lu X, Rosenthal GE, Ibrahim S, Cram P. Racial disparities in knee and hip total joint arthroplasty: an 18-year analysis of national Medicare data. *Ann Rheum Dis* 2014; **73**: 2107-2115 [PMID: 24047869 DOI: 10.1136/annrheumdis-2013-203494]
  - 18 **Franks MM**, Stephens MA, Rook KS, Franklin BA, Keteyian SJ, Artinian NT. Spouses' provision of health-related support and control to patients participating in cardiac rehabilitation. *J Fam Psychol* 2006; **20**: 311-318 [PMID: 16756407 DOI: 10.1037/0893-3200.20.2.311]
  - 19 **Aizer AA**, Chen MH, McCarthy EP, Mendu ML, Koo S, Wilhite TJ, Graham PL, Choueiri TK, Hoffman KE, Martin NE, Hu JC, Nguyen PL. Marital status and survival in patients with cancer. *J Clin Oncol* 2013; **31**: 3869-3876 [PMID: 24062405 DOI: 10.1200/JCO.2013.49.6489]
  - 20 **Roubion RC**, Fox RS, Townsend LA, Pollock GR, Leonardi C, Dasa V. Does Marital Status Impact Outcomes After Total Knee Arthroplasty? *J Arthroplasty* 2016; **31**: 2504-2507 [PMID: 27240961 DOI: 10.1016/j.arth.2016.04.017]
  - 21 **Lieberman JR**, Teuscher D, Berry DJ, Vail TP. AAOS' comments on CMS' Comprehensive Care for Joint Replacement Payment Model for Acute Care Hospitals Furnishing Lower Extremity Joint Replacement Services Proposed Rule [CMS-5516-P]. 2015. Available from: URL: <https://innovation.cms.gov/initiatives/cjr>
  - 22 **Otero JE**, Graves CM, Gao Y, Olson TS, Dickinson CC, Chalus RJ, Vittetoe DA, Goetz DD, Callaghan JJ. Patient-Reported Allergies Predict Worse Outcomes After Hip and Knee Arthroplasty: Results From a Prospective Cohort Study. *J Arthroplasty* 2016; **31**: 2746-2749 [PMID: 27600302 DOI: 10.1016/j.arth.2016.07.040]
  - 23 **McLawhorn AS**, Bjerke-Kroll BT, Blevins JL, Sculco PK, Lee YY, Jerabek SA. Patient-Reported Allergies Are Associated With Poorer Patient Satisfaction and Outcomes After Lower Extremity Arthroplasty: A Retrospective Cohort Study. *J Arthroplasty* 2015; **30**: 1132-1136 [PMID: 25702595 DOI: 10.1016/j.arth.2015.01.043]
  - 24 **Graves CM**, Otero JE, Gao Y, Goetz DD, Willenborg MD, Callaghan JJ. Patient reported allergies are a risk factor for poor outcomes in total hip and knee arthroplasty. *J Arthroplasty* 2014; **29**: 147-149 [PMID: 25034881 DOI: 10.1016/j.arth.2014.02.040]
  - 25 **Chen CJ**, Cheng CF, Lin HY, Hung SP, Chen WC, Lin MS. A comprehensive 4-year survey of adverse drug reactions using a network-based hospital system. *J Clin Pharm Ther* 2012; **37**: 647-651 [PMID: 22646235 DOI: 10.1111/j.1365-2710.2012.01359.x]
  - 26 **Patten SB**, Williams JV. Self-reported allergies and their relationship to several Axis I disorders in a community sample. *Int J Psychiatry Med* 2007; **37**: 11-22 [PMID: 17645194 DOI: 10.2190/L811-0738-10NG-7157]
  - 27 **Muppavarapu RC**, Chaurasia AR, Schwarzkopf R, Matzkin EG, Cassidy CC, Smith EL. Total joint arthroplasty surgery: does day of surgery matter? *J Arthroplasty* 2014; **29**: 1943-1945 [PMID: 25015754 DOI: 10.1016/j.arth.2014.06.004]
  - 28 **Earnest A**, Chen MI, Seow E. Exploring if day and time of admission is associated with average length of stay among inpatients from a tertiary hospital in Singapore: an analytic study based on routine admission data. *BMC Health Serv Res* 2006; **6**: 6 [PMID: 16426459 DOI: 10.1186/1472-6963-6-6]
  - 29 **Slaughter KN**, Frumovitz M, Schmelzer KM, Nick AM, Fleming ND, dos Reis R, Munsell MF, Westin SN, Soliman PT, Ramirez PT. Minimally invasive surgery for endometrial cancer: does operative start time impact surgical and oncologic outcomes? *Gynecol Oncol* 2014; **134**: 248-252 [PMID: 24945591 DOI: 10.1016/j.ygyno.2014.06.007]
  - 30 **Sebghatollahi V**, Ghomi K, Tamizifar B, Minakari M, Khodadoustan M. The Relationship between the Time of Endoscopy and Morbidity and Mortality Rates in Patients with Upper Gastrointestinal Bleeding. *Adv Biomed Res* 2017; **6**: 81 [PMID: 28808647]
  - 31 **Orsini J**, Rajayer S, Ahmad N, Din N, Morante J, Malik R, Shim A. Effects of time and day of admission on the outcome of critically ill patients admitted to ICU. *J Community Hosp Intern Med Perspect* 2016; **6**: 33478 [PMID: 27987290 DOI: 10.3402/jchimp.v6.33478]
  - 32 **Richards MK**, Yanez D, Goldin AB, Grieb T, Murphy WM, Drugas GT. Factors associated with 30-day unplanned pediatric surgical readmission. *Am J Surg* 2016; **212**: 426-432 [PMID: 26924805 DOI: 10.1016/j.amjsurg.2015.12.012]

**P- Reviewer:** Fenichel I, Wu CC **S- Editor:** Ji FF **L- Editor:** A  
**E- Editor:** Bian YN



## Observational Study

## Humeral retroversion and shoulder muscle changes in infants with internal rotation contractures following brachial plexus birth palsy

Fabian van de Bunt, Michael L Pearl, Tom van Essen, Johannes A van der Sluijs

Fabian van de Bunt, Tom van Essen, Johannes A van der Sluijs, Department of Orthopedics, Amsterdam UMC, VU University Medical Center, Amsterdam 1081 HV, Netherlands

Michael L Pearl, Department of Shoulder and Elbow Surgery, Kaiser Permanente Medical Center, Los Angeles, Ca 90027, United States

ORCID number: Fabian van de Bunt (0000-0002-4169-0322); Michael L Pearl (0000-0003-3407-481X); Tom van Essen (0000-0001-9256-9269); Johannes A van der Sluijs (0000-0002-9879-8908).

**Authorship:** All authors made significant contributions to the manuscript, conforming to the standard proposed by the ICMJE.

**Author contributions:** van de Bunt F designed the study, and performed data collection, analysis and interpretation of data, writing of (the first draft) of the manuscript, critical evaluation of the intelligent content of the final version; Pearl ML designed the study and performed data interpretation, writing of the manuscript, critical evaluation of the intelligent content of the final version; van Essen T performed data collection, analysis and interpretation of data, writing of (the first draft) manuscript; van der Sluijs JA designed the study and performed data interpretation, writing of the manuscript, and critical evaluation of the intelligent content of the final version.

**Institutional review board statement:** We are pleased to confirm that the Medical Research Involving Human Subjects Act (WMO) does not apply to the above-mentioned study and that an official approval of this study by our committee is not required.

**Informed consent statement:** We received an IRB waiver from the Institutional review board since this was a retrospective observational study, utilizing MRI scans made strictly for clinical purposes. MRIs were all anonymized by the Radiology department before conducting our study. See the attached IRB statement.

