ISSN 2218-5836 (online)

World Journal of *Orthopedics*

World J Orthop 2019 February 18; 10(2): 54-122

Published by Baishideng Publishing Group Inc

WJO

World Journal of Orthopedics

Contents

Monthly Volume 10 Number 2 February 18, 2019

ABOUT COVER

Associate Editor of *World Journal of Orthopedics*, Wasim S Khan, CCST, FRCS (Ed), FRCS (Hon), MBChB, MSc, PhD, Lecturer, Surgeon, Division of Trauma and Orthopaedic Surgery, Addenbrooke's Hospital, University of Cambridge, Cambridge CB2 2QQ, United Kingdom

AIMS 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, *etc*. 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, *etc*.

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

The *WJO* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Scopus, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Yun-Xiaojian Wu* **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

EDITORS-IN-CHIEF
Bao-Gan Peng

EDITORIAL BOARD MEMBERS
http://www.wjgnet.com/2218-5836/editorialboard.htm

EDITORIAL OFFICE
Jin-Lei Wang, Director

PUBLICATION DATE
February 18, 2019

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 February 18; 10(2): 54-62

DOI: 10.5312/wjo.v10.i2.54

ISSN 2218-5836 (online)

REVIEW

Osteoarticular manifestations of human brucellosis: A review

Seyed Mokhtar Esmaeilnejad-Ganji, Seyed Mohammad Reza Esmaeilnejad-Ganji

ORCID number: Seyed Mokhtar Esmaeilnejad-Ganji (0000-0001-7562-0835); Seyed Mohammad Reza Esmaeilnejad-Ganji (0000-0003-4152-5324).

Author contributions: Esmaeilnejad-Ganji SM contributed to study design; Esmaeilnejad-Ganji SM and Esmaeilnejad-Ganji SMR contributed to data collection and writing the draft; Esmaeilnejad-Ganji SM contributed to manuscript revision; all authors approved the final version of the manuscript.

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

Manuscript source: Unsolicited manuscript

Received: November 14, 2018
Peer-review started: November 15, 2018
First decision: November 29, 2018
Revised: November 30, 2018
Accepted: December 17, 2018
Article in press: December 17, 2018
Published online: February 18,

Seyed Mokhtar Esmaeilnejad-Ganji, Clinical Research Development Center, Shahid Beheshti Hospital, Babol University of Medical Sciences, Babol 47176-47745, Iran

Seyed Mokhtar Esmaeilnejad-Ganji, Department of Orthopedics, Babol University of Medical Sciences, Babol 47176-47745, Iran

Seyed Mokhtar Esmaeilnejad-Ganji, Infectious Diseases and Tropical Medicine Research Center, Health Research Institute, Babol University of Medical Sciences, Babol 47176-47745, Iran

Seyed Mohammad Reza Esmaeilnejad-Ganji, Boston University School of Medicine, Boston, MA 02118, United States

Corresponding author: Seyed Mokhtar Esmaeilnejad-Ganji, MD, Associate Professor, Department of Orthopedics, Babol University of Medical Sciences, Ganjafrooz Street, Babol 47176-47745, Mazandaran, Iran. smsnganji@yahoo.com
Telephone: +98-11-32199936
Fax: +98-11-32190181

Abstract

Brucellosis is a common global zoonotic disease, which is responsible for a range of clinical manifestations. Fever, sweating and musculoskeletal pains are observed in most patients. The most frequent complication of brucellosis is osteoarticular involvement, with 10% to 85% of patients affected. The sacroiliac (up to 80%) and spinal joints (up to 54%) are the most common affected sites. Spondylitis and spondylodiscitis are the most frequent complications of brucellar spinal involvement. Peripheral arthritis, osteomyelitis, discitis, bursitis and tenosynovitis are other osteoarticular manifestations, but with a lower prevalence. Spinal brucellosis has two forms: focal and diffuse. Epidural abscess is a rare complication of spinal brucellosis but can lead to permanent neurological deficits or even death if not treated promptly. Spondylodiscitis is the most severe form of osteoarticular involvement by brucellosis, and can have single- or multi-focal involvement. Early and appropriate diagnosis and treatment of the disease is important in order to have a successful management of the patients with osteoarticular brucellosis. Brucellosis should be considered as a differential diagnosis for sciatic and back pain, especially in endemic regions. Patients with septic arthritis living in endemic areas also need to be evaluated in terms of brucellosis. Physical examination, laboratory tests and imaging techniques are needed to diagnose the disease. Radiography, computed tomography, magnetic resonance imaging (MRI) and bone scintigraphy are imaging techniques for the diagnosis of osteoarticular brucellosis. MRI is helpful to differentiate between pyogenic spondylitis and brucellar spondylitis. Drug medications (antibiotics) and surgery are the only two options for the treatment and cure of osteoarticular

2019

brucellosis.

Key words: Brucellosis; Brucella; Osteoarticular manifestations; Musculoskeletal pain; Bone; Joint

Core tip: The most frequent complication of brucellosis is osteoarticular involvement, with a rate of 10%-85%. Sacroiliac and spinal joints are the most common affected sites. Spondylitis and spondylodiscitis are the most frequent complications of brucellar spinal involvement. Peripheral arthritis, osteomyelitis, discitis, bursitis and tenosynovitis are other osteoarticular manifestations. Epidural abscess is a rare complication of spinal brucellosis but can lead to permanent neurological deficits or even death if not treated promptly. Spondylodiscitis is the most severe form of osteoarticular involvement by brucellosis. Brucellosis should be considered as a differential diagnosis for sciatica, back pain and septic arthritis in endemic regions.

Citation: Esmaeilnejad-Ganji SM, Esmaeilnejad-Ganji SMR. Osteoarticular manifestations of human brucellosis: A review. *World J Orthop* 2019; 10(2): 54-62
URL: https://www.wjgnet.com/2218-5836/full/v10/i2/54.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i2.54

INTRODUCTION

Brucellosis is the most common microbial zoonotic disease in the world and found endemically in most developed and developing countries. Brucella, an intracellular bacterium, causes brucellosis and *Brucella melitensis* spp. is the most common of the *Brucella* species[1-3]. This disease was first diagnosed in the Mediterranean area, where it received its initial name "Malta fever"[4]. Thousands of new cases of brucellosis are reported annually worldwide: its annual incidence per million population was reported to be 238.6 in Iran, 262.2 in Turkey, 214.4 in Saudi Arabia and 278.4 in Iraq[5]. Humans can acquire the infection mainly through occupational contact (*e.g.*, veterinary, butcher, animal husbandry) or consumption of contaminated dairy products, especially milk, butter and cheese[6-8].

Brucellosis can involve the human body systemically. The most common clinical presentations of human brucellosis are fever, sweating, musculoskeletal pains, lymphadenopathy or hepatosplenomegaly[9,10]. The musculoskeletal system is particularly involved. Presentations of brucellosis are variable, deceptive and often non-specific, and they can mimic other infectious and non-infectious diseases[11-13].

For the diagnosis of brucellosis, after primary physical examination, serological tests [the Wright and 2-Mercaptoethanol (2-ME) tests], cultural and imaging methods (radiography, computed tomography, magnetic resonance imaging (MRI) and bone scintigraphy) should be helpful[14,15]. To definitely diagnose brucellosis, the organism needs to be isolated from blood, bone marrow, wounds, purulent discharge or other body tissues and fluids, with culture or molecular/histological assessment[16-18]. In the present review, we have examined the literature concerning the osteoarticular manifestations of brucellosis, aiming to help physicians and orthopedic surgeons to provide better clinical management for these patients.

OSTEOARTICULAR MANIFESTATIONS

Osteoarticular involvement is the most frequent complication of brucellosis and can occur in 10% to 85% of the patients infected with the disease[19]. It is usually seen as sacroiliitis, spondylitis, osteomyelitis, peripheral arthritis, bursitis and tenosynovitis[15,20]. The type of skeletal involvement mainly depends on a patient's age. This range of manifestations can lead patients to initially visit general practitioners, and ultimately orthopedic and rheumatology specialists. Variable clinical features and lack of specific symptoms often cause a delay in diagnosis of osteoarticular brucellosis.

Spinal brucellosis

The spine is one of the most common organs involved in brucellosis infection with a rate of 2%-54%, and the lumbar vertebrae are the most frequently affected[21,22]. It mainly manifests as spondylitis, spondylodiscitis and/or discitis. Back pain is the most common compliant in spinal brucellosis and reported by about half of the patients. Some patients with spinal brucellosis, who have back pain and sciatic radiculopathy, are misdiagnosed as having disease of an intervertebral disc and undergo surgery[23,24]. Given the high prevalence of backache, brucellosis should be considered as a differential diagnosis for sciatic and back pain, especially in the patients who are at occupational risk of brucellosis in endemic areas. Serological screening tests need to be conducted in all such patients[13,22,25,26], although serology may not be positive in all cases. A radionuclide scan can be a useful tool to determine the affected site[27,28]. MRI may be the best method to diagnosis and localize the cause of spondylodiscitis, epidural abscess, or compression on the spine and spinal nerves related to brucellosis. Epidural abscess is a rare complication of spinal brucellosis but can lead to severe outcomes, such as permanent neurological deficits, or even death if not treated timely.

Spondylitis

Spondylitis or vertebral osteomyelitis is inflammation and infection of vertebrae which has a prevalence rate of 2%-60% and mostly observed in men aged > 40 years old[22,29]. Lumbar (60%), sacral (19%) and cervical (12%) vertebrae were the most common affected sites, respectively, in a survey by Bozgeyik *et al*[30]. There are two types of spinal brucellosis, focal and diffuse. In focal involvement, osteomyelitis is localized in the anterior aspect of an endplate at the discovertebral junction, but in the diffuse type, osteomyelitis affects the entire vertebral endplate or the whole vertebral body[30,31]. Spondylitis is the dangerous complication of brucellosis due to its association with epidural, paravertebral and psoas abscess and potential resultant nerve compression. In one report, rapidly progressive spinal epidural abscess was observed following brucellar spondylitis, which was primarily misdiagnosed as a lumbar disc herniation[32]; delay in diagnosis and treatment were responsible for rapid progression of the disease. Another study reported a seronegative patient who developed a psoas abscess following brucellar spondylitis[33]. The basis of spondylitis diagnosis is microbiological or histopathological assessment of the tissue obtained by biopsy using a needle with computed tomography guidance. Epidural abscess is a rare complication of spondylitis and its diagnosis is difficult due to non-specific symptoms. Among the serological tests and radiological techniques, MRI is the most valuable method to diagnose spinal brucellosis or spinal epidural abscess[34,35]. MRI is also helpful to differentiate between pyogenic spondylitis and brucellar spondylitis[36].

Spondylodiscitis

This is simultaneous inflammation of vertebrae and disc, and usually occurs via hematogenous spread. It is the most severe form of osteoarticular involvement of brucellosis, because it makes a high rate of skeletal and neurological sequels despite therapy[32,37,38]. It is stated that 6%-85% of brucellosis osteoarticular involvements are related to brucellar spondylodiscitis. Lumbar (60%-69%), thoracic (19%) and cervical segments (6%-12%) are reported to be more involved in the spinal area[39-41]. Spondylodiscitis can be seen as single-focal and/or contiguous or non-contiguous multi-focal involvements. Multi-focal skeletal involvement in the spinal system was seen in 3%-14% of patients[41,42]. Radionuclide bone scintigraphy is an important technique in determination of musculoskeletal region of brucellosis. Increased uptake of the involved region on bone scintigraphy is more in favor of brucellar spondylodiscitis than tuberculous spondylodiscitis[43,44]. MRI is the choice for diagnosis of spondylodiscitis, epidural abscess and cord or root compression relevant to brucellosis[30,45,46]. In MRI, the lesion is found as destructive appearance (Pedro Pons' sign) at antero-superior corner of vertebrae accompanied by prominent osteosclerosis, which is a pathognomonic finding[47,48]. Back pain is the main symptom of spondylodiscitis, however, it is not a specific symptom and usually leads to a delay in diagnosis and late treatment. Therefore, in the endemic regions, it is necessary to consider spondylodiscitis as a differential diagnosis for long-term cervical, lumbar and sacral pain (especially among elderly patients) and perform screening serological tests to achieve early diagnosis and prevent its late complications[49,50].

Discitis

The intervertebral disc can be infected without spondylitis, which is named discitis. In addition to back pain, disc herniation and sciatica can be described by the patient with discitis[51,52], therefore, this disease should be considered in the differential diagnosis of those symptoms. It was observed that the simultaneous existence of spondylolysis and spondylolisthesis with brucellar discitis caused misdiagnosis[53].

Sacroiliitis

Large joints, like sacroiliac, are the most common regions of musculoskeletal involvement of brucellosis[31]. Sacroiliitis, or inflammation of sacroiliac joint, has been observed in nearly 80% of patients with focal complications and more frequently in adults[31,46]. Its clinical symptoms (septic or reactive forms) mimic acute low back pain or lumbar disc herniation and the back pain may radiate into the tight, however, chronic sacroiliitis is associated with chronic back pain[54,55]. Although low back pain is the important symptom, 24% of the patients were asymptomatic in a study[56]. It is reported that the rate of sacroiliitis is high in those patients who are infected with *B. melitensis* spp.[15,57]. Both of unilateral and bilateral forms of brucellar sacroiliitis have been reported[56,58]. Sacroiliitis was also simultaneously seen with dactylitis, olecranon bursitis, humerus osteomyelitis and iliac muscle abscess, and with other systemic diseases, like endocarditis, pyelonephritis and thyroiditis[59-62]. A study showed that high-resolution MRI has a higher sensitivity than scintigraphy in the diagnosis of brucellar sacroiliitis[63].

Limbs

Brucellosis with peripheral skeleton involvement is less prevalent compared with vertebral features. It can manifest as arthralgia, enthesopathy, osteomyelitis, arthritis, bursitis, tendonitis and tenosynovitis[64-67]. Arthritis occurs in 14%-26% of the patients suffering from acute, sub-acute or chronic brucellosis[68,69]. Knee, hip and ankle joints are among the most common peripheral regions affected by brucellosis and these patients present with arthritis[15,70]. Shoulders, wrists, elbows, interphalangeal and sternoclavicular joints may also be involved[28,69,71]. Chronic knee arthritis along with osteomyelitis have also been reported[72,73]. Multiple joint arthritis caused by brucellosis was reported in 17% of patients in a study[74]. In children, monoarthritis is the most common type of musculoskeletal brucellosis that mostly involves hip and knee joints, but adjacent bone osteomyelitis may also exist simultaneously[15,75,76]. Brucellosis can involve the peripheral joints through septic (with presence of pathogen) and reactive (lack of the pathogen) mechanisms[64,77].

Septic arthritis caused by brucellosis has been reported in the literature and it has been recommended that patients with septic arthritis living in the endemic areas, be examined in terms of brucellosis[68,74,78]. Septic arthritis in brucellosis progresses slowly and starts with small pericapsular erosions. Blood culture is positive in 20%–70% of such patients. Although synovial fluid assessment is the most useful diagnostic method, the isolation of the pathogen from synovial fluid is not easy[79]. In relation to the diagnosis of purulent arthritis, it may be necessary to rely on bone marrow culture in those patients with negative serology[80-82].

Knee arthritis has obvious symptoms and is less difficult to diagnose and treat due to easy access. However, the diagnosis and treatment of hip arthritis is more difficult and delay in diagnosis and treatment may lead to serious and irreparable complications, such as dislocation and necrosis of the femoral head[73,83]. Brucellosis should be considered in the differential diagnosis for a patient presenting with knee or hip arthritis symptoms in endemic regions to prevent misdiagnosis and serious complications. For example, misdiagnosis due to serological false negative test and improper interference in surgery was reported about brucellar arthritis of hip[84]. Almajid reported a rare case of brucellar olecranon bursitis whose serology was negative, but the blood and aspirate cultures were positive[85]. Brucellar arthritis following implantation of artificial knee and hip joints has been reported, which the medications may not be enough and removing the prosthesis might be needed[86-88]. Due to the synovial involvement of the disease, pathological evidence may not be found on radiograph in the early phase of infection.

Other manifestations

Spondyloarthritis following brucellosis was reported[77]. Sternal osteomyelitis caused by *B. melitensis* was observed following median sternotomy[89]. In a study by Ebrahimpour *et al*[69], brucellosis was attributed to sternoclavicular (4.5%), wrist (2.4%), elbow (1.07%) and shoulder (0.6%) arthritis. Delay in the diagnosis of brucellosis results in prolong disease duration which can lead to osteomyelitis or osteolytic lesions. Brucellar osteomyelitis has been observed in closed femur fracture and a pathologic humerus fracture[90,91]. It was also seen in association with prosthetic extra-articular hardware[92]. We reported the first case of brucellar osteomyelitis of pubic symphysis, who was symptom free within two-year follow-up despite inappropriate initial antibiotherapy[93].

LABORATORY INVESTIGATIONS

Laboratory tests following physical examinations are essential in order to diagnose brucellosis. Serology is often positive in the patients. In the acute infection, immunoglobulin M (IgM) antibody firstly appears, followed by immunoglobulin G (IgG) and immunoglobulin A (IgA)[14,94,95]. The Wright test, which is a standard agglutination test (SAT), measures the total amount of IgM and IgG antibodies, and the 2-ME test measures IgG antibody. In the endemic regions, a SAT titer ≥ 1:160 and 2-ME titer ≥ 1:80 is in favor of brucellosis diagnosis[94,96,97]. Enzyme-Linked Immunosorbent Assay (ELISA) is another type of serological test, but has less sensitivity and specificity[98]. Polymerase chain reaction (PCR) is a molecular method which can be very useful due to its quick procedure and high sensitivity and specificity, if it is available[99].

TREATMENT

The main purpose of antimicrobial medications in brucellosis is to treat the disease and its symptoms and signs, and to prevent the relapse. Combinations of doxycycline, streptomycin, gentamicin, ciprofloxacin, ofloxacin, co-trimoxazole (trimethoprim plus sulfamethoxazole) and rifampicin are used for antibiotherapy[100-102]. No standard therapy exists for osteoarticular brucellosis and physicians prescribe drugs based on their experiences and conditions of the disease (the involved site, and being complicated/uncomplicated). Triple regimen containing streptomycin (1 g daily) plus doxycycline (100 mg twice daily) plus rifampin (15 mg/kg daily) over 6 months had 100% efficacy on brucellar spondylitis[21]. Similar results were found using this regimen[103,104]. In contrast, double therapy with doxycycline and rifampin was associated with relapses[19,104]. With respect to brucellar spondylitis, patients need a long-term anti-bacterial medication (usually at least three months), mainly aiming to prevent relapses. Those patients who failed antibiotic therapy or presented with progressive neurological deficit, need surgical intervention[34,105,106]. The rate of surgical drainage in spinal brucellosis was reported in the range of 7.6%-33%[107]. In case of abscess in those patients with spondylodiscitis, treatment duration will be prolonged and surgery may be needed[47].