**Conflict-of-interest statement:** The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants;

participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

**STROBE statement:** The authors have read the STROBE Statement-checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-checklist of items.

**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

**Corresponding author to:** Fabian van de Bunt, MD, MSc, Doctor, MD, Department of Orthopedics, Amsterdam UMC, VU University Medical Center, De Boelelaan 1117, Amsterdam 1081 HV, Netherlands. [fabianvdbunt@gmail.com](mailto:fabianvdbunt@gmail.com)  
Telephone: +31-64-8482593

Received: August 22, 2018  
Peer-review started: August 22, 2018  
First decision: October 4, 2018  
Revised: October 16, 2018  
Accepted: November 15, 2018  
Article in press: November 15, 2018  
Published online: December 18, 2018

### Abstract

#### AIM

To examine humeral retroversion in infants who sus-

tained brachial plexus birth palsy (BPBI) and suffered from an internal rotation contracture. Additionally, the role of the infraspinatus (IS) and subscapularis (SSc) muscles in the genesis of this bony deformation is explored.

### METHODS

Bilateral magnetic resonance imaging (MRI) scans of 35 infants (age range: 2-7 mo old) with BPBI were retrospectively analyzed. Retroversion was measured according to two proximal axes and one distal axis (transepicondylar axis). The proximal axes were: (1) the perpendicular line to the borders of the articular surface (humeral centerline); and (2) the longest diameter through the humeral head. Muscle cross-sectional areas of the IS and SSc muscles were measured on the MRI-slides representing the largest muscle belly. The difference in retroversion was correlated with the ratio of muscle-sizes and passive external rotation measurements.

### RESULTS

Retroversion on the involved side was significantly decreased,  $1.0^\circ$  vs  $27.6^\circ$  (1) and  $8.5^\circ$  vs  $27.2^\circ$  (2), ( $P < 0.01$ ), as compared to the uninvolved side. The size of the SSc and IS muscles on the involved side was significantly decreased,  $2.26 \text{ cm}^2$  vs  $2.79 \text{ cm}^2$  and  $1.53 \text{ cm}^2$  vs  $2.19 \text{ cm}^2$ , respectively ( $P < 0.05$ ). Furthermore, the muscle ratio (SSc/IS) at the involved side was significantly smaller compared to the uninvolved side ( $P = 0.007$ ).

### CONCLUSION

Even in our youngest patient population, humeral retroversion has a high likelihood of being decreased. Altered humeral retroversion warrants attention as a structural change in any child being evaluated for the treatment of an internal rotation contracture.

**Key words:** Humeral retroversion; Infants; Brachial plexus; Brachial plexus neuropathies; Shoulder; Humerus

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** This study examines humeral retroversion in infants who sustained neonatal brachial plexus palsy and suffered from an internal rotation contracture. The existing common treatment options all strive for better function of the upper extremity through an improved position of the hand in space. Therefore, a thorough understanding of the development of the pathogenesis of this injury is important. We found a significant reduction of humeral retroversion in our study group (mean difference, 26.8). When treatment becomes warranted and contralateral humeral version measurements greatly differ, a humeral derotational osteotomy may offer the best improvement regarding the hand position.

van de Bunt F, Pearl ML, van Essen T, van der Sluijs JA. Humeral retroversion and shoulder muscle changes in infants with internal rotation contractures following brachial plexus birth palsy. *World J Orthop* 2018; 9(12): 292-299

URL: <https://www.wjgnet.com/2218-5836/full/v9/i12/292.htm>

DOI: <https://dx.doi.org/10.5312/wjo.v9.i12.292>

## INTRODUCTION

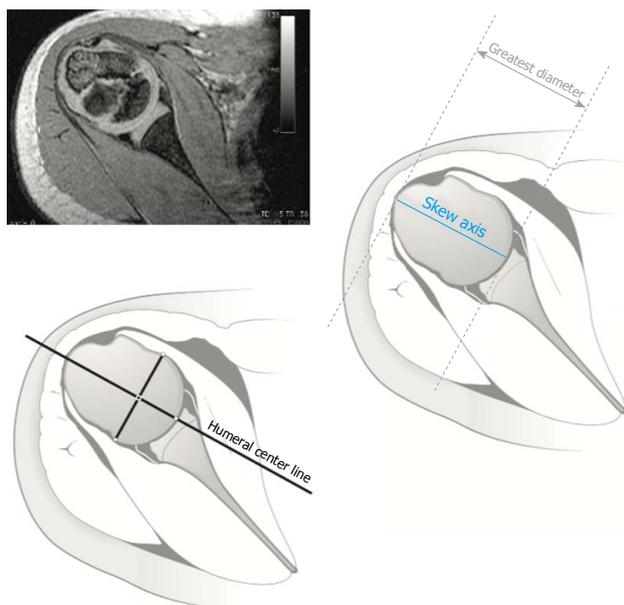
The most common musculoskeletal sequela of neurologic injury of brachial plexus birth palsy (BPBI) is an internal rotation contracture of the shoulder. This contracture is frequently associated with deformity of the glenohumeral joint<sup>[1-5]</sup>. These bony deformities have been thought to be a consequence of abnormal muscular development<sup>[6-8]</sup>.

The internal rotation contracture secondary to BPBI has been associated with alterations of humeral retroversion<sup>[9-12]</sup>. Previous studies presented opposite findings, as both older studies reported an increased humeral version angle<sup>[10,11]</sup>, while more recent studies reported a decrease in humeral retroversion<sup>[9,12]</sup>. Normal humeral retroversion is greatest at birth and gradually decreases through adolescence<sup>[13-15]</sup> to adult values averaging between 25-30 with well documented individual variation<sup>[16]</sup>. One well-studied exception is the throwing athlete, for whom retroversion has been shown to be greater on the dominant throwing side, due to repetitive throwing that usually begins in early childhood<sup>[17-21]</sup>.

The existing common treatment options consist of soft tissue procedures (releases and tendon transfers) and bone realignment procedures (rotational osteotomy) with the aim to provide better function of the upper extremity through an improved position of the hand in space<sup>[22-26]</sup>. This position is directly related to the humeral version angle. We studied humeral retroversion in 35 consecutive infants who were under evaluation for treatment of their internal rotation contractures secondary to unilateral BPBI in this retrospective observational study. Our main goal was to further elucidate the timing that these anatomic changes may occur; therefore, we included our youngest patient population. We hypothesized that the retroversion angle (RV-angle) on the involved side would be significantly decreased relative to the uninvolved side and that the difference would increase with age. Since the subscapularis (SSc) and infraspinatus (IS) muscles, are an agonist-antagonist muscle pair regarding humeral rotation, we hypothesized that an imbalance between these muscles would correlate with altered humeral version.

## MATERIALS AND METHODS

In this retrospective observational study, we included 37 Magnetic resonance imaging (MRI) -scans from a consecutive series of infants (< 1 year old) with a unilateral BPBI. All infants were potential candidates for neurosurgical interventions because of the severity of the



**Figure 1** Schematic illustration of measurement parameters applied to a magnetic resonance imaging slice from the proximal part of the normal uninvolved, humerus. (Reproduced with modification from: Pearl ML, *et al.* Geometry of the proximal humeral articular surface in young children: a study to define normal and analyze the dysplasia due to brachial plexus birth palsy. *J Shoulder Elbow Surg* 2013; **22**: 1274-84. Reproduced with permission from Elsevier.)

neurological lesion. This study was IRB approved.

MRI studies were performed on a 1.5-T MRI-unit (Magnetom 1.5 T Vision; Siemens, Erlangen, Germany). A FISP three-dimensional pulse acquisition sequence (repetition time, 25 msec; time to echo, 10 msec; flip angle 40°) with ranges from 0.8 to 1.5 mm partitions was used to obtain images from both shoulders and upper arms, representing the full humerus and glenohumeral joint in the axial plane. All children were given pethidine, droperidol and chlorpromazine intramuscularly. During sedation, they were monitored by electrocardiograph, measurement of oxygen saturation, and by video. Children were not moved during the imaging protocol.

From these 37 studies, two were insufficient for completing our detailed measurement protocol, as one study did not capture the entire humerus and motion artifacts compromised the other study.

Our Radiology department anonymized the MRI studies before performing our measurement protocol; Digital Imaging and Communications in Medicine files were imported as a numerical database into Osirix (Pixmeo, Geneva, Switzerland). For humeral version measurements, axial plane slides from the involved and uninvolved side that to our best efforts represented the midpoint of the humeral head were selected. For the measurement of muscle dimensions, axial plane slides representing the largest cross-sectional area of the SSc muscle and infraspinatus muscle were selected and exported as TIFF files. The TIFF files were imported into Geometer's Sketchpad version 5.03 (KCP Technologies, Emeryville, CA, United States) for further retroversion

analyses. The region of interest tool available in Osirix was used for muscle cross-sectional area measurements. The Narakas classifications were assigned as described by Narakas<sup>[27]</sup>. Passive external rotation was measured with the arm in the adducted position and the elbow by the side.

### Measure of retroversion

Retroversion was measured with respect to two different methods for the proximal humeral axis and the transepicondylar axis distally, introduced by Pearl *et al*<sup>[12]</sup>.

The first proximal reference axis was chosen to provide continuity with earlier retroversion analysis performed in this specific patient group<sup>[10,11]</sup>. This axis is conforming to the longest diameter through the humeral head. A line segment was created, which spanned the greatest distance from the periphery of the greater tuberosity to the medial articular surface and is labeled as the skew axis (SA) (Figure 1)<sup>[2]</sup>.

Retroversion was analyzed using the humeral center-line (HCL) as the proximal axis (Figure 1). This is a commonly used axis in various retroversion studies<sup>[19,28-32]</sup>. The HCL represents the perpendicular projection from the margins of the articular surface.

Based on the literature, retroversion of the humeral head is shown as a positive value and anteversion is shown as a negative value. Two investigators performed the humeral version measurements.

### Surface area measurements

Cross-sectional areas of the IS and SSc muscles were measured using the closed region-of-interest polygon tool in Osirix (Pixmeo). The MRI slides depicting the largest muscle bellies were identified for measurement of this cross-sectional area. Muscle size was determined by the muscle cross-sectional area in cm<sup>2</sup> and muscle percentage relative to the corresponding muscle at the uninvolved side. Furthermore, the ratio of the SSc and IS muscle (SSc/IS) was calculated to compare muscle balance between both sides and correlate these with the  $\Delta$ RV-angle.

### Analysis

Statistical analysis was performed using SPSS software (version 22.0; SPSS Inc., Chicago, IL, United States). The distribution analysis showed an approximately normal distribution.

Standard descriptive measures as mean, standard deviation, minimum and maximum values are reported for retroversion of the involved and uninvolved sides, as for the muscle surface area measurements, and their difference ( $\Delta$ ) within the study population. Pearson product-moment or Spearman rank correlation coefficients are estimated between each of these and passive external rotation and Narakas classification, as appropriate, based on the underlying distribution and type of the data. Paired data, such as involved vs uninvolved measurements regarding retroversion and muscle cross-sectional area measurements made on the same

Table 1 Demographics

Subject	Narakas	Age (mo)	External rotation (passive) (°)	Retroversion involved (HCL) (°)	Retroversion involved (SA) (°)	Retroversion uninvolved (HCL) (°)	Retroversion uninvolved (SA) (°)
1	3	2.6	-15	7.665	11.25	26.4	26.315
2	1	3.1	-5	-9.16	11.045	23.18	13.485
3	1	3.2	-40	-17.125	4.04	18.65	17.05
4	3	3.2	-30	14.175	23.395	30.56	31.865
5	3	3.3	0	-7.05	6.67	31.23	32.85
6	3	3.4	-10	-24.74	-19.26	41.72	31.705
7	3	3.4	0	7.67	7.905	30.145	29.165
8	3	3.5	-20	35.595	35.015	27.295	31.23
9	2	3.5	-5	-10.885	1.615	24.17	23.905
10	1	3.5	-20	4.54	2.05	32.21	26.49
11	3	3.6	-20	1.99	5.695	43.55	36.11
12	1	3.6	-20	3.6	22.565	54.905	47.955
13	3	3.8	-25	1.595	9.425	29.355	36.42
14	1	4.0	-5	-6.715	3.44	29.115	28.165
15	2	4.1	-15	-13.53	-1.035	21.59	25.605
16	1	4.1	-15	14.975	9.85	25.575	21.24
17	3	4.5	-25	0.065	-2.075	19.47	19.995
18	3	4.5	-45	24.195	20.195	34.19	34.55
19	1	4.5	-10	-4.115	6.1	24.305	20.175
20	2	4.6	-30	-7.205	11.675	13.465	14.06
21	3	4.6	-10	-3.14	7.29	15.445	12.14
22	1	4.7	-20	4.125	18.195	23.045	30.385
23	1	4.7	-20	-20.83	1.9	21.85	30.085
24	1	4.8	-40	4.875	9.95	15.655	20.11
25	3	4.9	-40	8.935	9.525	18.805	11.765
26	1	5.0	-15	38.24	33.53	20.055	15.945
27	1	5.0	0	-8.86	4.405	24.85	21.6
28	1	5.0	-15	-30.23	-20.135	38.975	23.31
29	1	5.0	-10	24.725	25.535	32.98	39.03
30	1	5.1	-5	8.79	10.05	20.115	-2.295
31	1	5.4	-20	-28.55	-11.965	47.445	39.185
32	3	5.6	-35	3.385	6.45	30.395	27.485
33	3	5.9	-15	-16.805	11.66	18.085	14.5
34	2	5.9	-30	11.89	7.225	28.56	35.075
35	1	6.5	-10	17.315	14.43	31.08	22.5
Mean		4.3	-18.3	0.8	8.5	27.7	25.4
Standard deviation		0.9	12	16.1	11.7	9.2	9.8
Minimum		2.6	-45	-30.23	-20.135	13.465	-2.295
Maximum		6.5	0	38.24	35.015	54.905	47.955

HCL: Humeral center-line; SA: Skew axis.

subject, were compared using paired t- or paired-samples Wilcoxon's signed-rank tests, as appropriate. Inter-rater reliability assessment by Intraclass correlations coefficient (ICC) was performed. A Bland-Altman plot was created to visualize potential differences in retroversion measuring methods<sup>[33]</sup>.

## RESULTS

The 35 children included in our study had a mean age of 4.3 mo (range of 2.1-6.5 mo), and they were classified according to the Narakas classification: Narakas I : 18 cases; Narakas II : 4 cases; Narakas III : 15 cases. Internal rotation contractures varied from -45° to 12°, with a mean of -18°, measured as passive external rotation with the elbow by the side (Table 1).