CONCLUSION

Brucellosis has variable clinical features and osteoarticular manifestations are the most common. Sacroiliac and spinal joints are the most frequently involved regions. Monoarthritis (knee/hip), sacroiliitis and spondylitis predominate in children, adults and the elderly, respectively. In order to diagnose the disease, physical examinations, laboratory tests and imaging techniques are needed. Brucellosis should be considered as a differential diagnosis for sciatic and back pain, especially in the endemic regions. Radiological assessments would be very helpful in such cases. Patients whose big joints, bone and artificial joints are involved, may be referred to a rheumatology center. Considering that these patients usually need orthopedic evaluation and treatment, it is recommended to refer them to an orthopedic center in order to prevent adverse effects caused by delay in the treatment. Early and appropriate diagnosis and treatment of the disease is the key of success in management of the patients with the osteoarticular manifestation of brucellosis. This is feasible by an early collaboration of orthopedic surgeon with a specialist in infectious diseases.

REFERENCES

1 **Dean AS**, Crump L, Greter H, Schelling E, Zinsstag J. Global burden of human brucellosis: a systematic review of disease frequency. *PLoS Negl Trop Dis* 2012; **6**: e1865 [PMID: 23145195 DOI: 10.1371/journal.pntd.0001865]

2 **Roushan MR**, Ahmadi SA, Gangi SM, Janmohammadi N, Amiri MJ. Childhood brucellosis in Babol, Iran. *Trop Doct* 2005; **35**: 229-231 [PMID: 16354479 DOI: 10.1258/004947505774938693]

3 **Seleem MN**, Boyle SM, Sriranganathan N. Brucellosis: a re-emerging zoonosis. *Vet Microbiol* 2010; **140**: 392-398 [PMID: 19604656 DOI: 10.1016/j.vetmic.2009.06.021]

4 **Papathanassiou BT**, Papachristou G, Hartofilakidis-Garofalidi. Brucellar spondylitis. Report of 6 cases. *Acta Orthop Scand* 1972; **43**: 384-391 [PMID: 4651059 DOI: 10.3109/17453677208998958]

5 **Al-Tawfiq JA**. Therapeutic options for human brucellosis. *Expert Rev Anti Infect Ther* 2008; **6**: 109-120 [PMID: 18251668 DOI: 10.1586/14787210.6.1.109]

6 **Hasanjani Roushan MR**, Mohrez M, Smailnejad Gangi SM, Soleimani Amiri MJ, Hajiahmadi M. Epidemiological features and clinical manifestations in 469 adult patients with brucellosis in Babol,

Northern Iran. *Epidemiol Infect* 2004; **132**: 1109-1114 [PMID: 15635968 DOI: 10.1017/S0950268804002833]
7 **Zhang J**, Sun GQ, Sun XD, Hou Q, Li M, Huang B, Wang H, Jin Z. Prediction and control of brucellosis transmission of dairy cattle in Zhejiang Province, China. *PLoS One* 2014; **9**: e108592 [PMID: 25386963 DOI: 10.1371/journal.pone.0108592]
8 **Adesokan HK**, Alabi PI, Ogundipe MA. Prevalence and predictors of risk factors for Brucellosis transmission by meat handlers and traditional healers' risk practices in Ibadan, Nigeria. *J Prev Med Hyg* 2016; **57**: E164-E171 [PMID: 27980381]
9 **Hasanjani Roushan MR**, Ebrahimpour S, Moulana Z. Different Clinical Presentations of Brucellosis. *Jundishapur J Microbiol* 2016; **9**: e33765 [PMID: 27284398 DOI: 10.5812/jjm.33765]
10 **Ahmadinejad Z**, Abdollahi A, Ziaee V, Domiraei Z, Najafizadeh SR, Jafari S, Ahmadinejad M. Prevalence of positive autoimmune biomarkers in the brucellosis patients. *Clin Rheumatol* 2016; **35**: 2573-2578 [PMID: 26781780 DOI: 10.1007/s10067-016-3171-7]
11 **Zheng R**, Xie S, Lu X, Sun L, Zhou Y, Zhang Y, Wang K. A Systematic Review and Meta-Analysis of Epidemiology and Clinical Manifestations of Human Brucellosis in China. *Biomed Res Int* 2018; **2018**: 5712920 [PMID: 29850535 DOI: 10.1155/2018/5712920]
12 **Ulu-Kilic A**, Metan G, Alp E. Clinical presentations and diagnosis of brucellosis. *Recent Pat Antiinfect Drug Discov* 2013; **8**: 34-41 [PMID: 22873352 DOI: 10.2174/1574891X11308010007]
13 **Dean AS**, Crump L, Greter H, Hattendorf J, Schelling E, Zinsstag J. Clinical manifestations of human brucellosis: a systematic review and meta-analysis. *PLoS Negl Trop Dis* 2012; **6**: e1929 [PMID: 23236528 DOI: 10.1371/journal.pntd.0001929]
14 **Galińska EM**, Zagórski J. Brucellosis in humans--etiology, diagnostics, clinical forms. *Ann Agric Environ Med* 2013; **20**: 233-238 [PMID: 23772567 DOI: 10.2166/wst.2013.207]
15 **Sanaei Dashti A**, Karimi A. Skeletal Involvement of Brucella melitensis in Children: A Systematic Review. *Iran J Med Sci* 2013; **38**: 286-292 [PMID: 24293781]
16 **Christopher S**, Umapathy BL, Ravikumar KL. Brucellosis: review on the recent trends in pathogenicity and laboratory diagnosis. *J Lab Physicians* 2010; **2**: 55-60 [PMID: 21346896 DOI: 10.4103/0974-2727.72149]
17 **Traxler RM**, Lehman MW, Bosserman EA, Guerra MA, Smith TL. A literature review of laboratory-acquired brucellosis. *J Clin Microbiol* 2013; **51**: 3055-3062 [PMID: 23824774 DOI: 10.1128/JCM.00135-13]
18 **Araj GF**. Update on laboratory diagnosis of human brucellosis. *Int J Antimicrob Agents* 2010; **36** Suppl 1: S12-S17 [PMID: 20692128 DOI: 10.1016/j.ijantimicag.2010.06.014]
19 **Ulu-Kilic A**, Karakas A, Erdem H, Turker T, Inal AS, Ak O, Turan H, Kazak E, Inan A, Duygu F, Demiraslan H, Kader C, Sener A, Dayan S, Deveci O, Tekin R, Saltoglu N, Aydın M, Horasan ES, Gul HC, Ceylan B, Kadanalı A, Karabay O, Karagoz G, Kayabas U, Turhan V, Engin D, Gulsun S, Elaldı N, Alabay S. Update on treatment options for spinal brucellosis. *Clin Microbiol Infect* 2014; **20**: O75-O82 [PMID: 24118178 DOI: 10.1111/1469-0691.12351]
20 **Lampropoulos C**, Kamposos P, Papaioannou I, Niarou V. Cervical epidural abscess caused by brucellosis. *BMJ Case Rep* 2012; **2012**: pii: bcr2012007070 [PMID: 23188848 DOI: 10.1136/bcr-2012-007070]
21 **Smailnejad Gangi SM**, Hasanjani Roushan MR, Janmohammadi N, Mehraeen R, Soleimani Amiri MJ, Khalilian E. Outcomes of treatment in 50 cases with spinal brucellosis in Babol, Northern Iran. *J Infect Dev Ctries* 2012; **6**: 654-659 [PMID: 23000864 DOI: 10.3855/jidc.2175]
22 **Lim KB**, Kwak YG, Kim DY, Kim YS, Kim JA. Back pain secondary to Brucella spondylitis in the lumbar region. *Ann Rehabil Med* 2012; **36**: 282-286 [PMID: 22639756 DOI: 10.5535/arm.2012.36.2.282]
23 **Yuksel KZ**, Senoglu M, Yuksel M, Gul M. Brucellar spondylo-discitis with rapidly progressive spinal epidural abscess presenting with sciatica. *Spinal Cord* 2006; **44**: 805-808 [PMID: 16683007 DOI: 10.1038/sj.sc.3101938]
24 **Samini F**, Gharedaghi M, Khajavi M, Samini M. The etiologies of low back pain in patients with lumbar disk herniation. *Iran Red Crescent Med J* 2014; **16**: e15670 [PMID: 25763198 DOI: 10.5812/ircmj.15670]
25 **Hartvigsen J**, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, Hoy D, Karppinen J, Pransky G, Sieper J, Smeets RJ, Underwood M; Lancet Low Back Pain Series Working Group. What low back pain is and why we need to pay attention. *Lancet* 2018; **391**: 2356-2367 [PMID: 29573870 DOI: 10.1016/S0140-6736(18)30480-X]
26 **Andriopoulos P**, Tsironi M, Deftereos S, Aessopos A, Assimakopoulos G. Acute brucellosis: presentation, diagnosis, and treatment of 144 cases. *Int J Infect Dis* 2007; **11**: 52-57 [PMID: 16651018 DOI: 10.1016/j.ijid.2005.10.011]
27 **Bosilkovski M**, Krteva L, Caparoska S, Dimzova M. Osteoarticular involvement in brucellosis: study of 196 cases in the Republic of Macedonia. *Croat Med J* 2004; **45**: 727-733 [PMID: 15578807 DOI: 10.1007/BF02914571]
28 **Bosilkovski M**, Zezoski M, Siskova D, Miskova S, Kotevska V, Labacevski N. Clinical characteristics of human brucellosis in patients with various monoarticular involvements. *Clin Rheumatol* 2016; **35**: 2579-2584 [PMID: 26861030 DOI: 10.1007/s10067-016-3207-z]
29 **Nickerson EK**, Sinha R. Vertebral osteomyelitis in adults: an update. *Br Med Bull* 2016; **117**: 121-138 [PMID: 26872859 DOI: 10.1093/bmb/ldw003]
30 **Bozgeyik Z**, Aglamis S, Bozdag PG, Denk A. Magnetic resonance imaging findings of musculoskeletal brucellosis. *Clin Imaging* 2014; **38**: 719-723 [PMID: 24849195 DOI: 10.1016/j.clinimag.2014.04.007]
31 **Arkun R**, Mete BD. Musculoskeletal brucellosis. *Semin Musculoskelet Radiol* 2011; **15**: 470-479 [PMID: 22081282 DOI: 10.1055/s-0031-1293493]
32 **Hu T**, Wu J, Zheng C, Wu D. Brucellar spondylodiscitis with rapidly progressive spinal epidural abscess showing cauda equina syndrome. *Spinal Cord Ser Cases* 2016; **2**: 15030 [PMID: 28053732 DOI: 10.1038/scsandc.2015.30]
33 **Bozbaş GT**, Ünübol Aİ, Gürer G. Seronegative brucellosis of the spine: A case of psoas abscess secondary to brucellar spondylitis. *Eur J Rheumatol* 2016; **3**: 185-187 [PMID: 28149665 DOI: 10.5152/eurjrheum.2015.15082]
34 **Reşorlu H**, Saçar S, Inceer BŞ, Akbal A, Gökmen F, Zateri C, Savaş Y. Cervical Spondylitis and Epidural Abscess Caused by Brucellosis: a Case Report and Literature Review. *Folia Med (Plovdiv)* 2016; **58**: 289-292 [PMID: 28068278 DOI: 10.1515/folmed-2016-0035]
35 **Bagheri AB**, Ahmadi K, Chokan NM, Abbasi B, Akhavan R, Bolvardi E, Soroureddin S. The Diagnostic Value of MRI in Brucella Spondylitis With Comparison to Clinical and Laboratory Findings. *Acta Inform*

Med 2016; **24**: 107-110 [PMID: 27147801 DOI: 10.5455/aim.2016.24.107-110]
36 **Li T**, Li W, Du Y, Gao M, Liu X, Wang G, Cui H, Jiang Z, Cui X, Sun J. Discrimination of pyogenic spondylitis from brucellar spondylitis on MRI. *Medicine (Baltimore)* 2018; **97**: e11195 [PMID: 29952971 DOI: 10.1097/MD.0000000000011195]
37 **Erdem H**, Elaldi N, Batirel A, Aliyu S, Sengoz G, Pehlivanoglu F, Ramosaco E, Gulsun S, Tekin R, Mete B, Balkan II, Sevgi DY, Giannitsioti E, Fragou A, Kaya S, Cetin B, Oktenoglu T, DoganCelik A, Karaca B, Horasan ES, Ulug M, Inan A, Kaya S, Arslanalp E, Ates-Guler S, Willke A, Senol S, Inan D, Guclu E, Tuncer-Ertem G, Meric-Koc M, Tasbakan M, Senbayrak S, Cicek-Senturk G, Sırmatel F, Ocal G, Kocagoz S, Kusoglu H, Guven T, Baran AI, Dede B, Yilmaz-Karadag F, Kose S, Yilmaz H, Aslan G, ALGallad DA, Cesur S, El-Sokkary R, Bekiroğlu N, Vahaboglu H. Comparison of brucellar and tuberculous spondylodiscitis patients: results of the multicenter "Backbone-1 Study". *Spine J* 2015; **15**: 2509-2517 [PMID: 26386176 DOI: 10.1016/j.spinee.2015.09.024]
38 **Mantur BG**, Amarnath SK, Shinde RS. Review of clinical and laboratory features of human brucellosis. *Indian J Med Microbiol* 2007; **25**: 188-202 [PMID: 17901634 DOI: 10.4103/0255-0857.34758]
39 **Tekaya R**, Tayeb MH, El Amri N, Sahli H, Saidane O, Mahmoud I, Abdelmoula L. THU0257 Brucella Spondylodiscitis: A Study of Nineteen Cases. *Ann Rheum Dis* 2015; **74**: 290 [DOI: 10.1136/annrheumdis-2015-eular.6083]
40 **Koubaa M**, Maaloul I, Marrakchi C, Lahiani D, Hammami B, Mnif Z, Ben Mahfoudh K, Hammami A, Ben Jemaa M. Spinal brucellosis in South of Tunisia: review of 32 cases. *Spine J* 2014; **14**: 1538-1544 [PMID: 24331843 DOI: 10.1016/j.spinee.2013.09.027]
41 **Chelli Bouaziz M**, Ladeb MF, Chakroun M, Chaabane S. Spinal brucellosis: a review. *Skeletal Radiol* 2008; **37**: 785-790 [PMID: 17962938 DOI: 10.1007/s00256-007-0371-x]
42 **Mrabet D**, Mizouni H, Khiari H, Rekik S, Chéour E, Meddeb N, Mnif E, Mrabet AB, Srairi HS, Sellami S. Brucellar spondylodiscitis affecting non-contiguous spine levels. *BMJ Case Rep* 2011; **2011**: pii: bcr0120113788 [PMID: 22700074 DOI: 10.1136/bcr.01.2011.3788]
43 **Colmenero JD**, Ruiz-Mesa JD, Plata A, Bermúdez P, Martín-Rico P, Queipo-Ortuño MI, Reguera JM. Clinical findings, therapeutic approach, and outcome of brucellar vertebral osteomyelitis. *Clin Infect Dis* 2008; **46**: 426-433 [PMID: 18181740 DOI: 10.1086/525266]
44 **Bouaziz MC**, Bougamra I, Kaffel D, Hamdi W, Ghannouchi M, Kchir MM. Noncontiguous multifocal spondylitis: an exceptional presentation of spinal brucellosis. *Tunis Med* 2010; **88**: 280-284 [PMID: 20446265]
45 **Yang X**, Zhang Q, Guo X. Value of magnetic resonance imaging in brucellar spondylodiscitis. *Radiol Med* 2014; **119**: 928-933 [PMID: 24862632 DOI: 10.1007/s11547-014-0416-x]
46 **Bozgeyik Z**, Ozdemir H, Demirdag K, Ozden M, Sonmezgoz F, Ozgocmen S. Clinical and MRI findings of brucellar spondylodiscitis. *Eur J Radiol* 2008; **67**: 153-158 [PMID: 17706906 DOI: 10.1016/j.ejrad.2007.07.002]
47 **Mehanic S**, Baljic R, Mulabdic V, Huric-Jusufi I, Pinjo F, Topalovic-Cetkovic J, Hadziosmanovic V. Osteoarticular manifestations of brucellosis. *Med Arch* 2012; **66**: 24-26 [PMID: 22937686 DOI: 10.5455/medarh.2012.66.s24-s26]
48 **Tuna N**, Ogutlu A, Gozdas HT, Karabay O. Pedro Pons' sign as a Brucellosis complication. *Indian J Pathol Microbiol* 2011; **54**: 183-184 [PMID: 21393913 DOI: 10.4103/0377-4929.77398]
49 **Raptopoulou A**, Karantanas AH, Poumboulidis K, Grollios G, Raptopoulou-Gigi M, Garyfallos A. Brucellar spondylodiscitis: noncontiguous multifocal involvement of the cervical, thoracic, and lumbar spine. *Clin Imaging* 2006; **30**: 214-217 [PMID: 16632160 DOI: 10.1016/j.clinimag.2005.10.006]
50 **Lebre A**, Velez J, Seixas D, Rabadão E, Oliveira J, Saraiva da Cunha J, Silvestre AM. [Brucellar spondylodiscitis: case series of the last 25 years]. *Acta Med Port* 2014; **27**: 204-210 [PMID: 24813488 DOI: 10.20344/amp.4117]
51 **Demirci I**. Brucella diskitis mimicking herniation without spondylitis; MRI findings. *Zentralbl Neurochir* 2003; **64**: 178-181 [PMID: 14634883 DOI: 10.1055/s-2003-44622]
52 **Yilmaz C**, Akar A, Civelek E, Köksay B, Kabatas S, Cansever T, Caner H. Brucellar discitis as a cause of lumbar disc herniation: a case report. *Neurol Neurochir Pol* 2010; **44**: 516-519 [PMID: 21082497 DOI: 10.1016/S0028-3843(14)60143-2]
53 **Guglielmino A**, Sorbello M, Murabito P, Naimo J, Palumbo A, Lo Giudice E, Giuffrida S, Fazzio S, Parisi G, Mangiameli S. A case of lumbar sciatica in a patient with spondylolysis and spondylolysthesis and underlying misdiagnosed brucellar discitis. *Minerva Anestesiol* 2007; **73**: 307-312 [PMID: 17529921 DOI: 10.1016/j.jclinane.2007.02.001]
54 **Ozgül A**, Yazicioğlu K, Gündüz S, Kalyon TA, Arpacioğlu O. Acute brucella sacroiliitis: clinical features. *Clin Rheumatol* 1998; **17**: 521-523 [PMID: 9890684 DOI: 10.1007/BF01451292]
55 **Thoma S**, Patsiogiannis N, Dempegiotis P, Filiopoulos K. A report of two cases of brucellar sacroiliitis without systemic manifestations in Greece. *J Pediatr Orthop* 2009; **29**: 375-379 [PMID: 19461380 DOI: 10.1097/BPO.0b013e3181a610c0]
56 **Gheita TA**, Sayed S, Azkalany GS, El Fishawy HS, Aboul-Ezz MA, Shaaban MH, Bassyouni RH. Subclinical sacroiliitis in brucellosis. Clinical presentation and MRI findings. *Z Rheumatol* 2015; **74**: 240-245 [PMID: 25090956 DOI: 10.1007/s00393-014-1465-1]
57 **Ariza J**, Pujol M, Valverde J, Nolla JM, Rufí G, Viladrich PF, Corredoira JM, Gudiol F. Brucellar sacroiliitis: findings in 63 episodes and current relevance. *Clin Infect Dis* 1993; **16**: 761-765 [PMID: 8329507 DOI: 10.1093/clind/16.6.761]
58 **Ozturk M**, Yavuz F, Altun D, Ulubay M, Firatligil FB. Postpartum Bilateral Sacroiliitis caused by Brucella Infection. *J Clin Diagn Res* 2015; **9**: QD07-QD08 [PMID: 26675497 DOI: 10.7860/JCDR/2015/14628.6765]
59 **Mamalis IP**, Panagopoulos MI, Papanastasiou DA, Bricteux G. [Sacroilitis and osteomyelitis of the humeral bone du to Brucella melitensis in an adolescent]. *Rev Med Liege* 2008; **63**: 742-745 [PMID: 19180835]
60 **Turan H**, Serefhanoglu K, Karadeli E, Timurkaynak F, Arslan H. A case of brucellosis with abscess of the iliacus muscle, olecranon bursitis, and sacroiliitis. *Int J Infect Dis* 2009; **13**: e485-e487 [PMID: 19398360 DOI: 10.1016/j.ijid.2009.02.002]
61 **Acar A**, Turhan V, Diktaş H, Oncül O, Cavuşlu S. [A case of brucellosis complicated with endocarditis, pyelonephritis, sacroileitis and thyroiditis]. *Mikrobiyol Bul* 2009; **43**: 141-145 [PMID: 19334391]
62 **Batmaz IB**, Tekin R, Sariyildiz MA, Deveci O, Cevik R. A Case of Brucellosis with simultaneous dactylitis and sacroiliitis. *Journal of Medical Cases* 2012; **3**: 304-307 [DOI: 10.4021/jmc701w]
63 **Bilgeturk A**, Gul HC, Karakas A, Mert G, Artuk C, Eyigun CP. Can imaging modalities be used as