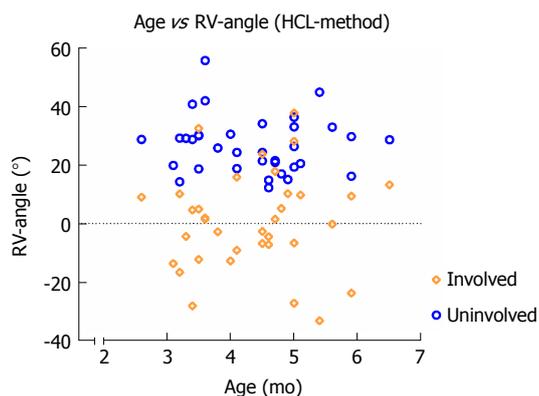
### Humeral retroversion by HCL

Retroversion measured according to the HCL and the

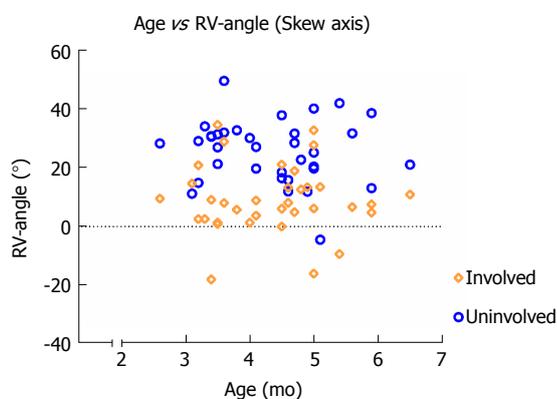
transepicondylar axis was significantly decreased on the involved side as measured by both observers. Mean RV-angles were 0.8° vs 27.7° ( $P < 0.001$ ). Paired differences averaged 26.8°, with a range from -18.4° to 77.8°. Figure 2 shows the distribution of the measurements. In two patients, retroversion increased on the involved side (Table 1). Age did not correlate with a decrease in humeral retroversion ( $r = -0.108$ ,  $P = 0.538$ ).

### Humeral retroversion by SA

Retroversion measured according to the SA and the transepicondylar axis was also significantly decreased on the involved side, as measured by both observers. Mean RV-angles were 8.5° vs 25.4° ( $P < 0.001$ ). Paired differences averaged 17.5°, with a range from -22.2° to 53.3°. Figure 3 shows the distribution of measurements. In five patients, retroversion was increased on the involved side (Table 1). Age was again not correlated with a decrease in humeral retroversion ( $r = -0.120$ ,  $P =$



**Figure 2** The distribution among measurements using the humeral center line as a proximal axis. HCL: Humeral center line; RV-angle: Retroversion angle.



**Figure 3** The distribution among measurements using the skew axis as a proximal axis. In the deformed humeral head, the skew axis yields systematically higher values compared to the humeral center line. RV-angle: Retroversion angle.

0.492).

### Muscle surface area

Both muscles were significantly smaller on the involved side. The IS muscle measured a mean surface area of 2.35 cm<sup>2</sup> vs 2.84 cm<sup>2</sup> (83%) ( $P < 0.001$ ), and the SSC muscle was 1.56 cm<sup>2</sup> vs 2.20 cm<sup>2</sup> (70%) ( $P < 0.001$ ).

Furthermore, the muscle ratio (SSc/IS) on the involved side was significantly smaller compared to the uninvolved side ( $P = 0.007$ ). In Table 2, the results of the muscle cross-sectional area measurements are summarized.

### Correlations

Pearson’s product correlation tests were performed for the retroversion measurements, the  $\Delta$ RV-angle and the muscle area ratios and muscle surface area measurements, however no significant correlations were found on the involved side. When correlating age with decrease of retroversion, the Spearman Rho test was performed for retroversion measurement and Narakas’ score and passive external rotation, no significant correlations were found ( $P > 0.05$ ).

### HCL method vs SA

For retroversion measured by HCL, the ICC for interrater reliability on the involved side was 0.934 (95%CI: 0.863-0.967;  $P < 0.001$ ). The ICC for interrater reliability on the uninvolved side was 0.889 (95%CI: 0.747-0.948;  $P < 0.001$ ). For retroversion measured using the SA, the ICC for interrater reliability on the involved side was 0.934 (95%CI: 0.897-0.970;  $P < 0.001$ ). The ICC for interrater reliability on the uninvolved side was 0.923 (95%CI: 0.853-0.960;  $P < 0.001$ ).

The distribution of measurements was larger on the involved side (Figure 4). Both measurement methods yielded comparable results in the uninvolved shoulder. However, the SA yielded systematically higher values in the deformed humeral head compared to the HCL.

## DISCUSSION

We found a significant reduction of humeral retroversion on the involved side compared to the uninvolved side in a consecutive series of patients with internal rotation contractures secondary to BPBI. Additionally, the size of the SSc and IS muscles on the involved side was significantly decreased, as was the muscle ratio (SSc/IS) on the involved side compared to the uninvolved side.

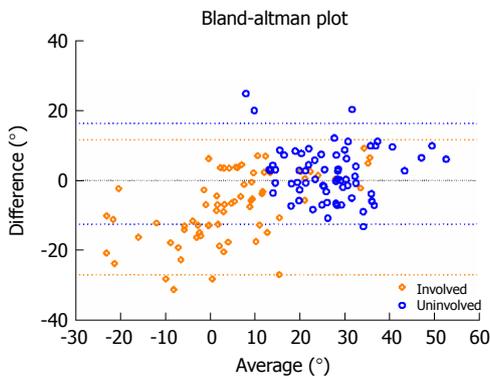
Considering the RV-angles measured, our results are similar to those reported by Pearl *et al.*, which were: 1.8° and 5.8° compared to 20.2° and 18.9°, respectively, depending on the method of measurement. However, the mean age of the study groups differed considerably, 3.2 years old vs 4.3 mo old. Our results suggest that declined humeral version is not something these children slowly grow into. The altered humeral version angle may already develop within the first weeks after birth, when the humerus is probably most prone to altered development caused by altered muscle forces gripping the humeral head. This is supported by the lack of significant correlation found between age and decreased retroversion on the involved side in both studies.

Of further note, the earliest reports by Scaglietti<sup>[11]</sup> and van der Sluijs *et al.*<sup>[10]</sup> found an increase in retroversion. Scaglietti’s study was in a very different era of imaging technology and presented his observations with little quantitative data. van der Sluijs *et al.*<sup>[10]</sup> utilized MRI, but nearly two decades ago in a somewhat older age group, when current software tools were not available for image analysis, and the lesser image quality might have influenced measurements. Perhaps these methodological differences explain these contradictory findings.

Consistent with the literature, we observed a significant decrease in muscle size on the involved side compared to the uninvolved side, with the SSc muscle being more affected than the IS muscle<sup>[6,34-36]</sup>. However, no significant correlation between the muscle ratio (SSc/IS) and the humeral RV-angle was observed. Nonetheless, the reduction in muscle ratio does not support the theory that the internal rotators overpower the injured (paralyzed) external rotators, but suggests

**Table 2** Main results of the muscle cross-sectional area measurements

Muscle area, cm <sup>2</sup>	Mean - involved	Mean - uninvolved	P value
Subscapularis muscle	1.56 ± 0.315	2.20 ± 0.372	< 0.001
Infraspinatus muscle	2.35 ± 0.520	2.84 ± 0.495	< 0.001
Ratio	68.51 ± 16.90	78.88 ± 15.45	0.007



**Figure 4** The distribution of measurement in the involved shoulder is larger than on the uninvolved side, indicating measurement differences between the skew axis and humeral center line are larger on the involved side. The blue and orange dotted lines represent the 95% limits of agreement.

that failure of the SSc to grow or develop may result in a contracted SSc, which restricts external rotation.

Another theory could be that the changes in humeral retroversion are partially related to injured muscles outside of the rotator cuff, perhaps those with at least some innervation outside of the original zone of injury. Further study of other muscles is warranted, looking for evidence as to whether they were also injured resulting in impaired growth<sup>[7,37]</sup>, or whether they recovered so strongly that they overwhelmed their antagonists or are used differently in children with varying levels of recovery.