follow-up criteria after brucellar sacroiliitis treatment? *J Infect Dev Ctries* 2017; **11**: 123-128 [PMID: 28248672 DOI: 10.3855/jidc.6599]
64 **Kazak E**, Akalın H, Yılmaz E, Heper Y, Mıstık R, Sınırtaş M, Özakın C, Göral G, Helvacı S. Brucellosis: a retrospective evaluation of 164 cases. *Singapore Med J* 2016; **57**: 624-629 [PMID: 26768063 DOI: 10.11622/smedj.2015163]
65 **Ismayilova R**, Nasirova E, Hanou C, Rivard RG, Bautista CT. Patterns of brucellosis infection symptoms in azerbaijan: a latent class cluster analysis. *J Trop Med* 2014; **2014**: 593873 [PMID: 25580137 DOI: 10.1155/2014/593873]
66 **Franco MP**, Mulder M, Gilman RH, Smits HL. Human brucellosis. *Lancet Infect Dis* 2007; **7**: 775-786 [PMID: 18045560 DOI: 10.1016/S1473-3099(07)70286-4]
67 **Tekin R**, Ceylan Tekin F, Ceylan Tekin R, Cevik R. Brucellosis as a primary cause of tenosynovitis of the extensor muscle of the arm. *Infez Med* 2015; **23**: 257-260 [PMID: 26397296]
68 **Wong TM**, Lou N, Jin W, Leung F, To M, Leung F. Septic arthritis caused by Brucella melitensis in urban Shenzhen, China: a case report. *J Med Case Rep* 2014; **8**: 367 [PMID: 25394500 DOI: 10.1186/1752-1947-8-367]
69 **Ebrahimpour S**, Bayani M, Moulana Z, Hasanjani Roushan MR. Skeletal complications of brucellosis: A study of 464 cases in Babol, Iran. *Caspian J Intern Med* 2017; **8**: 44-48 [PMID: 28503282]
70 **Geyik MF**, Gür A, Nas K, Cevik R, Saraç J, Dikici B, Ayaz C. Musculoskeletal involvement of brucellosis in different age groups: a study of 195 cases. *Swiss Med Wkly* 2002; **132**: 98-105 [PMID: 11971204]
71 **Mousa AR**, Muhtaseb SA, Almudallal DS, Khodeir SM, Marafie AA. Osteoarticular complications of brucellosis: a study of 169 cases. *Rev Infect Dis* 1987; **9**: 531-543 [PMID: 3496650 DOI: 10.1093/clinids/9.3.531]
72 **Wernaers P**, Handelberg F. Brucellar arthritis of the knee: a case report with delayed diagnosis. *Acta Orthop Belg* 2007; **73**: 795-798 [PMID: 18260497 DOI: 10.1080/17453670710014671]
73 **Ayaşlioğlu E**, Ozlük O, Kiliç D, Kaygusuz S, Kara S, Aydin G, Cokca F, Tekeli E. A case of brucellar septic arthritis of the knee with a prolonged clinical course. *Rheumatol Int* 2005; **25**: 69-71 [PMID: 15007623 DOI: 10.1007/s00296-004-0453-1]
74 **Charalambides C**, Papademetriou K, Sgouros S, Sakas D. Brucellosis of the spine affecting multiple non-contiguous levels. *Br J Neurosurg* 2010; **24**: 589-591 [PMID: 20707678 DOI: 10.3109/02688697.2010.499153]
75 **Fruchtman Y**, Segev RW, Golan AA, Dalem Y, Tailakh MA, Novak V, Peled N, Craiu M, Leibovitz E. Epidemiological, diagnostic, clinical, and therapeutic aspects of Brucella bacteremia in children in southern Israel: a 7-year retrospective study (2005-2011). *Vector Borne Zoonotic Dis* 2015; **15**: 195-201 [PMID: 25793475 DOI: 10.1089/vbz.2014.1726]
76 **Alshaalan MA**, Alalola SA, Almuneef MA, Albanyan EA, Balkhy HH, AlShahrani DA, AlJohani S. Brucellosis in children: Prevention, diagnosis and management guidelines for general pediatricians endorsed by the Saudi Pediatric Infectious Diseases Society (SPIDS). *IJPAM* 2014; **1**: 40-46 [DOI: 10.1016/j.ijpam.2014.09.004]
77 **Gotuzzo E**, Alarcón GS, Bocanegra TS, Carrillo C, Guerra JC, Rolando I, Espinoza LR. Articular involvement in human brucellosis: a retrospective analysis of 304 cases. *Semin Arthritis Rheum* 1982; **12**: 245-255 [PMID: 6101216 DOI: 10.1016/0049-0172(82)90064-6]
78 **Elzein FE**, Sherbeeni N. Brucella Septic Arthritis: Case Reports and Review of the Literature. *Case Rep Infect Dis* 2016; **2016**: 4687840 [PMID: 27200196 DOI: 10.1155/2016/4687840]
79 **Hasanoglu I**, Guven T, Maras Y, Guner R, Tasyaran MA, Acikgoz ZC. Brucellosis as an aetiology of septic arthritis. *Trop Doct* 2014; **44**: 48-49 [PMID: 24231687 DOI: 10.1177/0049475513512645]
80 **Işeri S**, Bulut C, Yetkin MA, Kinikli S, Demiröz AP, Tülek N. [Comparison of the diagnostic value of blood and bone marrow cultures in brucellosis]. *Mikrobiyol Bul* 2006; **40**: 201-206 [PMID: 17001849]
81 **Velan GJ**, Leitner J, Folman Y, Gepstein R. Brucellosis of the spine with a synchronous Staphylococcus aureus pyogenic elbow infection. *Eur Spine J* 1997; **6**: 284-285 [PMID: 9294756 DOI: 10.1007/BF01322454]
82 **Lee KH**, Kang H, Kim T, Choi S. A case of unusual septic knee arthritis with Brucella abortus after arthroscopic meniscus surgery. *Acta Orthop Traumatol Turc* 2016; **50**: 385-387 [PMID: 27130400 DOI: 10.3944/AOTT.2015.14.0287]
83 **Cerit ET**, Aydın M, Azap A. A case of brucellar monoarthritis and review of the literature. *Rheumatol Int* 2012; **32**: 1465-1468 [PMID: 21461852 DOI: 10.1007/s00296-011-1917-8]
84 **Janmohammadi N**, Roushan MR. False negative serological tests may lead to misdiagnosis and mismanagement in osteoarticular brucellosis. *Trop Doct* 2009; **39**: 88-90 [PMID: 19299290 DOI: 10.1258/td.2008.080042]
85 **Almajid FM**. A Rare Form of Brucella Bursitis with Negative Serology: A Case Report and Literature Review. *Case Rep Infect Dis* 2017; **2017**: 9802532 [PMID: 28337351 DOI: 10.1155/2017/9802532]
86 **Mortazavi SMJ**, Sobhan MR, Mazoochy H. Brucella Arthritis Following Total Knee Arthroplasty in a Patient with Hemophilia: A Case Report. *Arch Bone Jt Surg* 2017; **5**: 342-346 [PMID: 29226208]
87 **Lewis JM**, Folb J, Kalra S, Squire SB, Taegtmeyer M, Beeching NJ. Brucella melitensis prosthetic joint infection in a traveller returning to the UK from Thailand: Case report and review of the literature. *Travel Med Infect Dis* 2016; **14**: 444-450 [PMID: 27591088 DOI: 10.1016/j.tmaid.2016.08.010]
88 **Kasim RA**, Araj GF, Afeiche NE, Tabbarah ZA. Brucella infection in total hip replacement: case report and review of the literature. *Scand J Infect Dis* 2004; **36**: 65-67 [PMID: 15000565 DOI: 10.1080/00365540310017456]
89 **Chin YT**, Krishnan M, Burns P, Qamruddin A, Hasan R, Dodgson AR. Brucella melitensis sternal osteomyelitis following median sternotomy. *J Infect Chemother* 2014; **20**: 574-576 [PMID: 24910374 DOI: 10.1016/j.jiac.2014.04.011]
90 **Abrahams MA**, Tylkowski CM. Brucella osteomyelitis of a closed femur fracture. *Clin Orthop Relat Res* 1985; 194-196 [PMID: 3919984 DOI: 10.1097/00003086-198505000-00021]
91 **Luc M**, Armingeat T, Pham T, Legré V, Lafforgue P. Chronic Brucella infection of the humerus diagnosed after a spontaneous fracture. *Joint Bone Spine* 2008; **75**: 229-231 [PMID: 17977771 DOI: 10.1016/j.jbspin.2007.04.024]
92 **Navarro V**, Solera J, Martínez-Alfaro E, Sáez L, Escribano E, Pérez-Flores JC. Brucellar osteomyelitis involving prosthetic extra-articular hardware. *J Infect* 1997; **35**: 192-194 [PMID: 9354359 DOI: 10.1016/S0163-4453(97)91941-1]
93 **Mansoori D**, Gangi EN, Touzet P. [Brucellosis of the pubic symphysis. Apropos of a case. Review of the

literature]. *Rev Chir Orthop Reparatrice Appar Mot* 1996; **82**: 753-756 [PMID: 9097862]
94 **Pabuccuoglu O**, Ecemis T, El S, Coskun A, Akcali S, Sanlidag T. Evaluation of serological tests for diagnosis of brucellosis. *Jpn J Infect Dis* 2011; **64**: 272-276 [PMID: 21788700 DOI: 10.1016/j.medmal.2011.01.010]
95 **Al Dahouk S**, Nöckler K. Implications of laboratory diagnosis on brucellosis therapy. *Expert Rev Anti Infect Ther* 2011; **9**: 833-845 [PMID: 21810055 DOI: 10.1586/eri.11.55]
96 **Roushan MR**, Amiri MJ, Laly A, Mostafazadeh A, Bijani A. Follow-up standard agglutination and 2-mercaptoethanol tests in 175 clinically cured cases of human brucellosis. *Int J Infect Dis* 2010; **14**: e250-e253 [PMID: 19648045 DOI: 10.1016/j.ijid.2009.05.008]
97 **Nielsen K**, Yu WL. Serological diagnosis of brucellosis. *Prilozi* 2010; **31**: 65-89 [PMID: 20703184 DOI: 10.1080/00480169.1969.33804]
98 **Sanaei Dashti A**, Karimi A, Javad V, Shiva F, Fallah F, Alaei MR, Angoti G, Pournasiri Z. ELISA Cut-off Point for the Diagnosis of Human Brucellosis; a Comparison with Serum Agglutination Test. *Iran J Med Sci* 2012; **37**: 9-14 [PMID: 23115425]
99 **Wang Y**, Wang Z, Zhang Y, Bai L, Zhao Y, Liu C, Ma A, Yu H. Polymerase chain reaction-based assays for the diagnosis of human brucellosis. *Ann Clin Microbiol Antimicrob* 2014; **13**: 31 [PMID: 25082566 DOI: 10.1186/s12941-014-0031-7]
100 **Buzgan T**, Karahocagil MK, Irmak H, Baran AI, Karsen H, Evirgen O, Akdeniz H. Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. *Int J Infect Dis* 2010; **14**: e469-e478 [PMID: 19910232 DOI: 10.1016/j.ijid.2009.06.031]
101 **Ioannou S**, Karadima D, Pneumaticos S, Athanasiou H, Pontikis J, Zormpala A, Sipsas NV. Efficacy of prolonged antimicrobial chemotherapy for brucellar spondylodiscitis. *Clin Microbiol Infect* 2011; **17**: 756-762 [PMID: 20518794 DOI: 10.1111/j.1469-0691.2010.03272.x]
102 **Jia B**, Zhang F, Lu Y, Zhang W, Li J, Zhang Y, Ding J. The clinical features of 590 patients with brucellosis in Xinjiang, China with the emphasis on the treatment of complications. *PLoS Negl Trop Dis* 2017; **11**: e0005577 [PMID: 28459811 DOI: 10.1371/journal.pntd.0005577]
103 **Ulu-Kilic A**, Sayar MS, Tütüncü E, Sezen F, Sencan I. Complicated brucellar spondylodiscitis: experience from an endemic area. *Rheumatol Int* 2013; **33**: 2909-2912 [PMID: 23124695 DOI: 10.1007/s00296-012-2555-5]
104 **Bayindir Y**, Sonmez E, Aladag A, Buyukberber N. Comparison of five antimicrobial regimens for the treatment of brucellar spondylitis: a prospective, randomized study. *J Chemother* 2003; **15**: 466-471 [PMID: 14598939 DOI: 10.1179/joc.2003.15.5.466]
105 **Solera J**, Lozano E, Martínez-Alfaro E, Espinosa A, Castillejos ML, Abad L. Brucellar spondylitis: review of 35 cases and literature survey. *Clin Infect Dis* 1999; **29**: 1440-1449 [PMID: 10585793 DOI: 10.1086/313524]
106 **Alp E**, Doganay M. Current therapeutic strategy in spinal brucellosis. *Int J Infect Dis* 2008; **12**: 573-577 [PMID: 18539496 DOI: 10.1016/j.ijid.2008.03.014]
107 **Kaptan F**, Gulduren HM, Sarsilmaz A, Sucu HK, Ural S, Vardar I, Coskun NA. Brucellar spondylodiscitis: comparison of patients with and without abscesses. *Rheumatol Int* 2013; **33**: 985-992 [PMID: 22842981 DOI: 10.1007/s00296-012-2491-4]

P- Reviewer: Anand A, Papachristou G
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Wu YXJ

World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 February 18; 10(2): 63-70

DOI: 10.5312/wjo.v10.i2.63

ISSN 2218-5836 (online)

MINIREVIEWS

Allergy in total knee replacement surgery: Is it a real problem?

Maristella F Saccomanno, Giuseppe Sircana, Giulia Masci, Gianpiero Cazzato, Michela Florio, Luigi Capasso, Marco Passiatore, Giovanni Autore, Giulio Maccauro, Enrico Pola

ORCID number: Maristella Francesca Saccomanno (0000-0001-7399-8762); Giuseppe Sircana (0000-0002-4147-3520); Giulia Masci (0000-0002-2137-0145); Gianpiero Cazzato (0000-0002-3671-6989); Michela Florio (0000-0003-2273-7006); Luigi Capasso (0000-0002-2691-5239); Marco Passiatore (0000-0002-4361-6505); Giovanni Autore (0000-0002-5895-8313); Giulio Maccauro (0000-0002-7359-268X); Enrico Pola (0000-0001-5350-3910).

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

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

Manuscript source: Invited manuscript

Maristella F Saccomanno, Giuseppe Sircana, Giulia Masci, Gianpiero Cazzato, Michela Florio, Luigi Capasso, Marco Passiatore, Giovanni Autore, Giulio Maccauro, Enrico Pola, Department of Orthopaedics and Traumatology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome 00168, Italy

Corresponding author: Enrico Pola, MD, PhD, Associate Professor, Department of Orthopaedics and Traumatology, Fondazione Policlinico Universitario A. Gemelli IRCCS, L.go Agostino Gemelli, 8, Rome 00168, Italy. enrico.pola@tiscali.it
Telephone: +39-06-30154326
Fax: +39-06-3051161

Abstract

Total knee arthroplasty is a common procedure, with extremely good clinical results. Despite this success, it produces 20% unsatisfactory results. Among the causes of these failures is metal hypersensitivity. Metal sensitization is higher in patients with a knee arthroplasty than in the general population and is even higher in patients undergoing revision surgery. However, a clear correlation between metal sensitization and symptomatic knee after surgery has not been ascertained. Surely, patients with a clear history of metal allergy must be carefully examined through dermatological and laboratory testing before surgery. There is no globally accepted diagnostic algorithm or laboratory test to diagnose metal hypersensitivity or metal reactions. The patch test is the most common test to determine metal hypersensitivity, though presenting some limitations. Several laboratory assays have been developed, with a higher sensitivity compared to patch testing, yet their clinical availability is not widespread, due to high costs and technical complexity. Symptoms of a reaction to metal implants present across a wide spectrum, ranging from pain and cutaneous dermatitis to aseptic loosening of the arthroplasty. However, although cutaneous and systemic hypersensitivity reactions to metals have arisen, thereby increasing concern after joint arthroplasties, allergies against implant materials remain quite rare and not a well-known problem. The aim of the following paper is to provide an overview on diagnosis and management of metal hypersensitivity in patients who undergo a total knee arthroplasty in order clarify its real importance.