In addition, animal studies have shown that impaired longitudinal muscle growth and strength imbalance mechanisms are capable of producing shoulder deformities and impaired growth to a somewhat greater extent than muscle imbalance<sup>[8,38-41]</sup>. However, this has not yet been related to altered humeral version. For example, impaired growth and increased stiffness of the SSc muscle fibers may have a significant effect on humeral version development. In combination with other internal rotator muscles such as the pectoralis muscle, mechanical stiffness of these muscle fibers may not be directly related to cross-sectional muscle area measurements.

Further research is necessary to elucidate a causal relationship between those mechanisms and shoulder deformities, concerning both the humerus and glenoid, which will help guide clinical treatment decisions for BPBI.

This study has several limitations. The measurements made were based on axial slices of the humerus; measurements made from a 3D-reconstruction, as those performed by Sheehan and others, would have the potential for minimizing errors related to patient

positioning and inconsistent image acquisition. In our studied age group, the humeral head and epicondylar axis are mostly cartilaginous, making 3D-reconstruction of the humeral anatomy much more challenging than in a skeletally mature subject. While the software tools currently exist, they are labor intensive and extremely difficult to implement in clinical practice. Therefore, we chose to utilize methods often used in our clinic setting and shown in a prior publication<sup>[12]</sup>.

Analyses of the IS and SSc muscles are based on cross-sectional area measurements from the MRI-slice, depicting the largest muscle belly as used in multiple previous studies<sup>[6,35,36]</sup>. Capturing the full volume of both muscles would likely have been more informative; however, such software tools were not available to us. Furthermore, muscle thickness was only assessed for the IS and SSc muscles, and the measurement of other external and internal rotator muscles may offer additional insight into muscle behavior and its effect on humeral retroversion in this population.

The most common sequel and focus of surgical intervention in children with BPBI is an internal rotation contracture at the shoulder. These surgical interventions all aim for better function through an improved position of the hand in space. Humeral version undeniably affects hand functionality because with all other factors being equal, decreased humeral version results in an increase of the severity of the clinical presentation of an internal rotation contracture. A large reduction in humeral retroversion at a very young age could be a predictor (or an argument when apparent at an older age) for the necessity of a humeral derotational osteotomy to provide adequate improvement of hand and possibly elbow function. Furthermore, this study shows that secondary osseous changes can occur within several months in this patient population. A prospective study analyzing possible changes in humeral version in this patient population over time would be of interest, as it seems through these results and results from recent studies that changes in humeral version occur early, but that they may not change much after that.

In conclusion, humeral retroversion has a high likelihood of being significantly decreased in this patient population. These findings are relevant for any child under consideration for surgical intervention aiming to improve external rotation, since all other factors being equal, decreased humeral retroversion results in an increased severity of the clinical presentation of an internal rotation contracture. We measured these changes in infants 2-7 mo old and found that altered humeral development

can occur very early in life in a population where internal rotation contractures are apparent.

## ARTICLE HIGHLIGHTS

### Research background

The existing common treatment options for children suffering from brachial plexus birth palsy all strive for better function of the upper extremity through an improved position of the hand in space. This position is directly related to the humeral version angle.

### Research motivation

Since earlier studies did not reveal a correlation between age and decreased retroversion on the involved side, the question remained at what age this anatomic change may occur.

### Research objectives

Our objective was to elucidate the timing that decreased retroversion may occur; therefore, we included our youngest patient population (2-7 mo old).

### Research methods

We measured humeral version relative to two proximal axes and one distal axis (transepicondylar axis). The proximal axes were: (1) the perpendicular line to the borders of the articular surface (humeral centerline), and (2) the longest diameter through the humeral head. Additionally, cross-sectional areas of the infraspinatus (IS) and subscapularis (SSc) muscles were measured. The difference in retroversion was correlated with the ratio of muscle sizes.

### Research results

Retroversion on the involved side was significantly decreased,  $1.0^\circ$  vs  $27.6^\circ$  (1) and  $8.5^\circ$  vs  $27.2^\circ$  (2), ( $P < 0.01$ ), as compared to the uninvolved side. SSc and IS muscle size on the involved side was significantly decreased,  $2.26 \text{ cm}^2$  vs  $2.79 \text{ cm}^2$  and  $1.53 \text{ cm}^2$  vs  $2.19 \text{ cm}^2$ , respectively ( $P < 0.05$ ). Additionally, muscle ratio (SSc/IS) on the involved side was significantly smaller compared to the uninvolved side ( $P = 0.007$ ), but was not related to alterations in humeral version.

### Research conclusions

Our results show that altered humeral development can occur very early in life in a population where internal rotation contractures are apparent.

### Research perspectives

A large reduction in humeral retroversion at a very young age could be a predictor (or an argument when apparent at an older age), for the necessity of a humeral derotational osteotomy, to provide adequate improvement of hand and possibly elbow function. A prospective study analyzing changes in humeral version over time would be of interest to assess the predictive value of decreased retroversion at such a young age, concerning various treatment options (soft-tissue and bony).

## REFERENCES

- 1 **Pearl ML**, Edgerton BW. Glenoid deformity secondary to brachial plexus birth palsy. *J Bone Joint Surg Am* 1998; **80**: 659-667 [PMID: 9611026 DOI: 10.2106/00004623-199805000-00006]
- 2 **Pearl ML**, Woolwine S, van de Bunt F, Merton G, Burchette R. Geometry of the proximal humeral articular surface in young children: a study to define normal and analyze the dysplasia due to brachial plexus birth palsy. *J Shoulder Elbow Surg* 2013; **22**: 1274-1284 [PMID: 23478467 DOI: 10.1016/j.jse.2012.12.031]
- 3 **Kozin SH**. Correlation between external rotation of the glenohumeral joint and deformity after brachial plexus birth palsy. *J Pediatr Orthop* 2004; **24**: 189-193 [PMID: 15076606 DOI: 10.1097/01241398-200403000-00011]
- 4 **Waters PM**, Smith GR, Jaramillo D. Glenohumeral deformity

- secondary to brachial plexus birth palsy. *J Bone Joint Surg Am* 1998; **80**: 668-677 [PMID: 9611027 DOI: 10.2106/00004623-199805000-00007]
- 5 **van der Sluijs JA**, van Ouwerkerk 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]
- 6 **Waters PM**, Monica JT, Earp BE, Zurakowski D, Bae DS. Correlation of radiographic muscle cross-sectional area with glenohumeral deformity in children with brachial plexus birth palsy. *J Bone Joint Surg Am* 2009; **91**: 2367-2375 [PMID: 19797571 DOI: 10.2106/JBJS.H.00417]
- 7 **Nikolaou S**, Peterson E, Kim A, Wylie C, Cornwall R. Impaired growth of denervated muscle contributes to contracture formation following neonatal brachial plexus injury. *J Bone Joint Surg Am* 2011; **93**: 461-470 [PMID: 21368078 DOI: 10.2106/JBJS.J.00943]
- 8 **Soldado F**, Fontecha CG, Marotta M, Benito D, Casaccia M, Mascarenhas VV, Zlotolow D, Kozin SH. The role of muscle imbalance in the pathogenesis of shoulder contracture after neonatal brachial plexus palsy: a study in a rat model. *J Shoulder Elbow Surg* 2014; **23**: 1003-1009 [PMID: 24388715 DOI: 10.1016/j.jse.2013.09.031]
- 9 **Sheehan FT**, Brochard S, Behnam AJ, Alter KE. Three-dimensional humeral morphologic alterations and atrophy associated with obstetrical brachial plexus palsy. *J Shoulder Elbow Surg* 2014; **23**: 708-719 [PMID: 24291045 DOI: 10.1016/j.jse.2013.08.014]
- 10 **van der Sluijs JA**, van Ouwerkerk WJ, de Gast A, Wuisman P, Nollet F, Manoliu RA. Retroversion of the humeral head in children with an obstetric brachial plexus lesion. *J Bone Joint Surg Br* 2002; **84**: 583-587 [PMID: 12043783 DOI: 10.1302/0301-620x.84b4.12243]
- 11 **Scaglietti O**. The obstetrical shoulder trauma. *Surg Gynecol Obstet* 1938. pp. 868-877
- 12 **Pearl ML**, Batech M, van de Bunt F. Humeral Retroversion in Children with Shoulder Internal Rotation Contractures Secondary to Upper-Trunk Neonatal Brachial Plexus Palsy. *J Bone Joint Surg Am* 2016; **98**: 1988-1995 [PMID: 27926680 DOI: 10.2106/JBJS.15.01132]
- 13 **Krahl VE**. The torsion of the humerus; its localization, cause and duration in man. *Am J Anat* 1947; **80**: 275-319 [PMID: 20296010 DOI: 10.1002/aja.1000800302]
- 14 **Edelson G**. The development of humeral head retroversion. *J Shoulder Elbow Surg* 2000; **9**: 316-318 [PMID: 10979528 DOI: 10.1067/mse.2000.106085]
- 15 **Cowgill LW**. Humeral torsion revisited: a functional and ontogenetic model for populational variation. *Am J Phys Anthropol* 2007; **134**: 472-480 [PMID: 17657784 DOI: 10.1002/ajpa.20689]
- 16 **Edelson G**. Variations in the retroversion of the humeral head. *J Shoulder Elbow Surg* 1999; **8**: 142-145 [PMID: 10226966 DOI: 10.1016/s1058-2746(99)90007-1]
- 17 **Yamamoto N**, Itoi E, Minagawa H, Urayama M, Saito H, Seki N, Iwase T, Kashiwaguchi S, Matsuura T. Why is the humeral retroversion of throwing athletes greater in dominant shoulders than in nondominant shoulders? *J Shoulder Elbow Surg* 2006; **15**: 571-575 [PMID: 16979051 DOI: 10.1016/j.jse.2005.06.009]
- 18 **Whiteley R**, Adams R, Ginn K, Nicholson L. Playing level achieved, throwing history, and humeral torsion in Masters baseball players. *J Sports Sci* 2010; **28**: 1223-1232 [PMID: 20694888 DOI: 10.1080/02640414.2010.498484]
- 19 **Chant CB**, Litchfield R, Griffin S, Thain LM. Humeral head retroversion in competitive baseball players and its relationship to glenohumeral rotation range of motion. *J Orthop Sports Phys Ther* 2007; **37**: 514-520 [PMID: 17939610 DOI: 10.2519/jospt.2007.2449]
- 20 **Myers JB**, Oyama S, Rucinski TJ, Creighton RA. Humeral retrotorsion in collegiate baseball pitchers with throwing-related upper extremity injury history. *Sports Health* 2011; **3**: 383-389

- [PMID: 23016031 DOI: 10.1177/1941738111410636]
- 21 **Osbah 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 DOI: 10.1177/03635465020300030801]
  - 22 **Pearl ML**, Edgerton BW, Kazimiroff PA, Burchette RJ, Wong K. Arthroscopic release and latissimus dorsi transfer for shoulder internal rotation contractures and glenohumeral deformity secondary to brachial plexus birth palsy. *J Bone Joint Surg Am* 2006; **88**: 564-574 [PMID: 16510824 DOI: 10.2106/JBJS.D.02872]
  - 23 **Kozin SH**, Boardman MJ, Chafetz RS, Williams GR, Hanlon A. Arthroscopic treatment of internal rotation contracture and glenohumeral dysplasia in children with brachial plexus birth palsy. *J Shoulder Elbow Surg* 2010; **19**: 102-110 [PMID: 19664938 DOI: 10.1016/j.jse.2009.05.011]
  - 24 **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]
  - 25 **Gilbert A**, Brockman R, Carlioz H. Surgical treatment of brachial plexus birth palsy. *Clin Orthop Relat Res* 1991; : 39-47 [PMID: 1847671 DOI: 10.1097/00003086-199103000-00005]
  - 26 **Kirkos JM**, Kyrkos MJ, Kapetanios GA, Haritidis JH. Brachial plexus palsy secondary to birth injuries. *J Bone Joint Surg Br* 2005; **87**: 231-235 [PMID: 15736749 DOI: 10.1302/0301-620X.88B4.17641]
  - 27 **Birch R**. Obstetric brachial plexus palsy. *J Hand Surg Br* 2002; **27**: 3-8 [PMID: 11895337 DOI: 10.1054/jhsb.2001.0722]
  - 28 **Boileau P**, Bicknell RT, Mazzoleni N, Walch G, Urien JP. CT scan method accurately assesses humeral head retroversion. *Clin Orthop Relat Res* 2008; **466**: 661-669 [PMID: 18264854 DOI: 10.1007/s11999-007-0089-z]
  - 29 **DeLude JA**, Bicknell RT, MacKenzie GA, Ferreira LM, Dunning CE, King GJ, Johnson JA, Drosdowech DS. An anthropometric study of the bilateral anatomy of the humerus. *J Shoulder Elbow Surg* 2007; **16**: 477-483 [PMID: 17363290 DOI: 10.1016/j.jse.2006.09.016]
  - 30 **Harrold F**, Wigderowitz C. A three-dimensional analysis of humeral head retroversion. *J Shoulder Elbow Surg* 2012; **21**: 612-617 [PMID: 21783384 DOI: 10.1016/j.jse.2011.04.005]
  - 31 **Hernigou P**, Duparc F, Hernigou A. Determining humeral retroversion with computed tomography. *J Bone Joint Surg Am* 2002; **84-A**: 1753-1762 [PMID: 12377904 DOI: 10.2106/00004623-200306000-00035]
  - 32 **Matsumura N**, Ogawa K, Kobayashi S, Oki S, Watanabe A, Ikegami H, Toyama Y. Morphologic features of humeral head and glenoid version in the normal glenohumeral joint. *J Shoulder Elbow Surg* 2014; **23**: 1724-1730 [PMID: 24862249 DOI: 10.1016/j.jse.2014.02.020]
  - 33 **Bland JM**, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307-310 [PMID: 2868172 DOI: 10.1016/S0140-6736(86)90837-8]
  - 34 **Hogendoorn S**, van Overvest KL, Watt I, Duijsens AH, Nelissen RG. Structural changes in muscle and glenohumeral joint deformity in neonatal brachial plexus palsy. *J Bone Joint Surg Am* 2010; **92**: 935-942 [PMID: 20360518 DOI: 10.2106/JBJS.I.00193]
  - 35 **Van Gelein Vitringa VM**, Jaspers R, Mullender M, Ouwkerk WJ, Van Der Sluijs JA. Early effects of muscle atrophy on shoulder joint development in infants with unilateral birth brachial plexus injury. *Dev Med Child Neurol* 2011; **53**: 173-178 [PMID: 20846159 DOI: 10.1111/j.1469-8749.2010.03783.x]
  - 36 **Pöyhkä TH**, Nietosvaara YA, Remes VM, Kirjavainen MO, Peltonen JI, Lamminen AE. MRI of rotator cuff muscle atrophy in relation to glenohumeral joint incongruence in brachial plexus birth injury. *Pediatr Radiol* 2005; **35**: 402-409 [PMID: 15635469 DOI: 10.1007/s00247-004-1377-3]
  - 37 **Einarsson F**, Hultgren T, Ljung BO, Runesson E, Fridén J. Subscapularis muscle mechanics in children with obstetric brachial plexus palsy. *J Hand Surg Eur Vol* 2008; **33**: 507-512 [PMID: 18687840 DOI: 10.1177/1753193408090764]
  - 38 **Crouch DL**, Hutchinson ID, Plate JF, Antoniono J, Gong H, Cao G, Li Z, Saul KR. Biomechanical Basis of Shoulder Osseous Deformity and Contracture in a Rat Model of Brachial Plexus Birth Palsy. *J Bone Joint Surg Am* 2015; **97**: 1264-1271 [PMID: 26246261 DOI: 10.2106/JBJS.N.01247]
  - 39 **Li Z**, Barnwell J, Tan J, Koman LA, Smith BP. Microcomputed tomography characterization of shoulder osseous deformity after brachial plexus birth palsy: a rat model study. *J Bone Joint Surg Am* 2010; **92**: 2583-2588 [PMID: 21048177 DOI: 10.2106/JBJS.1.01660]
  - 40 **Li Z**, Ma J, Apel P, Carlson CS, Smith TL, Koman LA. Brachial plexus birth palsy-associated shoulder deformity: a rat model study. *J Hand Surg Am* 2008; **33**: 308-312 [PMID: 18343282 DOI: 10.1016/j.jhsa.2007.11.017]
  - 41 **Soldado F**, Benito-Castillo D, Fontecha CG, Barber I, Marotta M, Haddad S, Menendez ME, Mascarenhas VV, Kozin SH. Muscular and glenohumeral changes in the shoulder after brachial plexus birth palsy: an MRI study in a rat model. *J Brachial Plex Peripher Nerve Inj* 2012; **7**: 9 [PMID: 23217052 DOI: 10.1186/1749-7221-7-9]