Key words: Knee arthroplasty; Total knee arthroplasty; Metal hypersensitivity; Metal allergy; Non-allergenic implants

Received: October 7, 2018
Peer-review started: October 7, 2018
First decision: October 19, 2018
Revised: December 26, 2018
Accepted: January 5, 2019
Article in press: January 6, 2019
Published online: February 18, 2019

Core tip: Metal hypersensitivity may be a cause of failure for total knee arthroplasty, although a clear correlation between metal sensitization and symptomatic knee after surgery has not been ascertained. Patients with a clear history of metal allergy, must be carefully examined through dermatological and laboratory testing before surgery. However, despite the increase in cutaneous and systemic hypersensitivity reactions to metals, which raise concern about joint arthroplasties, allergies against implant materials remain quite rare and an unexplored issue.

Citation: Saccomanno MF, Sircana G, Masci G, Cazzato G, Florio M, Capasso L, Passiatore M, Autore G, Maccauro G, Pola E. Allergy in total knee replacement surgery: Is it a real problem? *World J Orthop* 2019; 10(2): 63-70
URL: https://www.wjgnet.com/2218-5836/full/v10/i2/63.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i2.63

INTRODUCTION

Osteoarthritis is a degenerative disease affecting an important part of the population aged 65 or older, with a reported prevalence higher than 30% in the United States[1]. Its incidence increases with age and overweight status[2]. Its aetiology has not been completely clarified, but likely entails a multifactorial interplay of mechanical and biological causes. Various molecular mediators involved in the development of osteoarthritis have been identified[3-4], although their clinical relevance has yet to be demonstrated. Surgical therapy is required in cases of advanced osteoarthritis.

Total knee arthroplasty (TKA) is a common procedure performed in increasing numbers worldwide[5]. Despite its great success, up to 20% of patients still complain of unsatisfactory results[6]. Although several causes, such as infection or malalignment, have been shown to be most commonly responsible for dissatisfaction and poor outcomes, in the last decades another possible explanation has gained popularity: implant-related metal (or less frequently cement) hypersensitivity. In other words, an immunological reaction to the metallic portion of TKA components or to the bone cement[7,8]. The hypothesis is supported by studies showing a higher prevalence of positive patch tests after TKA implantation[9-11]. However, even if local and systemic exposure to metals deriving from the implanted device can cause sensitization, the positivity of a metal test cannot be held as a proof of symptom causality[12]. As a matter of fact, it has also been shown that many patients who underwent TKA did not develop any complication after surgery, despite being sensitive to metal[13].

Looking at the epidemiologic data, 10% to 15% of the general population present dermatologic symptoms caused by metal hypersensitivity. Nickel is responsible in the majority of cases, while cobalt, chromium, beryllium and less frequently tantalum, titanium and vanadium are responsible for dermal symptomatology in a smaller number of cases[14]. However, taking into consideration patients undergoing TKA revision, it has been reported that less than 2% showed “metal related pathologies”[15]. Bone cement hypersensitivity is even more rare[16]. Therefore, it appears quite clear that the role of metal or cement allergies in TKA failures remains a controversial issue. The aim of the following paper is to provide an overview on diagnosis and management of metal hypersensitivity in patients who undergo a TKA in order clarify its real importance.

CAN PATIENTS WITH AN INCREASED RISK OF METAL HYPERSENSITIVITY BE RECOGNIZED BEFORE SURGERY?

Patient-reported allergies and history (family history, exposure, occupation, and self-reported allergies) are of utmost importance as a first diagnostic step. Although there are no guidelines, routine preoperative evaluation in patients reporting no history of adverse cutaneous reactions to metals or history of adverse events related to previous implant of metallic devices is not necessary and therefore not recommended. Moreover, use of conventional cobalt-chromium implants is also allowed without additional preoperative investigation, even in patients reporting only mild cutaneous reactions. An opposite consideration is that it is mandatory for patients reporting substantial cutaneous or systemic reactions to undergo patch testing before TKA[9,17]

(Figure 1).

SYMPTOMS AND DIAGNOSIS

After TKA implantation, clinical presentation of metal hypersensitivity is unspecific and symptoms are common to other complications. Metal hypersensitivity is a very rare condition and is usually a diagnosis of exclusion. The most common symptoms are joint effusion, swelling, stiffness, persistent pain at rest and decreased range of motion; less frequently, it is characterized by eczematous dermatitis, which can be local or generalized, extended to the neck, buttock and extremities[18]. Rarely, a general complication may occur, such as rhinitis, itching or asthma, hair loss and alopecia. The time range of first symptoms is variable, from 4 wk to 2 yr[19].

As a matter of fact, residual pain after TKA has many causes that need to be ruled out before a metal hypersensitivity is taken into consideration (Figure 2). An infection must be first ruled out by blood tests (erythrocyte sedimentation rate and C-reactive protein) and joint synovial fluid aspirations. Moreover, other common causes of pain, such as midflexion instability, component malalignment with patellar maltracking, crepitation and patellar clunk, can be ruled out by physical examination. Less common causes are early aseptic loosening and avascular necrosis of the patella[20]. Surely, a metal hypersensitivity should be suspected in patients with a clear self-reported history of metal reactions.

Radiographic images can show osteolytic lesions in the proximity of the femoral and tibial components, which formed as a result of the inflammatory response and can lead to aseptic loosening of the implant, loss of tibial posterior slope and setting of the tibial base plate into varus, as compared to the previous images taken after surgery[21]. The diagnostic algorithm is based on metal hypersensitivity aetiology. The immunological reactive mechanism to metallic components is still an unclear and debated issue. Metal hypersensitivity is generally a type IV allergic reaction, meaning that immune response acts through a delayed cell-mediated response, with activation of specific CD4+ T lymphocytes, macrophages, dendritic cells and other immune cells found within the synovial tissue. This response produces tissue inflammation and periprosthetic tissue damage, powered by the incretion of cytokines involved in the pro-inflammatory pathway, including interleukin (IL)-1, IL-12, IL-6, tumour necrosis factor and interferon-gamma. In particular, it must be highlighted that this mechanism of metal hypersensitivity is different from those that characterize lymphocyte-dominated non-septic vasculitis-associated lesions and pseudotumours that are reported as adverse local tissue reactions after metal-on-metal total hip arthtroplasty[18].

No generally accepted and reliable tests are available for the clinical diagnosis of metal hypersensitivity after TKA[22]. Patch test is the most frequent method used to diagnose contact allergy to metals and is, up to now, considered the gold standard. However, its validity faces a lot of controversy, and its sensitivity and specificity are 77% and 71%, respectively[18]. It is an *in vivo* test, widely available and easy to apply, so it can provide results within a few days. The hypothesis that cutaneous and systemic hypersensitivities are strictly related to the presence of metal after TKA is supported by a series of studies that found an important prevalence of positive patch tests after implantation of metallic TKA components. As already highlighted, the most common sensitizations to metal are with nickel, chromium and cobalt[19]. Patch test can be performed not only for metals but also for cement components, by using adhesive patches loaded with a known concentration of specific allergens compared with vaseline. However, patch tests also present some important limitations, namely skin reactions that are different compared with deep tissue layers and the joint environment, with the potential of an antigen-presenting mechanism being altered thereby. Patch tests also have different preparation and plots which can differ from subject to subject and tester to tester[23]. According to the published guidelines of the German Contact Allergy Group, patch testing should be exclusively regarded as a mean to "verify or exclude metal allergy in patients with a corresponding history"[24]. The American Contact Dermatitis Society has defined criteria for the diagnosis of post-implantation metal hypersensitivity contact dermatitis[25]. In particular, they proposed four major and six minor criteria, reported here in Table 1.

Several laboratory assays have been proposed over the years. Lymphocyte transformation test is an *in vitro* test which analyses the proliferation of lymphocytes obtained by peripheral blood draw after contact with a metallic implant. It compares peripheral blood lymphocyte proliferation upon a 7 d incubation period, with and without the addition of metal antigen. Lymphocyte transformation test sensitivity is higher than patch testing, and provides quantifiable data and is very reproducible.

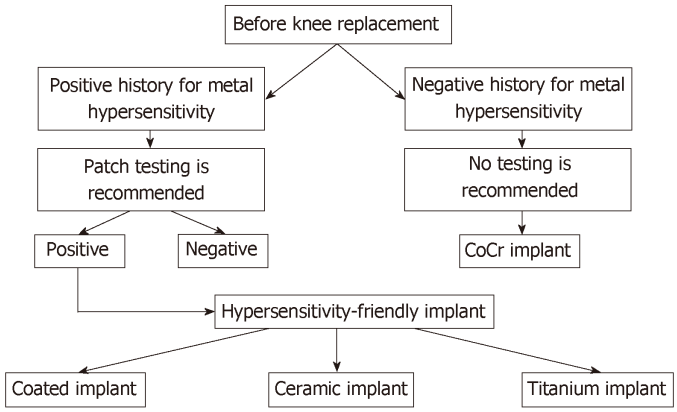

Figure 1 Preoperative diagnostic algorithm to select patients requiring hypersensitivity-friendly implants.

Despite these positive aspects, this test is poorly available and there are a limited number of allergens that can be tested[19].

Even if many cytokines may be overexpressed in other conditions and diseases, enzyme-linked immunosorbent assay (commonly known as ELISA) testing can be used for measurement of cytokines released by stimulated cells.

Other *in vitro* tests are the Modified Lymphocyte Stimulation Test, the Lymphocyte Activation Test and the Leukocyte Migration Inhibition Test. The Modified Lymphocyte Stimulation Test has been described as a reliable test to diagnose systemic metal hypersensitivity, but it is currently impossible to use in large-scale settings because of its costs and limited availability[26]. The Lymphocyte Activation Test quantifies the expression of specific receptors (CD69) on circulating mononuclear cells after stimulation with metals. The Leukocyte Migration Inhibition Test measures the speed of migration of leukocytes after contact with sensitizing allergens. Another technique, even if not yet disseminated, is confocal microscopy, which can demonstrate intracellular abnormalities of the stimulated cells after contact with metals by 3D images obtained by computer tomography[23].

If the implant has to be removed, intra-operative biopsies and a consequential histopathological work-up can be used to confirm implant-related hypersensitivity. In those cases, periprosthetic membranes are characterized by a pronounced lymphocytes' infiltration[19]. At the histologic analysis of the synovial membrane, the characteristic pattern is granulation tissue and fibrosis, along with numerous giant cells and calcification. In support of the hypothesis that a chronic inflammatory response is the cause of synovitis, lymphocytic and plasma cell infiltrates in the surrounding synovial tissue have also been reported[18].

MANAGEMENT

Management of patients with a suspicion of metal hypersensitivity is still not well defined. Once again, several authors have reported that patients with an ascertained diagnosis of metal allergy who underwent knee replacement with a metal-containing prosthetic device present no clinical evidence of metal hypersensitivity[27], and that no correlation between metal hypersensitivity and complications connected with the prosthesis could be found[28]. Therefore, although implant removal is surely a definitive solution, it must be considered very carefully, as a last option.

Good results have been reported after short-term therapy including topical steroids in the treatment of cutaneous dermatitis and non-steroidal anti-inflammatory drugs or physical therapy to manage pain caused by synovitis[29,30]. By the end, if the symptoms do not resolve, one-stage revision surgery with a hypoallergenic implant should be considered. Resolution of symptoms after revision surgery is expected in 2-3 mo after surgery.

“HYPERSENSITIVITY-FRIENDLY” IMPLANTS

When a metal hypersensitivity has been diagnosed, surgeons need safe implants; many “hypersensitivity-friendly” knee arthroplasty components are currently available from various manufacturers. They can be divided in two categories: Coated

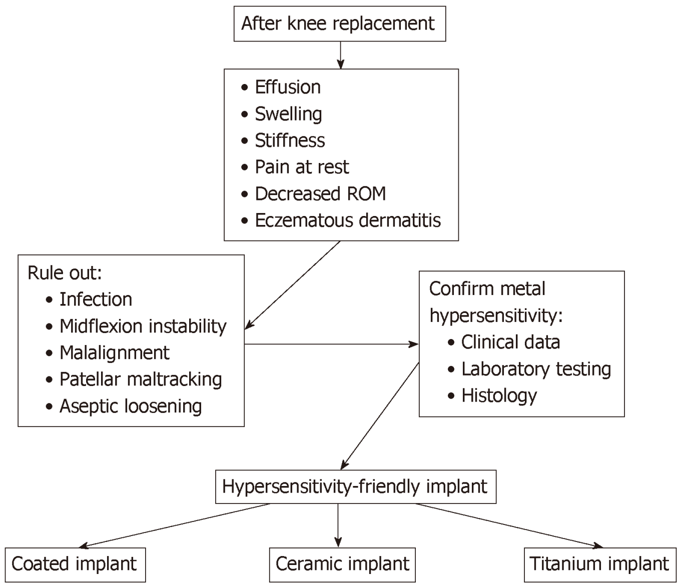

Figure 2 Algorithm for diagnosis and treatment for metal hypersensitivity-related adverse reactions.

implants and non-allergenic implants[23,31].

Cobalt chrome (CoCr) implants coated with a hypersensitivity-friendly thin layer provide the advantage of retaining part of the superior tribological properties of CoCr; yet, the hypersensitivity-friendly layer, after scratching or wear can become damaged, exposing the underlying allergenic alloy[31]. Non-allergenic implants are made of non-CoCr alloys; while reducing the risk of exposure to allergenic metals, they usually show inferior physical properties compared to CoCr alloys[31]. They can be made of oxidized zirconium, pure titanium or ceramic femoral components associated with a tibial tray made of titanium or polyethylene[23].

The aim of the development of the Titanium Nitride (TiN) coating of knee implants was to improve their biocompatibility and mechanical properties[32]. TiN is applied as a 3–4 μm layer on CoCr implants[32]. In biomechanical studies, it has been shown to provide a 98% reduction of polyethylene wear[33]. Specifically, TiN showed a high resistance to adhesive wear and less adhesion to polyethylene; in addition, while CoCr catalyses polyethylene degradation, TiN is inert[34]. Sealing the CoCr surface, TiN reduces the cobalt and chromium ions release[32,35], avoiding hypersensitivity reactions. Despite this theoretical advantage, in a clinical trial, no difference in metal sensitization and blood ion concentration has been found between coated and uncoated arthroplasties[26]. TiN-coated implants have shown good clinical and radiological results[36]. They were shown to have a 95.1% survival rate for any reason at 10 yr. When compared to a standard CoCr implant, they showed no difference in functional outcome, range of motion, revision rate and postoperative pain[37]. The titanium niobium nitride-coated implants showed similar results; comparison of the titanium niobium nitride implants with standard CrCo implants resulted in no statistical difference in clinical outcome scores, range of motion or radiographic evaluation at 1-yr follow-up[38].

Zirconium is a metal with physical properties resembling those of titanium. Its oxide, named zirconia, is a ceramic material. The coupled zirconium-oxidized zirconium has been used as a hybrid material to produce knee arthroplasty implants. It is composed of a core of solid metal, surrounded by a ceramic zirconium oxide (ZrOx) layer which cannot be considered as a coating but instead as the surface of the metal alloy[39]. This material couples the superficial wear characteristics of the ceramic zirconia and the strength of the internal metal. ZrOx causes less wear of the polyethylene than CoCr components and shows a better resistance to abrasion[40]. In an *in vitro* study, a reduction of 42% of polyethylene wear was demonstrated[41]. Containing no nickel, it is absolutely safe in metal-sensitive patients[37]. The ZrOx femoral component is usually coupled with a pure titanium tibial baseplate. A survival rate of 95%-98.7% has been reported at a 5-10 yr follow-up[42,43]. No radiographic failures have been found in short-term[44] or long-term[43] follow up. In a clinical study comparing the results of ZrOx and CoCr arthroplasties implanted in patients undergoing simultaneous bilateral knee replacement, 44% of the patients perceived their knees as equivalent at a 5-yr follow-up[45].

Table 1 Diagnostic criteria for post-implantation metal hypersensitivity[25]

Major criteria
Eruption overlying the metal implant
Positive patch test reaction to a metal used in the implant
Complete recovery after removal of the offending implant
Chronic dermatitis beginning weeks to months after metallic implantation
Minor criteria
Unexplained pain and/or failure of the offending implant
Dermatitis reaction is resistant to therapy
Morphology consistent with dermatitis (erythema, induration, papules, vesicles)
Systemic allergic dermatitis reaction
Histology consistent with allergic contact dermatitis
Positive *in vitro* test to metals (*e.g.*, lymphocytes transformation test)

Ceramic implants, being bioinert, represent a further choice for patients with metal hypersensitivity. These materials have a load to scratch that is 5 times greater than that of ZrOx and 10 times greater than CoCr, resulting in less wear of the surface and, consequently, less third-body wear of the polyethylene[46]. Among ceramics, zirconia is especially suitable for development of implants because of its tensile stress resistance and the possibility to shape it with a thickness similar to that of CoCr components[47]. Good clinical and radiographic results have been reported with these implants[47-49]; at 2-yr and 5-yr follow-up, neither clinical or radiological outcome nor revision rate difference between the CoCr and ceramic implants could be found[48,49], and a survival rate of 97.4% at 10 yr and 94% at 15 yr has been reported[50,51].

All-polyethylene tibial implants should provide the advantages of a thinner bone resection, thicker polyethylene implant and absence of locking mechanisms[52]. In a meta-analysis, no increased revision rates were found at 5 yr and 10 yr, when compared to metal-backed tibial components. No difference could be found for clinical and functional outcomes as well[53]. Should the patient be allergic to a substance contained in the cement, cementless implants are available. Advantages of cementless fixation are preservation of bone stock, provision of a biological fixation of the implant to the bone and avoidance of cement and its wear particles[54]. At 10 yr, a survival rate of 98.9% has been found[55]. In a recent meta-analysis, no difference could be found in terms of implant survivorship, clinical outcomes, radiological outcomes and complications between cemented and cementless implants[54].

CONCLUSIONS

Metal hypersensitivity is a rare condition. Routine allergy testing or patch testing prior to TKA is not recommended, unless a clear history of local or systemic reactions has been reported. In cases of positive history and positive tests, a hypersensitivity-friendly implant should be considered. However, there is still a lack of evidence regarding correlation between metal hypersensitivity and implant-related complications. As a matter of fact, after TKA, one-stage revision surgery for metal or bone cement hypersensitivity should be considered only after ruling out most common causes of TKA failure and even after a short-term therapy aiming to solve cutaneous dermatitis and pain. In this paper, we report the up-to-date knowledge on metal hypersensitivity, suggesting how to make diagnosis of metal hypersensitivity, to treat the symptoms, and to avoid its presentation. Further studies are needed in order to reach a definitive conclusion on the role of metal ions in sensitization and development of implant-related metal hypersensitivity.