**P- Reviewer:** Emara KM, Wyatt MC **S- Editor:** Dou Y  
**L- Editor:** Filipodia **E- Editor:** Bian YN



## Metallosis following a clip breakage in a total knee arthroplasty implant: A case report

Ahmed Isam Saad, Shafiq Arif Shahban, Richard Fernandes

Ahmed Isam Saad, Shafiq Arif Shahban, Richard Fernandes, Good Hope Hospital Part of the University Hospital Birmingham, Birmingham B75 7RR, United Kingdom

ORCID number: Ahmed Isam Saad (0000-0002-5796-069X); Shafiq Arif Shahban (0000-0002-8807-8026); Richard Fernandes (0000-0002-5837-4385).

Author contributions: Saad AI, Shahban SA and Fernandes R contributed equally to this work, they designed the research and contributed to writing the paper equally.

Informed consent statement: Informed consent has been taken from this patient and form provided with manuscript.

Conflict-of-interest statement: No conflicts of interest.

CARE Checklist (2016) statement: The CARE checklist (2016) has been added to the content of 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: Unsolicited manuscript

Corresponding author to: Ahmed Isam Saad, MBBS, Surgeon, Good Hope Hospital Part of the University Hospital Birmingham, West Midlands, Birmingham B16 8EQ, United Kingdom. [ahmed.saad3@nhs.net](mailto:ahmed.saad3@nhs.net)  
Telephone: +44-740-5775343  
Fax: +44-121-3712000

Received: October 2, 2018

Peer-review started: October 2, 2018

First decision: November 16, 2018

Revised: November 22, 2018

Accepted: December 13, 2018

Article in press: December 13, 2018

Published online: December 18, 2018

### Abstract

#### BACKGROUND

Metallosis describes the build-up of metal debris in the soft tissues after a period of metal on metal articulation. This debris can be asymptomatic or lead to catastrophic implant failure, which can present acutely, as in this case, or over a period of time. This report highlights how a metal clip used to hold the polyethylene liner to the tibial base plate broke 5 years after implantation, dislodged from its original position and went on to cause post-operative knee metallosis.

#### CASE SUMMARY

We present a case of a 63 year old lady admitted to our unit with an acute onset of right knee pain on top of a previous right total knee replacement. There was no associated trauma and examination revealed an erythematous, swollen and tender right knee. Blood investigations went on to display significantly raised inflammatory markers, raising the suspicion of a septic joint. This patient was taken to theatre for a knee arthrotomy and lavage of what was thought to be a septic joint when she was found to have extensive knee metallosis. On further inspection the metal clip, normally used to secure the polyethylene insert to the tibial base plate, had broken, dislodged, and had triggered this response. After the initial washout, this lady went back to theatre, once the appropriate implants were in stock, for an exchange of liner and metal clip.

#### CONCLUSION

This case highlights this very rare complication which has never been reported in the literature and the success of this patient's management.

**Key words:** Case report; Metallosis; Total knee replacement; Vanguard<sup>®</sup>

© The Author(s) 2018. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Metallosis describes the build-up of metal debris in the soft tissues after a period of metal on metal articulation. This can present acutely, as in this case, or gradually. This case report highlights how a metal clip used to hold the polyethylene liner to the tibial base plate broke 5 years after implantation, dislodged from its original position and went on to cause post-operative knee metallosis. The success to this patient's management came from thorough debridement, and replacement of the components involved.

Saad AI, Shahban SA, Fernandes R. Metallosis following a clip breakage in a total knee arthroplasty implant: A case report. *World J Orthop* 2018; 9(12): 300-303

URL: <https://www.wjgnet.com/2218-5836/full/v9/i12/300.htm>

DOI: <https://dx.doi.org/10.5312/wjo.v9.i12.300>

## INTRODUCTION

Metallosis is a rare condition that has been recognised to affect both knee and hip arthroplasties. The most common cause leading to this malady is abrasive wear of the polyethylene component, inadvertently allowing two or more of the metal components to come into contact. This subsequently leads to a serious and debilitating synovial reaction.

Though the majority of cases documented in the literature of metallosis involve the wear of the polyethylene component; we present a rare and interesting case of metallosis in the knee following breakage of the metal clip used to hold the polyethylene insert of a Vanguard® implant in place. This consequently allowed the femoral and tibial components to come into contact leading to the acute metal induced synovitis.

## CASE PRESENTATION

### Case report

A 63 years old lady had a right total knee replacement (TKR) in 2013 using the Vanguard® knee system - Biomet implant. She was admitted into hospital in March 2018 - approximately five years following her initial TKR. She presented with an insidious and acute onset of worsening right knee pain and swelling, not associated with any trauma. The pain was affecting her mobility, limiting her ability to weight bear on that joint.

On clinical assessment, she had an erythematous and fluctuant right knee with a moderate joint effusion. Along with this, she had a tender joint line with a limited range of movement. There was no evidence of wound breakdown, equally in 2013 following her primary procedure, she had an uncomplicated recovery period. She had a core body temperature of 37.3 °C, with no accompanying fevers or rigors, and the rest of her

physiological markers were unremarkable.

Her initial blood investigations revealed significantly raised inflammatory markers with a white cell count (WCC) of  $20.27 \times 10^9/L$ , neutrophils of  $16.68 \times 10^9/L$  and C - reactive protein (CRP) of 186 mg/L, suggesting an acute infection. Radiographs of the knee showed a relatively well positioned in-situ TKR, with no evidence of loosening, with the possibility of a joint effusion (Figure 1A and B).

Given this patient's history, examination and biochemical findings, a right knee septic arthritis could not be excluded, and as such she was taken to theatre for a knee arthrotomy with a view to debride the joint, and potentially replacement of the polyethylene liner.