REFERENCES

1 **Arden N**, Nevitt MC. Osteoarthritis: epidemiology. *Best Pract Res Clin Rheumatol* 2006; **20**: 3-25 [PMID: 16483904 DOI: 10.1016/j.berh.2005.09.007]

2 **Jüni P**, Hari R, Rutjes AW, Fischer R, Silletta MG, Reichenbach S, da Costa BR. Intra-articular corticosteroid for knee osteoarthritis. *Cochrane Database Syst Rev* 2015; CD005328 [PMID: 26490760 DOI: 10.1002/14651858.CD005328.pub3]

3 **Giunta S**, Castorina A, Marzagalli R, Szychlinska MA, Pichler K, Mobasheri 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]

4 **Musumeci G**, Castrogiovanni P, Trovato FM, Imbesi R, Giunta S, Szychlinska MA, Loreto C, Castorina S, Mobasheri 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]

5 **Castorina S**, Guglielmino C, Castrogiovanni P, Szychlinska MA, Ioppolo F, Massimino P, Leonardi P, Maci C, Iannuzzi M, Di Giunta A, Musumeci G. Clinical evidence of traditional *vs* fast track recovery methodologies after total arthroplasty for osteoarthritic knee treatment. A retrospective observational study. *Muscles Ligaments Tendons J* 2018; **7**: 504-513 [PMID: 29387645 DOI: 10.11138/mltj/2017.7.3.504]

6 **Pacheco KA**. Allergy to Surgical Implants. *J Allergy Clin Immunol Pract* 2015; **3**: 683-695 [PMID: 26362550 DOI: 10.1016/j.jaip.2015.07.011]

7 **Bloemke AD**, Clarke HD. Prevalence of self-reported metal allergy in patients undergoing primary total knee arthroplasty. *J Knee Surg* 2015; **28**: 243-246 [PMID: 24949984 DOI: 10.1055/s-0034-1381959]

8 **Razak A**, Ebinesan AD, Charalambous CP. Metal Hypersensitivity in Patients with Conventional Orthopaedic Implants. *JBJS Rev* 2014; **2**: pii: 01874474-201402000-00004 [PMID: 27490934 DOI: 10.2106/JBJS.RVW.M.00082]

9 **Atanaskova Mesinkovska N**, Tellez A, Molina L, Honari G, Sood A, Barsoum W, Taylor JS. The effect of patch testing on surgical practices and outcomes in orthopedic patients with metal implants. *Arch Dermatol* 2012; **148**: 687-693 [PMID: 22351785 DOI: 10.1001/archdermatol.2011.2561]

10 **Basko-Plluska JL**, Thyssen JP, Schalock PC. Cutaneous and systemic hypersensitivity reactions to metallic implants. *Dermatitis* 2011; **22**: 65-79 [PMID: 21504692 DOI: 10.2310/6620.2011.10055]

11 **Schalock PC**, Menné T, Johansen JD, Taylor JS, Maibach HI, Lidén C, Bruze M, Thyssen JP. Hypersensitivity reactions to metallic implants - diagnostic algorithm and suggested patch test series for clinical use. *Contact Dermatitis* 2012; **66**: 4-19 [PMID: 21957996 DOI: 10.1111/j.1600-0536.2011.01971.x]

12 **Thomsen M**, Rozak M, Thomas P. Pain in a chromium-allergic patient with total knee arthroplasty: disappearance of symptoms after revision with a special surface-coated TKA--a case report. *Acta Orthop* 2011; **82**: 386-388 [PMID: 21504368 DOI: 10.3109/17453674.2011.579521]

13 **Middleton S**, Toms A. Allergy in total knee arthroplasty: a review of the facts. *Bone Joint J* 2016; **98-B**: 437-441 [PMID: 27037424 DOI: 10.1302/0301-620X.98B4.36767]

14 **Frigerio E**, Pigatto PD, Guzzi G, Altomare G. Metal sensitivity in patients with orthopaedic implants: a prospective study. *Contact Dermatitis* 2011; **64**: 273-279 [PMID: 21480913 DOI: 10.1111/j.1600-0536.2011.01886.x]

15 Australian Orthopaedic Association National Joint Replacement Registry. Annual Report. Adelaide: AOA 2014;

16 **Stathopoulos IP**, Andrianopoulos N, Paschaloglou D, Tsarouchas I. Revision total knee arthroplasty due to bone cement and metal hypersensitivity. *Arch Orthop Trauma Surg* 2017; **137**: 267-271 [PMID: 28070650 DOI: 10.1007/s00402-016-2614-6]

17 **Granchi D**, Cenni E, Giunti A, Baldini N. Metal hypersensitivity testing in patients undergoing joint replacement: a systematic review. *J Bone Joint Surg Br* 2012; **94**: 1126-1134 [PMID: 22844057 DOI: 10.1302/0301-620X.94B8.28135]

18 **Akil S**, Newman JM, Shah NV, Ahmed N, Deshmukh AJ, Maheshwari AV. Metal hypersensitivity in total hip and knee arthroplasty: Current concepts. *J Clin Orthop Trauma* 2018; **9**: 3-6 [PMID: 29628676 DOI: 10.1016/j.jcot.2017.10.003]

19 **Faschingbauer M**, Renner L, Boettner F. Allergy in Total Knee Replacement. Does It Exist?: Review Article. *HSS J* 2017; **13**: 12-19 [PMID: 28167868 DOI: 10.1007/s11420-016-9514-8]

20 **Park CN**, White PB, Meftah M, Ranawat AS, Ranawat CS. Diagnostic Algorithm for Residual Pain After Total Knee Arthroplasty. *Orthopedics* 2016; **39**: e246-e252 [PMID: 26811953 DOI: 10.3928/01477447-20160119-06]

21 **Gupta R**, Phan D, Schwarzkopf R. Total Knee Arthroplasty Failure Induced by Metal Hypersensitivity. *Am J Case Rep* 2015; **16**: 542-547 [PMID: 26278890 DOI: 10.12659/AJCR.893609]

22 **Lachiewicz PF**, Watters TS, Jacobs JJ. Metal Hypersensitivity and Total Knee Arthroplasty. *J Am Acad Orthop Surg* 2016; **24**: 106-112 [PMID: 26752739 DOI: 10.5435/JAAOS-D-14-00290]

23 **Innocenti M**, Vieri B, Melani T, Paoli T, Carulli C. Metal hypersensitivity after knee arthroplasty: fact or fiction? *Acta Biomed* 2017; **88**: 78-83 [PMID: 28657568 DOI: 10.23750/abm.v88i2-S.6517]

24 **Wawrzynski J**, Gil JA, Goodman AD, Waryasz GR. Hypersensitivity to Orthopedic Implants: A Review of the Literature. *Rheumatol Ther* 2017; **4**: 45-56 [PMID: 28364382 DOI: 10.1007/s40744-017-0062-6]

25 **Schalock PC**, Crawford G, Nedorost S, Scheinman PL, Atwater AR, Mowad C, Brod B, Ehrlich A, Watsky KL, Sasseville D, Silvestri D, Worobec SM, Elliott JF, Honari G, Powell DL, Taylor J, DeKoven J. Patch Testing for Evaluation of Hypersensitivity to Implanted Metal Devices: A Perspective From the American Contact Dermatitis Society. *Dermatitis* 2016; **27**: 241-247 [PMID: 27649347 DOI: 10.1097/DER.0000000000000210]

26 **Lützner J**, Hartmann A, Dinnebier G, Spornraft-Ragaller P, Hamann C, Kirschner S. Metal hypersensitivity and metal ion levels in patients with coated or uncoated total knee arthroplasty: a randomised controlled study. *Int Orthop* 2013; **37**: 1925-1931 [PMID: 23860793 DOI: 10.1007/s00264-013-2010-6]

27 **Carlsson A**, Möller H. Implantation of orthopaedic devices in patients with metal allergy. *Acta Derm Venereol* 1989; **69**: 62-66 [PMID: 2563611]

28 **Webley M**, Kates A, Snaith ML. Metal sensitivity in patients with a hinge arthroplasty of the knee. *Ann Rheum Dis* 1978; **37**: 373-375 [PMID: 686871 DOI: 10.1136/ard.37.4.373]

29 **Pinson ML**, Coop CA, Webb CN. Metal hypersensitivity in total joint arthroplasty. *Ann Allergy Asthma Immunol* 2014; **113**: 131-136 [PMID: 24934108 DOI: 10.1016/j.anai.2014.05.012]

30 **Verma SB**, Mody B, Gawkrodger DJ. Dermatitis on the knee following knee replacement: a minority of cases show contact allergy to chromate, cobalt or nickel but a causal association is unproven. *Contact Dermatitis* 2006; **54**: 228-229 [PMID: 16650111 DOI: 10.1111/j.0105-1873.2006.0775o.x]

31 **Ajwani SH**, Charalambous CP. Availability of Total Knee Arthroplasty Implants for Metal Hypersensitivity Patients. *Knee Surg Relat Res* 2016; **28**: 312-318 [PMID: 27894179 DOI: 10.5792/ksrr.16.018]

32 **Wisbey A**, Gregson PJ, Tuke M. Application of PVD TiN coating to Co-Cr-Mo based surgical implants. *Biomaterials* 1987; **8**: 477-480 [PMID: 3427147 DOI: 10.1016/0142-9612(87)90085-8]
33 **Pappas MJ**, Makris G, Buechel FF. Titanium nitride ceramic film against polyethylene. A 48 million cycle wear test. *Clin Orthop Relat Res* 1995; 64-70 [PMID: 7671497 DOI: 10.1021/cen-v078n027.p003]
34 **Galetz MC**, Seiferth SH, Theile B, Glatzel U. Potential for adhesive wear in friction couples of UHMWPE running against oxidized zirconium, titanium nitride coatings, and cobalt-chromium alloys. *J Biomed Mater Res B Appl Biomater* 2010; **93**: 468-475 [PMID: 20186822 DOI: 10.1002/jbm.b.31604]
35 **Goldberg JR**, Gilbert JL. The electrochemical and mechanical behavior of passivated and TiN/AlN-coated CoCrMo and Ti6Al4V alloys. *Biomaterials* 2004; **25**: 851-864 [PMID: 14609674 DOI: 10.1016/S0142-9612(03)00606-9]
36 **Choi NY**, In Y, Bae JH, Do JH, Chung SJ, Koh IJ. Are Midterm Patient-Reported Outcome Measures Between Rotating-Platform Mobile-Bearing Prosthesis and Medial-Pivot Prosthesis Different? A Minimum of 5-Year Follow-Up Study. *J Arthroplasty* 2017; **32**: 824-829 [PMID: 27667531 DOI: 10.1016/j.arth.2016.08.028]
37 **van Hove RP**, Brohet RM, van Royen BJ, Nolte PA. No clinical benefit of titanium nitride coating in cementless mobile-bearing total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 1833-1840 [PMID: 25283502 DOI: 10.1007/s00167-014-3359-9]
38 **Thienpont E**. Titanium niobium nitride knee implants are not inferior to chrome cobalt components for primary total knee arthroplasty. *Arch Orthop Trauma Surg* 2015; **135**: 1749-1754 [PMID: 26318754 DOI: 10.1007/s00402-015-2320-9]
39 **Ries MD**, Salehi A, Widding K, Hunter G. Polyethylene wear performance of oxidized zirconium and cobalt-chromium knee components under abrasive conditions. *J Bone Joint Surg Am* 2002; **84-A** Suppl 2: 129-135 [PMID: 12479351 DOI: 10.2106/00004623-200200002-00018]
40 **Patel AM**, Spector M. Tribological evaluation of oxidized zirconium using an articular cartilage counterface: a novel material for potential use in hemiarthroplasty. *Biomaterials* 1997; **18**: 441-447 [PMID: 9061186 DOI: 10.1016/S0142-9612(96)00152-4]
41 **Ezzet KA**, Hermida JC, Colwell CW, D'Lima DD. Oxidized zirconium femoral components reduce polyethylene wear in a knee wear simulator. *Clin Orthop Relat Res* 2004; 120-124 [PMID: 15534531 DOI: 10.1097/01.blo.0000148576.70780.13]
42 **Innocenti M**, Civinini R, Carulli C, Matassi F, Villano M. The 5-year results of an oxidized zirconium femoral component for TKA. *Clin Orthop Relat Res* 2010; **468**: 1258-1263 [PMID: 19798541 DOI: 10.1007/s11999-009-1109-y]
43 **Hofer JK**, Ezzet KA. A minimum 5-year follow-up of an oxidized zirconium femoral prosthesis used for total knee arthroplasty. *Knee* 2014; **21**: 168-171 [PMID: 24161449 DOI: 10.1016/j.knee.2013.08.015]
44 **Laskin RS**. An oxidized Zr ceramic surfaced femoral component for total knee arthroplasty. *Clin Orthop Relat Res* 2003; 191-196 [PMID: 14646761 DOI: 10.1097/01.blo.0000093003.90435.1f]
45 **Hui C**, Salmon L, Maeno S, Roe J, Walsh W, Pinczewski L. Five-year comparison of oxidized zirconium and cobalt-chromium femoral components in total knee arthroplasty: a randomized controlled trial. *J Bone Joint Surg Am* 2011; **93**: 624-630 [PMID: 21471415 DOI: 10.2106/JBJS.I.01753]
46 **Solarino G**, Piconi C, De Santis V, Piazzolla A, Moretti B. Ceramic Total Knee Arthroplasty: Ready to Go? *Joints* 2017; **5**: 224-228 [PMID: 29270560 DOI: 10.1055/s-0037-1607428]
47 **Bergschmidt P**, Bader R, Ganzer D, Hauzeur C, Lohmann C, Rüther W, Tigani D, Rani N, Prats FL, Zorzi C, Madonna V, Rigotti S, Benazzo F, Rossi SM, Kundt G, Bloch HR, Mittelmeier W. Ceramic femoral components in total knee arthroplasty - two year follow-up results of an international prospective multi-centre study. *Open Orthop J* 2012; **6**: 172-178 [PMID: 22582104 DOI: 10.2174/1874325001206010172]
48 **Bergschmidt P**, Ellenrieder M, Bader R, Kluess D, Finze S, Schwemmer B, Mittelmeier W. Prospective comparative clinical study of ceramic and metallic femoral components for total knee arthroplasty over a five-year follow-up period. *Knee* 2016; **23**: 871-876 [PMID: 27338511 DOI: 10.1016/j.knee.2016.06.001]
49 **Bergschmidt P**, Bader R, Kluess D, Zietz C, Schwemmer B, Kundt G, Mittelmeier W. Total knee replacement system with a ceramic femoral component versus two traditional metallic designs: a prospective short-term study. *J Orthop Surg (Hong Kong)* 2013; **21**: 294-299 [PMID: 24366787 DOI: 10.1177/230949901302100306]
50 **Nakamura S**, Kobayashi M, Ito H, Nakamura K, Ueo T, Nakamura T. The Bi-Surface total knee arthroplasty: minimum 10-year follow-up study. *Knee* 2010; **17**: 274-278 [PMID: 20303765 DOI: 10.1016/j.knee.2010.02.015]
51 **Nakamura S**, Ito H, Nakamura K, Kuriyama S, Furu M, Matsuda S. Long-Term Durability of Ceramic Tri-Condylar Knee Implants: A Minimum 15-Year Follow-Up. *J Arthroplasty* 2017; **32**: 1874-1879 [PMID: 28209274 DOI: 10.1016/j.arth.2017.01.016]
52 **Gioe TJ**, Maheshwari AV. The all-polyethylene tibial component in primary total knee arthroplasty. *J Bone Joint Surg Am* 2010; **92**: 478-487 [PMID: 20124081 DOI: 10.2106/JBJS.I.00842]
53 **Nouta KA**, Verra WC, Pijls BG, Schoones JW, Nelissen RG. All-polyethylene tibial components are equal to metal-backed components: systematic review and meta-regression. *Clin Orthop Relat Res* 2012; **470**: 3549-3559 [PMID: 22972656 DOI: 10.1007/s11999-012-2582-2]
54 **Zhou K**, Yu H, Li J, Wang H, Zhou Z, Pei F. No difference in implant survivorship and clinical outcomes between full-cementless and full-cemented fixation in primary total knee arthroplasty: A systematic review and meta-analysis. *Int J Surg* 2018; **53**: 312-319 [PMID: 29656129 DOI: 10.1016/j.ijsu.2018.04.015]
55 **Napier RJ**, O'Neill C, O'Brien S, Doran E, Mockford B, Boldt J, Beverland DE. A prospective evaluation of a largely cementless total knee arthroplasty cohort without patellar resurfacing: 10-year outcomes and survivorship. *BMC Musculoskelet Disord* 2018; **19**: 205 [PMID: 29945574 DOI: 10.1186/s12891-018-2128-1]

P- Reviewer: Anand A, Musumeci G, Papachristou G, Yu B

S- Editor: Yan JP **L- Editor:** A **E- Editor:** Wu YXJ

World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 February 18; 10(2): 71-80

DOI: 10.5312/wjo.v10.i2.71

ISSN 2218-5836 (online)

MINIREVIEWS

Update on diagnosis and management of cuboid fractures

Antonios G Angoules, Nikolaos A Angoules, Michalis Georgoudis, Stylianos Kapetanakis

ORCID number: Antonios G Angoules (0000-0002-7118-958X); Nikolaos A Angoules (0000-0003-3435-0757); Michalis Georgoudis (0000-0003-2688-7538); Stylianos Kapetanakis (0000-0001-6276-2447).

Author contributions: All authors equally contributed to this paper, from the conception of the study and the writing of the discussion through the final structure and design of the paper.

Conflict-of-interest statement: Antonios G Angoules, Nikolaos A Angoules, and Michalis Georgoudis declare that they have no conflict of interests. Stylianos Kapetanakis is a reference doctor for joimax® GmbH and receives payments for teaching.

Manuscript source: Invited manuscript

Received: October 24, 2018
Peer-review started: October 24, 2018
First decision: November 1, 2018
Revised: December 11, 2018

Antonios G Angoules, Michalis Georgoudis, Orthopaedic Department, Athens Medical Center, Athens 15125, Greece

Nikolaos A Angoules, School of Physiotherapy, AMC Metropolitan College, Athens 15125, Greece

Stylianos Kapetanakis, Spine Department and Deformities, Interbalkan European Medical Center, Thessaloniki 55535, Greece

Corresponding author: Antonios G Angoules, MD, PhD, Surgeon, Orthopaedic Department, Athens Medical Center, Distomou 5-7, Marousi, Athens 15125, Greece. angoules@teiath.gr
Telephone: +30-69-77011617
Fax: +30-21-6198555

Abstract

Cuboid fractures due to the particular bone anatomy and its protected location in the midfoot are rare, and they are usually associated with complex injuries of the foot. Clinical examination to diagnose these fractures should be detailed and the differential diagnosis, especially in the case of vague symptoms, should include the exclusion of all lateral foot pain causes. Conventional radiographs do not always reveal occult fractures, which can be under diagnosed especially in children. In this case, further investigation including magnetic resonance imaging or scintigraphy may be required. The treatment of these injuries depends on the particular fracture characteristics. Non-displaced isolated fractures of the cuboid bone can be effectively treated conservatively by immobilization and by avoiding weight bearing on the injured leg. In the case of shortening of the lateral column > 3 mm or articular displacement > 1 mm, surgical management of the fracture is mandatory in order to avoid negative biomechanical and functional consequences for the foot and adverse effects such as arthritis and stiffness as well as painful gait. In this review, an update on diagnosis and management of cuboid fractures is presented.

Key words: Cuboid; Fracture; Diagnosis; Treatment; Surgery

Core tip: The cuboid bone is an essential anatomic element of the midfoot contributing greatly to foot biomechanics. Cuboid fractures are rare and usually associated with complex foot fractures and dislocations. Such fractures require a high level of attention in order to ensure a timely diagnosis. Besides a detailed physical examination, further radiological assessment will identify the presence and type of fracture. Although simple cuboid fractures are effectively treated conservatively, displaced fractures require

Accepted: January 5, 2019
Article in press: January 6, 2019
Published online: February 18, 2019

surgical treatment in order to avoid future devastating consequences. Because of the lack of adequate scientific evidence, the ideal surgical approach is still not universally accepted.

Citation: Angoules AG, Angoules NA, Georgoudis M, Kapetanakis S. Update on diagnosis and management of cuboid fractures. *World J Orthop* 2019; 10(2): 71-80
URL: https://www.wjgnet.com/2218-5836/full/v10/i2/71.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i2.71

INTRODUCTION

Cuboid single fractures are rare due to the particular bone anatomy and the protected location of the midfoot. Their annual frequency reaches 1.8 per 100000 in the United Kingdom[1] and typically occur in combination with other midfoot fractures such as navicular or cuneiforms fractures or are associated with Lisfranc and Chopart fractures and dislocations[2,3].

Cuboid fractures can be the result of bone injury due to compression after a car accident or direct crush of the lateral aspect of the dorsum of the foot as it may happen after a heavy object falls on the foot. They may also be the result of avulsion injury involving any ligamentous attachments of the cuboid *e.g.*, calcaneocuboid ligament. Such an injury is attributed to ankle sprain as a result of a twisting injury of the foot with the hindfoot inverted and the forefoot adducted. A particular type of isolated cuboid fracture was presented in the literature by Hermel and Gershon-Cohen[6] in 1953 who coined the term "nutcracker fracture" in order to describe a cuboid fracture that is caused by compression between the calcaneus proximally and the bases of the fourth and fifth metatarsals distally. This fracture is the result of forced plantar flexion of the hindfoot and midfoot against the fixed and forced abduction forefoot[2,4-6]. This injury is also described as a result of equestrian-related injuries in children and adolescents where compression cuboid fractures are combined with other midfoot injuries such as avulsion and compression navicular or cuneiform fractures[7].

Cuboid stress fractures are less common than fractures in other tarsal bones such as calcaneus and navicular because the cuboid is not a weight-bearing bone[8]. These fractures may occur in both toddlers[9-13] and adults[8,14-17] and may be a result of overuse affecting athletes[8,15] or military recruits[18]. They may also follow osteoporosis and reduced bone strength[17]. Although they are successfully treated non-operatively without having adverse effects due to vague symptoms, they may initially not come to attention[5].

Cuboid fractures are not always recognized promptly due to the special anatomy of the foot and the difficulty in interpreting the radiologic findings. However, delayed identification and effective treatment of these injuries may have adverse effects on the biomechanics of the foot, such as loss of length of the lateral column resulting in forefoot abduction and also lesser metatarsals lateral subluxation, resulting in planus deformity associated with compensatory hindfoot eversion and posterior tibial tendon insufficiency[4,19]. Anatomical disorder of the bone articulations with tarsal bones of may lead to foot stiffness and painful arthritis as well as foot deformity[20].

This review analyzes the modern diagnostic and therapeutic approach of these rare though challenging fractures whose inappropriate and delayed management, according to their specific characteristics can have significant negative consequences on the mechanics and functionality of the foot, causing pain and stiffness to the injured limb with a final negative impact on a patient's quality of life.

CLINICAL ANATOMY

The cuboid is one of the seven bones of the midfoot and hindfoot located most laterally in the distal tarsal row in the center of the foot lateral column. It has a pyramidal shape with five articular surfaces that are articulated with the bases of the fourth and fifth metatarsal bones in front with the calcaneus on the back as well as with the lateral cuneiform and navicular medially (Figure 1). Hence it is the only bone of the tarsus involved both in the tarsometatarsal joint (Lisfranc complex) and in the midtarsal joint (Chopart's joint). It also links the lateral column to the transverse plantar arch[4,19,21-24]. Its articulation with the fourth and fifth metatarsals provides mobility three times greater than the mobility of the first through third tarsometatarsal joints and has the largest contribution to the dorsiflexion and plantar flexion of the midfoot[19,23]. It also has a primary contribution to pronation and supination assisted in this function by the calcaneocuboid joint[19].

Due to its special anatomy and its position, the cuboid is the main supporting element of the rigid and static lateral column and ensures that its length is maintained. Its role is supported by a number of ligamentous, capsuloligamentous, and tendinous restraints. Although it does not participate directly in weight bearing, it receives significant forces during standing and ambulation, and its contribution is important in the mobility of the foot lateral column and the adaptation of the foot when walking on an uneven terrain[14,23]. The dorsal surface of the bone is bare, but on its plantar surface there is a groove that runs obliquely distal and medially and from which the tendon of peroneus longus passes acting as a fulcrum for the peroneus longus muscle contraction[4] (Figure 2). Gathering forces in this area during activities such as running can cause stress fractures[8].

Cuboid vascularization is ensured by the lateral plantar artery where anastomosis exists between the medial plantar artery. The satisfactory blood supply of the bone also explains the satisfactory bone consolidation following a fracture and the rare occurrence of events such as nonunion or osteonecrosis[4].

CLASSIFICATION

Although there is not a universally accepted classification system, cuboid fractures are classified according to their characteristics regarding the displacement of the fragments, the involvement of the articular surfaces, and the avulsion or comminuted type of fracture[23].

The Orthopaedic Trauma Association subdivides these fractures into three main categories[25]. Group A includes the simple extraarticular fractures, Group B includes calcaneocuboid or metatarsocuboid joint fractures, and Group C includes fractures involving both joints. This classification further subdivides the cuboid fractures from the simplest ones up to the most complex in each category according to the level and the particular anatomical position of each fracture. The fractures of each group are denoted with numbers with the most complex fractures being characterized by higher numbers.

Fenton *et al*[19] proposed the classification of cuboid fractures into five groups. A type 1 fracture is the most common type of avulsion fracture involving the capsule of the calcaneocuboid joint. Type 2 includes stable isolated extra-articular injuries of the fracture that do not require surgical treatment because the length of the foot lateral column is maintained, and there is no intra-articular involvement. Type 3 injuries are isolated intra-articular fractures within the body of the cuboid involving the calcaneocuboid, the tarsometatarsal joint, or both of them. The fractures of this category are treated conservatively. Type 4 fractures are associated with disruption of the midfoot as well as with tarsometatarsal injuries. These intra-articular fractures require anatomic reduction and stabilization. Finally, type 5 fractures are high-energy crushing injuries of the cuboid that may be accompanied by disruption of the mid-tarsal joint and loss of length of the lateral column alone or in combination with the medial column. These fractures are mostly treated surgically except in cases where the length of the foot lateral column is maintained.

CLINICAL EVALUATION

The diagnosis of cuboid fractures, particularly of those that are not accompanied by other foot injuries, may be difficult. The early detection of these fractures requires a high degree of suspicion[26]. Regarding children, local swelling and antalgic limp with refusal to bear weight on the lateral side of the foot may accompany a fracture of the cuboid[11,27]. Cuboid fractures may be associated with lateral foot pain especially with push off when walking[28]. Typically there is tenderness to direct palpation of the cuboid over the lateral aspect of the midfoot (Figure 3) while the fracture can be accompanied by deformity, ecchymosis, or fracture blisters[5,22,23]. In the event that the calcaneocuboid joint is unstable, diagnostic maneuvers that control the integrity of this joint can cause pain[28].

Stress fractures of the cuboid may have no obvious clinical signs. Painful gait and mild tenderness on the lateral side of the foot may be present without swelling or evident hematoma[16]. Pain may be mild with a progressive nature and accompany a

Figure 1 Cuboid bone lateral view.

recent increase in athletic or other daily activity level of an individual. If there is significant periosteal reaction or sclerosis in the fracture area, then a palpable mass may be present in the area of maximum tenderness. The placement of a vibrating tuning fork just above the area of maximum tenderness can cause an increase in pain intensity and has been proposed as a diagnostic method for stress fractures[29].

IMAGING METHODS

Plain X-ray radiography usually diagnoses simple fractures of the cuboid and includes the anterior, posterior, lateral, and standard oblique view of the foot[4]. Imaging examination should include contralateral foot for the comparison and determination of the length of the foot lateral column as well as for the appropriate preoperative planning. The integrity of the foot lateral column can be evaluated by the anteroposterior view, which also allows the detection of any transverse plane deformity. The lateral radiograph assesses the congruity of the calcaneocuboid joint and can also reveal avulsion fractures[28]. The standard medial oblique view is particularly useful for assessing cuboid fractures because it allows the view of the cuboid and its articulation with the metatarsals and the calcaneus, free of superimposition of the bones with the open and equal cuboid joint. It also contributes to the evaluation of the length of the lateral column[4,23].

Although conventional radiography can provide a lot of information about the nature of the cuboid bone injury, the considerable overlap of bony structures in the foot leads to a failure regarding the depiction of occult cuboid fractures[30]. Miller *et al*[2] found that in 17 patients with pain over the lateral aspect of the midfoot, the X-ray radiography revealed cuboid fractures in only seven of them.

Computed tomography

Computed tomography (CT) may provide additional information regarding the size, exact location, and pattern of fractures of the cuboid, as well as associated injuries such as other fractures and dislocations of other bones of the foot[7,8]. It clearly depicts tarsometatarsal joints and Lisfranc joint and also provides information on the fracture healing progression[8,31].

Magnetic resonance imaging

In the case of non-diagnostic radiography findings using plain film radiographs the contribution of magnetic resonance imaging (MRI) is a valuable, sensitive examination for the diagnosis of cuboid fractures in both children and adults[24,32,33] (Figure 4). Miller *et al*[2] found that in 17 adults with isolated occult cuboid fractures, the presence of a fracture was confirmed by MRI in eight of them. In their recent study, O’Dell *et al*[24] used MRI to confirm cuboid fractures in 19 children aged 18 mo to 17 years, nine of whom the initial radiography was negative for fracture. This radiology examination revealed fractures that were the result of acute trauma or were stress fractures linear in configuration and most commonly adjacent to the tarsometatarsal joint.

In the case of cuboid fractures in the T1 weighted sequence, continuous hypointense signals are revealed in the cuboid bone extending from the cuneiform joint surface toward the lateral side as well as fat suppression[16], while in the T2 sequence a hyperintense signal in the bone as well as the loss of the bone marrow signal is detected[5].

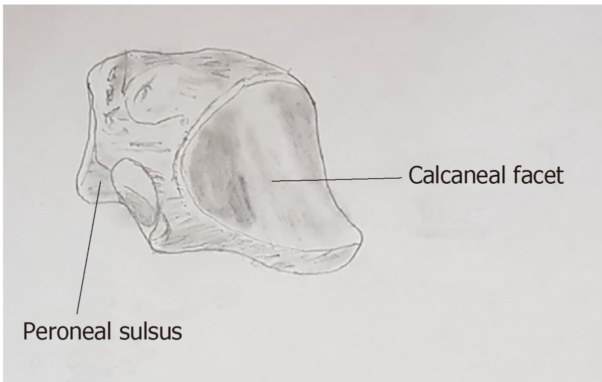

Figure 2 Posterolateral view of cuboid depicting peroneal groove (modified from Greys Anatomy, 1918).

Sonography

Sonography, although not the method of choice for the detection of cuboid fractures, is a reliable and quick method when painful swelling adjacent to the bone is present in the case of subtle cuboid fractures with non-diagnostic plain radiography[5,30]. Bilateral ultrasonography that includes longitudinal and transverse scan planes reveals a cortical discontinuity and cortical step in the area of the fracture as well as soft tissue edema[5]. Wang *et al*[30] reported a study of 268 patients with post-traumatic pain in the area of the foot and ankle with negative findings in the initial radiology examination, where ultrasound examination revealed a fracture in 24 of them. Two of the patients examined suffered cuboid fractures.

Scintigraphy

Scintigraphy may reveal focal uptake in the cuboid and contribute to the early diagnosis of cuboid fractures, particularly in stress fractures in children in the case of a negative initial physical examination and non-diagnostic radiographs[9,12,13,15]. However, it should be taken into account that due to the complex anatomy of the midfoot, it is difficult to ascertain the exact intake area of the radiopharmaceutical, which reduces the diagnostic accuracy of the method[5].

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes bony causes of lateral foot pain such as ankle sprain, stress fractures of the foot, fracture of the fifth metatarsal distal to tuberosity, avulsion of the anterior process of the calcaneus, Lisfranc injuries, tarsal coalition, cuboid syndrome, and os perineum injury. Furthermore, soft tissue pathogens such as peroneus, longus tendon tenosynovitis or partial tearing, subluxing peroneal tendons, extensordigitorum, tendonitis, sinus tarsi syndrome, and lateral plantar nervous entrapment may have a similar clinical picture to cuboid fractures and should be excluded during the initial diagnosis in the case of negative radiology evaluation with a clinical picture similar to a cuboid fracture[2,28,34,35] (Table 1).

Cuboid syndrome is caused by the structural congruity of the calcaneocuboid joint and subluxation of the cuboid and usually concerns athletes or dancers. It is characterized by pain in the area of the plantar surface of the cuboid or in the foot. Two clinical maneuvers have been proposed for the clinical diagnosis of the syndrome, namely the midtarsal adduction and the midtarsal supination test[28,36].

Os perineum is an accessory bone located within the peroneus longus tendon adjacent to the lateral plantar aspect of the cuboid, which can cause foot pain. It is found in 4% to 30% of normal feet[28,37]. In most cases, it is asymptomatic but may be the cause of acute and chronic foot pain as in cases of stress fracture or diastasis. For the diagnosis of the syndrome, plain radiography films may be diagnostic or further examination by CT, MRI and/or sonography may be required[28].

TREATMENT

The therapeutic approach of cuboid fractures is adjusted according to the severity of the fracture. Non-displaced low energy fractures such as avulsion fractures and stress fractures are effectively treated with conservative methods of treatment while

Figure 3 Local tenderness to direct palpation of the cuboid bone following foot injury may suggest cuboid fracture.

complex high-energy injuries involving complex fractures with significant displacement and intra-articular involvement require anatomic reduction and external or internal osteosynthesis depending on the particular fracture characteristics.

Conservative treatment

In cuboid fractures with minimal pain and swelling, treating with an elastic bandage or with a fracture boot and walking with partial weight bearing until the satisfactory regression of the symptoms, may be enough. In the case of severe initial pain, a short walking cast for 4-6 wk is recommended[30]. Stress fractures require limiting the activity and use of the limb while it is recommended to have plantar arch support[16]. Avulsion fractures are treated with protected weight bearing as tolerated and a fracture boot for 4 to 6 wk[23]. These fractures require regular radiographic evaluation every month as they may be complicated with fibrous non-union. In this case as well as in the presence of recalcitrant pain, excisional surgery may be necessary[28].

Surgical approach

According to Borrelli *et al*[4], open cuboid fractures are the only absolute indication for urgent surgical management. Surgery is also recommended when there is an articular displacement greater than 1 mm or a shortening of the foot lateral column length[22]. According to Holbein *et al*[38], this shortening requires surgical treatment of the fracture if it is greater than 3 mm. Surgical management of cuboid fractures includes external fixators, open reduction, and internal fixation with or without bone grafting and midtarsal arthrodesis[22]. The purpose of this surgical intervention is to restore the length of the lateral column as well as the normal anatomy and mobility of the surrounding joints, and in particular of the calcaneocuboid joint as well as of the fourth and fifth tarsometatarsal joints[20].

In the case of a severe comminution and displacement of fracture fragments and poor skin quality that does not allow open fixation, the application of spanning external fixation ensures that the length of the lateral column is restored[4,23].

The internal osteosynthesis of cuboid fractures can be conducted with lumbar or epidural anesthesia. The patient is placed in the supine position with a thigh tourniquet and a bump under the ipsilateral hip to avoid excessive external rotation of the foot and to ensure better access to the cuboid bone. A 6 cm lateral longitudinal incision over the cuboid from the tip of the fibula to the tip of the fifth metatarsal reveals the calcaneocuboid and tarsometatarsal joints and allows the anatomic reduction of the fracture or fractures[23] (Figure 5). The extension of this section, 5 mm centrally of the calcaneocuboid joint and beyond the level of the lateral base of the fifth metatarsal, allows a better view of the joints and the anatomic reduction of the fractures[4]. The incision is maintained at the lateral border of the extensor digitorum brevis muscle and proximal to the sural nerve, which must be identified and protected[4,22]. Further dissection is performed to visualize the extensor digitorum brevis and then the muscle belly is partially elevated off the periosteum to allow inspection of the cuboid as well as of the calcaneocuboid and tarsometatarsal joints[4,23].

After restoring the length of the cuboid, the dorsolateral wall is reconstructed. The articular surfaces should be reconstructed starting from the media fragments using the intact side of the joint as a model[20]. To maintain the reduction provisional fixation with small Kirschner wires may be required. The internal osteosynthesis is completed using locking or unlocking screws or mini fragment plates under fluoroscopy[4,23]. Any

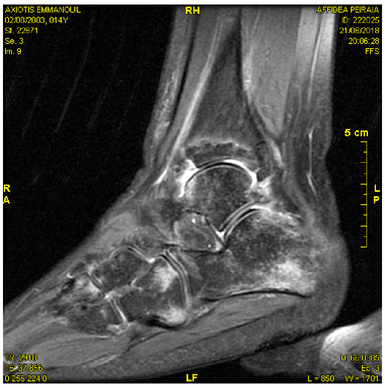

Figure 4 Sagittal view of the right ankle obtained via magnetic resonance imaging. Undisplaced cuboid fracture extending to the middle of the calcaneocuboid joint.

void is filled with autografts, allogenic, or cancellous bone chips, and an anatomic plate is placed over the cuboid to maintain the length. Postoperatively, the patient ambulates without weight bearing for 4-6 wk and for another 6 wk with partial weight bearing and with a walking cast. Full weight bearing walking is allowed after 12 wk[4,7,22].