After the initial arthrotomy was made, significant purulent, dark coloured fluid extruded from the joint. The knee joint was formally opened and at this point no pus was seen, however there was a significant amount of metallosis debris deeply embedded into the soft tissues surrounding the knee prostheses (Figure 2A). On further inspection, it was clear that the metal clip which is normally used to secure the polyethylene insert to the tibial base plate had broken and dislodged (Figures 2B and C). Despite this broken metal clip, the polyethylene liner was still in its original position, and on further examination the femoral, tibial and patella implants were all well fixed with no evidence of loosening. There was also no evidence of significant macroscopic wear of the femoral and tibial components.

The broken metal clip was retrieved successfully and in whole (part being dislodged and part being well fixed in the polyethylene liner). The Vanguard® TKR system is no longer used in our trust, and consequently we were unable to replace the liner and metal clip. This lady therefore went on to have a thorough soft tissue debridement of her metallosis and lavage with copious normal saline solution. She later had a second staged procedure (after a total of 18 d) at which point we were able to obtain the correct implants, and thus provide her with a new polyethylene liner and metal clip to secure it in place. In the interim, between stages, she was prescribed a course of two grams of intravenous flucloxacillin antibiotics (to complete a six week course) and was restricted with her weight bearing, to prevent polyethylene liner displacement.

Superficial and deep tissue samples from the time of her 1<sup>st</sup> procedure did not grow any organisms. The histology report demonstrated areas of black necrosis with reactive fibrosis, a giant cell foreign body reaction triggered by black, irregular metallic particles, confirming the diagnosis of metallosis.

## OUTCOME AND FOLLOW UP

Post-operatively, the patient's inflammatory markers started to improve with a fall in the CRP to 52 mg/L and WCC of  $12 \times 10^9$ . There was also marked improvement in her symptoms, pain and range of movement of the knee. She was later discharged whilst being able to fully



Figure 1 Initial radiographs of the right knee. A: Anterior-posterior radiograph of the right knee; B: Lateral radiograph of the right knee.

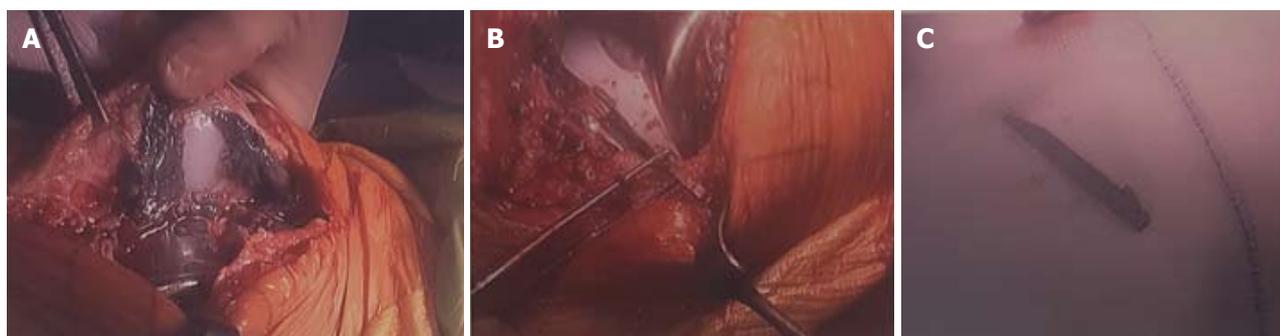


Figure 2 Intraoperative images of the soft tissues surrounding the *in-situ* total knee replacement. A: Intraoperative Image of extensive soft tissue metallosis; B, C: The retrieved broken metal clip.

weight bear and with a much improved knee. At the six week stage, in the outpatient clinic, she had complete resolution of her symptoms and was happily discharged from clinic.

## DISCUSSION

Metallosis is an uncommon synovial reaction that can lead to serious complications and almost always requires revision surgery. It is therefore critical to understand the causes that lead to this condition. Avoidance of this essentially comes down to trying to ensure that the individual metal components of any part of the prosthetic joint are not allowed to come into contact and abrade against each other. Most case reports in the literature document the development of metallosis following significant wear of the interposed polyethylene component<sup>[1]</sup>. In this report we found no significant wear of the polyethylene insert, but rather, ensuing metallosis which was allowed to occur due a metal clip which had broken and dislodged, allowing for metal-on-metal (MOM) abrasion of the components.

As the inflammation progresses, often over a prolonged period of time, patients with knee metallosis usually present with gradual worsening knee pain and, occasionally, a noticeable rash (indicating necrosis). Prosthetic dislocation is often a late sign and demonstrates significant polyethylene wear<sup>[2]</sup>. This almost always goes

on to require revision surgical intervention.

Different companies have different ways in which one can secure the polyethylene liner to the tibial base plate. In the case of the Vanguard® TKR system, one is required to slide the metal clip through both the liner and tibial component, thus allowing for a secure hold of the two. Clip breakage is not a recognised complication of TKR, and very rarely occurs. One would expect that when the clip breaks, this disrupts the position of the polyethylene component, which would ultimately lead to displacement or even dislocation of the knee joint. In our case, though we found the insert to be stable, we concluded that the broken and loose part of metal clip was abrading the metal back components of the joint, and thus triggering the metallosis inflammatory reaction.

When there is a suspicion of post-operative knee metallosis, imaging may help in coming to this diagnosis. Described in the literature are the metal-line sign and the cloud sign which occasionally can be seen on plain radiographs<sup>[2,3]</sup>.

With regards to the pre-operative radiographic images (Figures 1A and B) it was not immediately recognised that the clip had broken and moved out of position. In retrospect, there is a suspicion that the broken metal clip is visible in the initial set of radiographs. Whether or not pre-operative recognition would have aided in planning is debatable, as the decision to debride the joint was made on clinical grounds of a possible diagnosis of septic

arthritis. Liner exchange could not be carried out at the first instance due to non-availability of the insert and clip as these components were no longer used by the trust - something which, with more detailed pre-operative imaging, potentially could have been planned for and potentially could have allowed her to have a single staged procedure.

## CONCLUSION

Metallosis is most commonly caused by wear of the polyethylene insert, leading to a chronic inflammatory process with signs that may or may not be easily identifiable on plain radiographs. Septic arthritis is potentially fatal and thus requires a thorough work up. Once septic arthritis is excluded, early diagnosis of metallosis is key and often requires revision surgery in terms of debridement with or without implant exchange.

We present a rare case of metallosis from what was thought to be a robust mechanism of polyethylene liner stabilisation. We urge all clinicians to bear this in mind when dealing with prostheses which have the potential to allow any form of MOM interaction(s).

## REFERENCES

- 1 **Argenson JN**, Parratte S. The unicompartmental knee: design and technical considerations in minimizing wear. *Clin Orthop Relat Res* 2006; **452**: 137-142 [PMID: 16906108 DOI: 10.1097/01.blo.0000229358.19867.60]
- 2 **Romesburg JW**, Wasserman PL, Schoppe CH. Metallosis and Metal-Induced Synovitis Following Total Knee Arthroplasty: Review of Radiographic and CT Findings. *J Radiol Case Rep* 2010; **4**: 7-17 [PMID: 22470753 DOI: 10.3941/jrcr.v4i9.423]
- 3 **Paydar A**, Chew FS, Manner PA. Severe Periprosthetic Metallosis and Polyethylene Liner Failure Complicating Total Hip Replacement: The Cloud Sign. *Radiol Case Rep* 2015; **2**: 115 [PMID: 27303496 DOI: 10.2484/rcr.v2i4.115]

**P- Reviewer:** Drosos GI, Erkan S   **S- Editor:** Ma YJ   **L- Editor:** A  
**E- Editor:** Bian YN





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <https://www.f6publishing.com/helpdesk>  
<https://www.wjgnet.com>