Midtarsal primary arthrodesis is a surgical treatment method recommended for severe crush injuries with extensive comminution of the cuboid bone and articular involvement. However, this method presents the disadvantage of significant loss in lateral column motion and is mainly applied to less active patients[23,27]. In the case of failed internal fixation and persistent pain, secondary fusion may be an alternative treatment method[22].

DISCUSSION AND CONCLUSION

The cuboid bone is located at the center of the lateral midfoot and its anatomic position provides a relative protection[17]. However, it is subject to a series of compressive and shearing forces[24]. Cuboid fractures, although rare, may be the result of direct or indirect pressure in the foot and usually associated with other fractures and dislocations in the area. Thus, these fractures can be the result of compression or crush of the lateral aspect foot[2].

Cuboid stress fractures are less frequent than other foot fractures as this bone is not weight bearing[8]. Although they are slightly more common in children, they have been are also described in adults[14]. They may be the result of increased athletic activity or involve bones with reduced strength such as after a prolonged corticosteroid uptake period[17]. A possible mechanism of this fracture assumes that these fractures are the result of the repetitive pull of the peroneus longus tendon as it passes through the peroneal groove of the cuboid[8].

Due to their vague symptoms and the complex anatomy of the area, cuboid fractures may not be detected initially. The diagnosis of these fractures should be immediate because their delayed detection and treatment can cause a shortening of the foot lateral column with particularly negative consequences for the biomechanics of the foot such as a painful flatfoot deformity associated with posterior tibial tendon insufficiency[20].

Conventional radiography includes the anterior, posterior, lateral, and standard oblique view of the foot[5]. The latest view provides useful information about the condition of the joints between the cuboid and the base of the fourth and fifth metatarsals as well as the length of the lateral column. CT is a diagnostic method that offers the best visualization for assessing fracture patterns and articular displacements[4]. In the presence of occult radiographs, further imaging modalities such as ultrasound examination, MRI, or scintigraphy can contribute to the early detection of the fracture and help avoid future adverse effects regarding foot function. Particularly in children these fractures often go undiagnosed due to non-diagnostic plain X-ray radiography and the difficulties faced in the clinical examination that constitutes the contribution of these modern imaging methods very useful[24,27].

Treatment depends on the type of the fracture. Factors that determine the method of treatment include the involvement of the articular surfaces of the bone, the disorder of joints architecture in which the bone is involved, the reduction of the length of the foot lateral column, and the presence of fractures and dislocations of the other bones

Table 1 Differential diagnosis of lateral foot pain[2,28,34,35].

Differential diagnosis of lateral foot pain
Ankle sprain
Peroneal tendonitis
Peroneus longus tendon tear
Subluxing peroneal tendons
Stress fracture
Fracture of the shaft of the fifth metatarsal
Avulsion of the base of the fifth metatarsal
Apophysitis of the fifth metatarsal
Jones fracture
Avulsion of the anterior process of the calcaneus
Lisfranc injuries
Tarsal coalition
Cuboid syndrome
Os peroneum fracture
Sinus tarsi syndrome
Lateral plantar nerve entrapment

in the area[4]. Non-displaced stable fractures can be treated conservatively by splinting or casting with or without restriction of weight bearing[20]. Open fractures, complex comminuted fractures, and fractures accompanied by a shortening of the length of the foot lateral column greater than 3 mm or articular displacement greater than 1 mm require surgical treatment[22,38]. The purpose of this therapeutic approach is to restore the lateral column length and plantar support of the midfoot, to restore the integrity of the articular surfaces of the calcaneocuboid and tarsometatarsal joints, and the mobility of the cuboid joints to the fourth and fifth metatarsal bases[20,22].

As there is no sufficient scientific evidence to allow safe conclusions about the optimal management of cuboid fractures, the current therapeutic approach is based presumably on personal experience and beliefs[25]. For example, some authors support that Kirschner wires are more reliable in maintaining reduction than external fixation[39] whilst another postulates that fixation of the fractured cuboid bone with plates is preferable than screws, which are not associated with satisfactory results[25]. More sophisticated surgical approaches such as preoperative planning locking plates based on 3D CT may contribute to the anatomical reduction of the fracture and therefore may provide more favorable outcomes[40]. Still, further research is needed, including studies of high quality with a focus to resolve uncertainties of management and determine which patients could be treated non-operatively or are candidates to develop arthrosis and warrant primary fusion[19,39].

Figure 5 The lateral longitudinal surgical incision for the internal fixation of cuboid fractures.

REFERENCES

1 **Court-Brown C**, Zinna S, Ekrol I. Classification and epidemiology of midfoot fractures. *Foot* 2006; **16**: 138-141 [DOI: 10.1016/j.foot.2006.03.003]

2 **Miller TT**, Pavlov H, Gupta M, Schultz E, Greben C. Isolated injury of the cuboid bone. *Emerg Radiol* 2002; **9**: 272-277 [PMID: 15290553 DOI: 10.1007/s10140-002-0240-9]

3 **Ohmori T**, Katsuo S, Sunayama C, Mizuno K, Ojima T, Yamakado K, Ando T, Watanabe S, Hayashi S, Tsuchiya H. A Case Report of Isolated Cuboid Nutcracker Fracture. *Case Rep Orthop* 2016; **2016**: 3264172 [PMID: 27313925 DOI: 10.1155/2016/3264172]

4 **Borrelli J**, De S, VanPelt M. Fracture of the cuboid. *J Am Acad Orthop Surg* 2012; **20**: 472-477 [PMID: 22751166 DOI: 10.5435/JAAOS-20-07-472]

5 **Enns P**, Pavlidis T, Stahl JP, Horas U, Schnettler R. Sonographic detection of an isolated cuboid bone fracture not visualized on plain radiographs. *J Clin Ultrasound* 2004; **32**: 154-157 [PMID: 14994258 DOI: 10.1002/jcu.20009]

6 **Hermel MB**, GERSHON-COHEN J. The nutcracker fracture of the cuboid by indirect violence. *Radiology* 1953; **60**: 850-854 [PMID: 13064390 DOI: 10.1148/60.6.850]

7 **Ceroni D**, De Rosa V, De Coulon G, Kaelin A. Cuboid nutcracker fracture due to horseback riding in children: Case series and review of the literature. *J Pediatr Orthop* 2007; **27**: 557-561 [PMID: 17585267 DOI: 10.1097/01.bpb.0000279031.66774.c0]

8 **Chen JB**. Cuboid stress fracture. A case report. *J Am Podiatr Med Assoc* 1993; **83**: 153-155 [PMID: 8468697 DOI: 10.7547/87507315-83-3-153]

9 **Blumberg K**, Patterson RJ. The toddler's cuboid fracture. *Radiology* 1991; **179**: 93-94 [PMID: 2006311 DOI: 10.1148/radiology.179.1.2006311]

10 **Blumberg K**, Patterson RJ. Fractures of the cuboid bone in toddlers. *Pediatr Radiol* 1999; **29**: 563 [PMID: 10398800 DOI: 10.1007/s002470050647]

11 **Senaran H**, Mason D, De Pellegrin M. Cuboid fractures in preschool children. *J Pediatr Orthop* 2006; **26**: 741-744 [PMID: 17065937 DOI: 10.1097/01.bpo.0000242378.87724.7b]

12 **Joo SY**, Jeong C. Stress fracture of tarsal cuboid bone in early childhood. *Eur J Orthop Surg Traumatol* 2015; **25**: 595-599 [PMID: 25249481 DOI: 10.1007/s00590-014-1543-8]

13 **Simonian PT**, Vahey JW, Rosenbaum DM, Mosca VS, Staheli LT. Fracture of the cuboid in children. A source of leg symptoms. *J Bone Joint Surg Br* 1995; **77**: 104-106 [PMID: 7822362 DOI: 10.1302/0301-620X.77B1.7822362]

14 **Yu SM**, Dardani M, Yu JS. MRI of isolated cuboid stress fractures in adults. *AJR Am J Roentgenol* 2013; **201**: 1325-1330 [PMID: 24147421 DOI: 10.2214/AJR.13.10543]

15 **Beaman DN**, Roeser WM, Holmes JR, Saltzman CL. Cuboid stress fractures: a report of two cases. *Foot Ankle* 1993; **14**: 525-528 [PMID: 8314188 DOI: 10.1177/107110079301400907]

16 **Hagino T**, Ochiai S, Watanabe Y, Senga S, Takayama Y, Haro H. A case of a cuboid bone stress fracture in a senior high school rugby athlete. *AP-SMART* 2014; **1**: 132-135 [DOI: 10.1016/j.asmart.2014.09.001]

17 **Franco M**, Albano L, Kacso I, Gaïd H, Jaeger P. An uncommon cause of foot pain: The cuboid insufficiency stress fracture. *Joint Bone Spine* 2005; **72**: 76-78 [PMID: 15681254 DOI: 10.1016/j.jbspin.2004.03.001]

18 **Greaney RB**, Gerber FH, Laughlin RL, Kmet JP, Metz CD, Kilcheski TS, Rao BR, Silverman ED. Distribution and natural history of stress fractures in U.S. Marine recruits. *Radiology* 1983; **146**: 339-346 [PMID: 6217486 DOI: 10.1148/radiology.146.2.6217486]

19 **Fenton P**, Al-Nammari S, Blundell C, Davies M. The patterns of injury and management of cuboid fractures: a retrospective case series. *Bone Joint J* 2016; **98-B**: 1003-1008 [PMID: 27365481 DOI: 10.1302/0301-620X.98B7.36639]

20 **Mihalich RM**, Early JS. Management of cuboid crush injuries. *Foot Ankle Clin* 2006; **11**: 121-126, ix [PMID: 16564457 DOI: 10.1016/j.fcl.2005.11.001]

21 **Kolker D**, Marti CB, Gautier E. Pericuboid fracture-dislocation with cuboid subluxation. *Foot Ankle Int* 2002; **23**: 163-167 [PMID: 11858339 DOI: 10.1177/107110070202300215]

22 **Yu G**, Yu T, Yang Y, Li B, Yuan F, Zhou J. Nutcracker fracture of the cuboid: management and results. *Acta Orthop Belg* 2012; **78**: 216-219 [PMID: 22696993 DOI: 10.1007/s00132-012-1903-1]

23 **Clements JR**, Dijour F, Leong W. Surgical Management Navicular and Cuboid Fractures. *Clin Podiatr Med Surg* 2018; **35**: 145-159 [PMID: 29482786 DOI: 10.1016/j.cpm.2017.12.001]

24 **O'Dell MC**, Chauvin NA, Jaramillo D, Biko DM. MR imaging features of cuboid fractures in children. *Pediatr Radiol* 2018; **48**: 680-685 [PMID: 29427027 DOI: 10.1007/s00247-018-4076-1]

25 **Pountos I**, Panteli M, Giannoudis PV. Cuboid Injuries. *Indian J Orthop* 2018; **52**: 297-303 [PMID:

29887632 DOI: 10.4103/ortho.IJOrtho_610_17]

26 **Lucerna A**, Espinosa J, Butler N, Wenke A, Caltabiano N. Nutcracker Cuboid Fracture: A Case Report and Review. *Case Rep Emerg Med* 2018; **2018**: 3804642 [PMID: 29850286 DOI: 10.1155/2018/3804642]

27 **Holbein O**, Bauer G, Kinzl L. Fracture of the cuboid in children: case report and review of the literature. *J Pediatr Orthop* 1998; **18**: 466-468 [PMID: 9661854 DOI: 10.1097/00004694-199807000-00012]

28 **Traister E**, Simons S. Diagnostic considerations of lateral column foot pain in athletes. *Curr Sports Med Rep* 2014; **13**: 370-376 [PMID: 25391092 DOI: 10.1249/JSR.0000000000000099]

29 **Dodson NB**, Dodson EE, Shromoff PJ. Imaging strategies for diagnosing calcaneal and cuboid stress fractures. *Clin Podiatr Med Surg* 2008; **25**: 183-201, vi [PMID: 18346590 DOI: 10.1016/j.cpm.2007.12.001]

30 **Wang CL**, Shieh JY, Wang TG, Hsieh FJ. Sonographic detection of occult fractures in the foot and ankle. *J Clin Ultrasound* 1999; **27**: 421-425 [PMID: 10477883 DOI: 10.1002/(SICI)1097-0096(199910)27:8<421::AID-JCU2>3.0.CO;2-E]

31 **Preidler KW**, Peicha G, Lajtai G, Seibert FJ, Fock C, Szolar DM, Raith H. Conventional radiography, CT, and MR imaging in patients with hyperflexion injuries of the foot: diagnostic accuracy in the detection of bony and ligamentous changes. *AJR Am J Roentgenol* 1999; **173**: 1673-1677 [PMID: 10584818 DOI: 10.2214/ajr.173.6.10584818]

32 **Sadineni RT**, Pasumarthy A, Bellapa NC, Velicheti S. Imaging Patterns in MRI in Recent Bone Injuries Following Negative or Inconclusive Plain Radiographs. *J Clin Diagn Res* 2015; **9**: TC10-TC13 [PMID: 26557590 DOI: 10.7860/JCDR/2015/15451.6685]

33 **Feldman F**, Staron R, Zwass A, Rubin S, Haramati N. MR imaging: its role in detecting occult fractures. *Skeletal Radiol* 1994; **23**: 439-444 [PMID: 7992109 DOI: 10.1007/BF00204604]

34 **Unnithan S**, Thomas J. Not all ankle injuries are ankle sprains - Case of an isolated cuboid stress fracture. *Clin Pract* 2018; **8**: 1093 [PMID: 30090220 DOI: 10.4081/cp.2018.1093]

35 **Patterson SM**. Cuboid syndrome: a review of the literature. *J Sports Sci Med* 2006; **5**: 597-606 [PMID: 24357955 DOI: 10.1016/j.jsams.2006.07.006]

36 **Durall CJ**. Examination and treatment of cuboid syndrome: A literature review. *Sports Health* 2011; **3**: 514-519 [PMID: 23016051 DOI: 10.1177/1941738111405965]

37 **Schick F**, Karanjia H, Daniel J, Dheer S, Langman C, Taweel N, Sullivan P, Lebaron T. Spontaneous Fracture of the Os Peroneum With Rupture of the Peroneus Longus Tendon. *J Foot Ankle Surg* 2018; **57**: 790-793 [PMID: 29631970 DOI: 10.1053/j.jfas.2017.11.007]

38 **Holbein O**, Bauer G, Kinzl K. Displaced fractures of the cuboid: four case reports and review of the literature. *Foot and Ankle Surgery* 1997; **3**: 85-93 [DOI: 10.1046/j.1460-9584.1997.00052.x]

39 **Ahmed A**, Westrick E. Management of Midfoot Fractures and Dislocations. *Curr Rev Musculoskelet Med* 2018; **11**: 529-536 [PMID: 30196386 DOI: 10.1007/s12178-018-9518-8]

40 **Rony L**, de Sainte Hermine P, Steiger V, Ferchaud F, Cronier P. Clinical and radiological outcomes of a cohort of 9 patients with anatomical fractures of the cuboid treated by locking plate fixation. *Orthop Traumatol Surg Res* 2018; **104**: 245-249 [PMID: 29408687 DOI: 10.1016/j.otsr.2017.12.012]

P- Reviewer: Tawonsawatruk T, Vulcano E, Yukata K

S- Editor: Ji FF **L- Editor:** Filipodia **E- Editor:** Wu YXJ

World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 February 18; 10(2): 81-89

DOI: 10.5312/wjo.v10.i2.81

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Retrospective Study

Mandated health insurance increases rates of elective knee surgery

Daniel Kim, Woo Do, Shahein Tajmir, Brandon Mahal, Joe DeAngelis, Arun Ramappa

ORCID number: Daniel Kim (0000-0003-0625-3466); Woo Do (0000-0002-9641-9505); Shahein Tajmir (0000-0003-0407-1554); Brandon Mahal (0000-0003-3036-334X); Joseph DeAngelis (0000-0003-2833-4521); Arun Ramappa (0000-0003-2833-4523).

Author contributions: Kim D, Do W, Tajmir S, Mahal B, DeAngelis J and Ramappa A substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Institutional review board statement: This certifies that the action on the research study referenced was reviewed by the Committee on Clinical Investigations (CCI), the appropriately authorized Institutional Review Board and Privacy Board appointed to review research involving human subjects. This action was reviewed via Expedited review. This study approved for continuation for a period of one year with waiver of informed consent and authorization under expedited category #8.

Conflict-of-interest statement: Nothing.

Daniel Kim, Brandon Mahal, Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, United States

Woo Do, Department of Surgery, Madigan Army Medical Center, Tacoma, WA 98431, United States

Shahein Tajmir, Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, United States

Joe DeAngelis, Arun Ramappa, Department of Orthopaedic Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, United States

Corresponding author: Arun Ramappa, MD, Chief Doctor, Associate Professor, Department of Orthopaedic Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Shapiro 2, 330 Brookline Avenue, Boston, MA02215, United States. aramappa@bidmc.harvard.edu
Telephone: +1-617-6673940
Fax: +1-617-6672155

Abstract

BACKGROUND

The recent federal ruling to against Affordable Care Act (ACA), specifically the mandate requiring people to buy insurance, has once again brought the healthcare reform debate to the spotlight. The ACA increased the number of insured Americans through the development of subsidized healthcare plans and health insurance exchanges. Insurance-based differences in the rate of upper extremity elective orthopaedic surgery have been described before and after healthcare reform in Massachusetts, where a similar mandate was put into place years before the ACA was passed. However, no comprehensive study has evaluated insurance-based differences of knee elective surgery before and after reform.

AIM

To investigate how an individual mandate to purchase health insurance affects rates of knee surgery.

METHODS

A retrospective review was performed within an orthopaedic surgery department at a tertiary-care, academic medical center in Massachusetts. The rate of elective knee surgery performed before and after the healthcare reform (2005-2006 and 2007-2010, respectively) was calculated. The patients were categorized by insurance type (Commonwealth Care, Medicare, Medicaid, private insurance, Workers' Compensation, TriCare, and Uninsured). Using χ^2 testing, differences in rates of surgery between the pre-reform and post-reform period and among

Manuscript source: Unsolicited manuscript

Received: December 22, 2018
Peer-review started: December 23, 2018
First decision: December 30, 2018
Revised: January 11, 2019
Accepted: January 26, 2019
Article in press: January 26, 2019
Published online: February 18, 2019

insurance subgroups were calculated.

RESULTS

Rate of surgery increased in the post-reform period (pre-reform 8.07% (95%CI: 7.03%-9.11%), post-reform 9.38% (95%CI: 8.74%-10.03%) (P = 0.04) and was statistically significant. When the insurance groups and insurance types were compared, the rates of surgery are not significantly different before or after reform.

CONCLUSION

The increase in the rate of elective knee surgery in the post-reform period suggests that health care reform in Massachusetts has been successful in decreasing the uninsured population and may increase health care expenditures. This is a hypothesis generating study that suggests further avenues of study on how mandated coverage may change healthcare utilization and cost.

Key words: Healthcare reform; Elective surgery; Lower extremity; Affordable Care Act; Orthopaedic surgery

Core tip: We examined how an individual mandate in the United States may affect rates of knee surgery. This topic is of great interest as the United States thinks about moving to a universal coverage model and to countries that already have such a system. We found that the rate of surgery increased after the implementation of mandated universal coverage. Also, we found that patients on lesser reimbursing insurance plans were not discriminated against compared to private insurance plans.

Citation: Kim D, Do W, Tajmir S, Mahal B, DeAngelis J, Ramappa A. Mandated health insurance increases rates of elective knee surgery. *World J Orthop* 2019; 10(2): 81-89
URL: https://www.wjgnet.com/2218-5836/full/v10/i2/81.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i2.81

INTRODUCTION

The passage of the Affordable Care Act (ACA) nationally under the Obama administration in March 2010 stimulated discussion over how the individual mandate and other provisions of the law would affect the utilization and delivery of healthcare. With annual costs of $849 billion a year, orthopaedic care delivery accounts for nearly 7.7% of the GDP, affects 77 million Americans annually, and is an essential component to the successful reformation of United States healthcare[1]. Recently, the ACA was struck down by a federal judge on the grounds that the mandate requiring people to buy health insurance was unconstitutional[2,3]. This ruling has the potential to result to seismic shifts to the healthcare market and brings the debate of healthcare reform back into the spotlight.

In 2007 Massachusetts was the first state to pass a sweeping healthcare reform law. Because its provisions are very similar to the ACA (a universal coverage mandate, a government-run healthcare exchange (Commonwealth Connector), and novel partially-subsidized managed care plans (Commonwealth Care), eyes are once again focused on the Massachusetts as a test case for how ACA will affect the rest of the country. Given the similarities between the Massachusetts law and the ACA, it is very likely that changes in orthopaedic care delivery in post-reform Massachusetts will reflect future changes nationally. One area of particular interest is how much care utilization might change with mandated coverage as the one of the primary costs of healthcare reform is how to control costs.

One important component of these laws is their effect on rate of elective orthopaedic surgery. Previous studies have documented insurance-based differences in rates of elective upper extremity orthopaedic surgery. However, there have been no studies comparing pre- and post-reform rates for knee surgery[4-6]. Given the renewed attention and likely heated debate that will follow this recent ruling, study the Massachusetts experience with mandated coverage is important.

Therefore, we sought to examine a cohort of patients at a single academic orthopaedic practice in Massachusetts to determine if there were insurance-based differences in the rate of elective knee surgery (ROS) pre- and post-reform. We hypothesized that the ROS post-reform would be higher due to increased access and utilization.

MATERIALS AND METHODS

Approval for this investigation was obtained from the Institutional Review Board. A retrospective review was performed within the department of orthopedics at a tertiary-care, academic medical center in Massachusetts. The departmental billing database was queried to identify all International Classification of Diseases, Ninth Revision, Clinical Modification codes related to the knee. In an effort to validate the cohort, the ten most common diagnosis codes were identified for two periods in time: Pre-reform (calendar years 2005-2006) and post-reform (calendar years 2007-2010) periods for three orthopaedic surgeons. When compared, the pre- and post-reform ICD-9 codes were found to be identical, suggesting that the spectrum of disease in both periods was similar (Appendix A). These ten diagnosis codes were then used to identify all new patients seen by three surgeons in pre-reform (2005-2006) and post-reform (2007-2010) periods (n = 10420).

Although the healthcare reform was passed on April 12, 2006, the law did not take effect until the beginning of 2007. In keeping with prior investigations, the calendar year 2006 was considered pre-reform[5,6]. To control for confounders, eligible patients were limited to those seeking care from three orthopaedic surgeons with established practices at one academic institution throughout both study periods.

For each patient, age, sex, highest level of education, body mass index (BMI), dates of service, ICD-9 codes, and insurance status at time of presentation were recorded. The billing database contained twenty-one different providers. These different payers were grouped into four insurance groups (uninsured, government, private, Workers' Compensation) and seven insurance types (Medicaid, Medicare, Worker's Compensation, private insurance, uninsured, Commonwealth Care, and TriCare) allowed for continuity with previous investigations[5,6].

The ROS was defined as the number of patients who underwent surgery divided by the total number of unique patients in that cohort. For each insurance type at both points in time, the ROS was calculated. In keeping with the method described by McGlaston *et al*[6], an effect size of greater than or equal to 10% in the rate of surgery was considered clinically significant. An a priori sample size analysis indicated that a 10% difference in the rate of surgery between insurance categories with an α of 0.05 and a β of 0.20 (power = 0.80) could be achieved with 300 persons per insurance category.

The ROS was compared using a Pearson-type χ^2 test with Yate's continuity correction for the entire cohort, each group (uninsured *vs* government insurance *vs* private insurance *vs* Workers' Compensation) and the seven types of insurance (uninsured *vs* Commonwealth Care *vs* Medicare *vs* Medicaid *vs* TriCare *vs* private insurance *vs* Workers' Compensation) pre-reform and post-reform. A two-tailed P-value less than or equal to 0.05 was considered significant.

RESULTS

In this study, 2640 patients were enrolled from the pre-reform period and 7780 during the post reform. While gender did not significantly differ between the two study periods, comparison of the cohort's demographics reveals several disparities (Table 1).

Self-reported racial groups demonstrated a significant increase in "White" patients and significant decreases in "Other" and "Unknown/Unreported". The highest level of education showed a significant increase in all groups except "I did not attend school" and "8th grade or less". BMI showed a significant increase in "Overweight" and a significant decrease in "Unreported." The population of uninsured patients dropped significantly post-reform from 8% to 3%, and the population of private insurance increased significantly from 57% to 61%. When divided into insurance subgroups, TriCare subgroup's increase was statistically significant from 1% to 2% as was Medicaid's statistically significant decrease post-reform from 10% to 9%. Of note, Commonwealth Care did not exist before the reform.

Insurance grouping

There were 21 different payers present in the patient cohort. These different payers

Table 1 Demographic characteristics of the pre- and post-reform cohorts

		Pre-reform (*n*)	(%)	Post-reform (*n*)	(%)	*P*-value
Total		2640		7780		
Gender						
	Female	1551	59%	4419	57%	0.08
	Male	1089	41%	3361	43%	
Race						
	White	1592	60%	4997	64%	0.00
	Black	440	17%	1320	17%	0.72
	Asian	98	4%	323	4%	0.32
	Hispanic	208	8%	594	8%	0.69
	Native American	2	0%	8	0%	0.70
	Other	114	4%	242	3%	0.00
	Unknown/Unreported	186	7%	296	4%	0.00
Highest Education						
	Unreported	948	36%	398	5%	0.00
	I did not attend school	12	0%	41	1%	0.65
	8th grade or less	61	2%	215	3%	0.21
	Some high school	86	3%	341	4%	0.01
	Graduated from high school or GED	380	14%	1528	20%	0.00
	Some college/vocational/technical pgrm	222	8%	1033	13%	0.00
	Graduated from college, graduate or post	692	26%	3192	41%	0.00
	Other	22	1%	151	2%	0.00
	Patient declined to answer	133	5%	656	8%	0.00
	Patient unavailable to answer	84	3%	225	3%	0.47
BMI						
	Unreported	1279	48%	3221	41%	0.00
	Underweight/normal (0-18.49)	20	1%	42	1%	0.21
	Overweight (18.5-24.9)	249	9%	947	12%	0.00
	Obese, Class I (25-29.9)	436	17%	1385	18%	0.13
	Obese, Class II (30-34.9)	319	12%	1107	14%	0.06
	Obese, Class III (35+)	337	13%	1078	14%	0.16
Insurance Type						
	Uninsured	199	8%	204	3%	0.00
	Private	1507	57%	4715	61%	0.00
	Government	854	32%	2646	34%	0.12
	Workers' compensation	80	3%	215	3%	0.48
Insurance sub-types						
	Medicare	563	21%	1593	20%	0.35
	Medicaid	271	10%	694	9%	0.04
	CommCare	0	0%	240	3%	0.00
	TriCare	20	1%	119	2%	0.00
	Private	1507	57%	4715	61%	0.00
	Workers Comp	80	3%	215	3%	0.48
	Uninsured	199	8%	204	3%	0.00

were grouped into four insurance groups (uninsured, government, private, and workers' compensation) and seven insurance types (Medicaid, Medicare, Worker's Compensation, private, uninsured, Commonwealth Care, and TriCare). Figure 1 details the distribution of patients in each group.

Whole cohort rates of surgery: Pre-reform vs post-reform

Comparing all-patients pre-reform and post-reform, the pre-reform ROS was 8.07% (95%CI: 7.03%-9.11%) and 9.38% in the post-reform period (95%CI: 8.74%-10.03%; P = 0.04) (Figure 2).

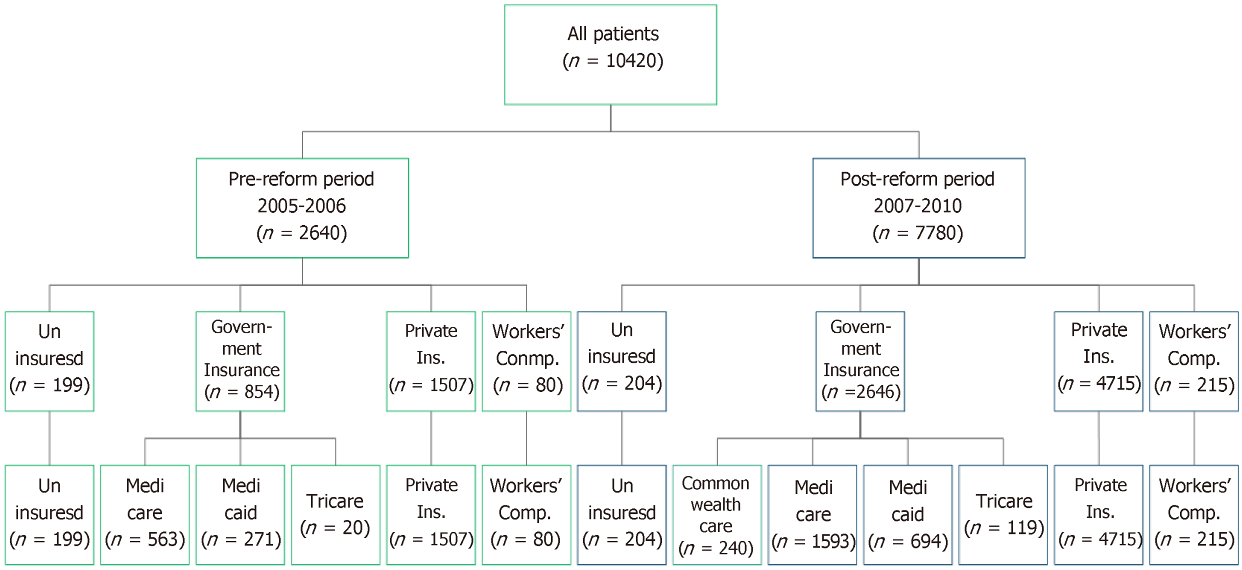

Figure 1 Cohort distribution by payer group.

Four insurance group rates of surgery: Pre-reform *vs* post-reform

When the groups were compared by their type of insurance (uninsured, private, government-sponsored, and Workers' Compensation, no significant differences were found before and after healthcare reform (Figure 3).

Seven insurance group rates of surgery: Pre-reform *vs* post-reform

Insurance subgroup analysis further subdivided the patients within the government group into Medicare, Medicaid, TriCare, and Commonwealth Care. Each group's rate of surgery pre-reform and post-reform was computed and compared using chi-square analysis. Rates of Surgery were as follows: Medicare 6.6% pre-reform and 8.0% post-reform (P = 0.26162); Medicaid 11.8% pre-reform and 9.7% post-reform (P = 0.32167); TriCare 20.0% pre-reform and 15.1% post-reform (P = 0.82471); Private patients' 7.8% pre-reform and 9.4% post-reform (P = 0.0582); Workers' Compensation 10.0% pre-reform and 16.7% post-reform (P = 0.2070); and uninsured patients' 7.0% pre-reform and 8.3% post-reform (P = 0.6249). Rates of surgery across these six groups were not significantly different when compared between the two periods (Figure 4).

DISCUSSION

This investigation sought to compare the rate of elective knee orthopaedic surgery in a large academic practice before and after healthcare reform in Massachusetts. Given the similarity between the ACA and the mandated coverage stipulated by the Massachusetts law in 2007, this study provides insight into how the rate of elective orthopaedic surgery may change nationally in light of the recent ruling against the ACA and the mandated coverage requirement. It is hypothesis generating and suggests avenues for further research into mandated coverage within Massachusetts and nationally.

Comparing the overall rate of surgery during the pre- and post-reform periods, there was a significant increase in the ROS following mandated coverage. When the cohort is examined by insurance group (uninsured, government, private, Workers' Compensation), there is no difference in ROS (Figure 3). Similarly, when the individual insurance types (Medicaid, Medicare, Worker's Compensation, private insurance, uninsured, Commonwealth Care, and TriCare) are considered, the ROS before and after reform remains unchanged (Figure 4).

This finding suggests that with increased insurance coverage (near-universal), patients enjoy increased access to medical services, and, in turn, there may be a higher ROS for musculoskeletal problems. This explanation assumes that there are patients without insurance with operative diagnoses that are now becoming surgical candidates because they are insured. This idea is supported by a significant decrease in the number of uninsured patients. It is possible that a musculoskeletal problem, which was neglected while a patient was uninsured, might require a surgery once they have coverage.

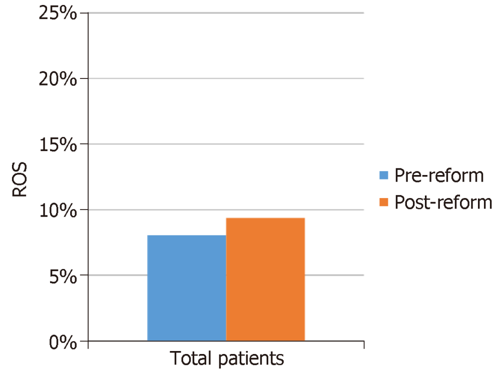

Figure 2 Rates of Surgery Increased from 8.07% to 9.38% post-healthcare reform. ROS: Rate of elective knee surgery.

The absence of a statistically significant difference in the ROS in both insurance group and insurance type before and after reform is mostly likely due to the limited size of this investigation. From the a priori sample size analysis, each subgroup would require 300 individuals in order to identify a 10% change in the ROS. Despite starting with more than 10000 eligible patients, many of the subgroups (both insurance groups and type) had less than the recommended 300 individuals participating. Specifically, in the four sub-group analysis, the Workers' Compensation and uninsured categories were underpowered. In the seven sub-group analysis, all groups were underpowered, except the Medicare insurance group.

The overall comparison of ROS is interesting given that the post-reform period had a significantly higher number of elective surgeries performed. This change may be due to greater access to surgery with the mandated insurance coverage. In this sense, the post-reform period has captured previously uninsured people who would have otherwise not had an elective procedure. However, it is difficult to assess whether a previously uninsured person obtained insurance and then had an elective procedure they would have formerly forgone. Similarly, another potential confound is how physician behavior may have changed in response to mandated coverage. Hypothetically, if government-supported plans offer lower reimbursement, it is possible that the fee change might influence a surgeon's willingness to operate. While this effect was not studied implicity, the data suggest that such an effect is unlikely because private and subsided plans had similar rates of surgery. In this way, these data support the argument that obtaining health insurance is helpful in decreasing healthcare disparities in orthopaedics, a finding that has been described in elective upper extremity surgery[6]. While this investigation was performed within an academic center, physician remuneration in this practice is based on cash collections, not relative value units or a productivity metric. As a result, the financial benefit associated with surgical treatment and fostering a better payer mix do not appear to have influenced physician behavior.

In Massachusetts, healthcare reform has been deemed a success because the number of uninsured people has decreased. The uninsured rate in Massachusetts has fallen from 10.9% in 2006 to 5.5% in 2007 (US average: 17.1% in 2006 and 16.6% in 2007)[7]. In the practice studied, the drop in uninsured patients was equally impressive, declining from 8% in the pre-reform period to 3% post-reform. However, the system has struggled to contain cost.

The price of health care in Massachusetts despite reform is concerning[8,9]. In May 2012 the non-partisan Kaiser Family Foundation Executive Summary found that since the law's enactment, the Commonwealth is struggling with rising health care costs. Per capita spending is 15% higher than the national average and Massachusetts continues to have the highest individual premiums in the country[10]. Furthermore, per capita health care spending increased from $8002 in 2006 to $9278 in 2009, 36% higher than the national average $6815[10].

Because the ROS increased in the post-reform period, it is possible that mandated coverage in Massachusetts leads to rising costs in a time when national health care spending has leveled off for the first time in over a decade[7,11]. While the reasons behind the slowdown in national health care spending are hotly debated, there is no question that cost containment is a priority and drives the health care debate today.

To strengthen this analysis, the entire cohort of patient was selected for the specified diagnoses to minimize selection bias. The sample size provided sufficient statistical power for a comparative analysis. As a single-institution, potentially

Figure 3 No significant difference in rate of elective knee surgery when compared by insurance type. ROS: Rate of elective knee surgery.

confounding site-specific and geographic variables were avoided. However, as a retrospective review, this study has its limitations. Certain insurance subgroups included fewer than 300 persons, increasing the probability of a type II error. This highlights an inherent challenge in studying groups that constitute a relatively small proportion of the overall population. While performing subgroup analysis may reduce statistical power, it should not be avoided, as previous work has shown that insurance-based differences in operative rates are subtle and may be masked by the method of insurance stratification[5,6]. Future studies of larger cohorts may address this issue. Generalizability may be an issue if orthopaedic care differs from institution to institution.

At baseline, there were some differences in the two cohorts. Among self-reported race, education, and BMI groups, there were statistically significant disparities. In the pre-reform period, the data had a higher chance of being unknown for a given group when compared to the post-reform period. This leads to significant increases within the individual categories while decreasing the unreported or unknown category. Whether the significant increase in the white racial group was due to a true demographic change or improved reporting is unclear. The highest reported level of education experienced a similar pattern. In the pre-reform period, 36% of patients did not report their highest level of education compared with the 5% post-reform did not. This difference may have led to the statistically significant increases in all education categories seen in the post-reform period. Interestingly, BMI also experienced a decrease in the unreported fraction from 48% to 41%. This change resulted in a statistically significant increase from 9% to 12%.

Despite its limitations, this investigation offers several avenues for future study. A more comprehensive evaluation of orthopaedic practices before and after the enactment of health care reform laws in Massachusetts would enable further clarification of the effect of mandated coverage on health care spending. The statistically significant increase in rate of elective orthopaedic knee surgery in the post-reform period suggests that health care reform in Massachusetts, while successful in decreasing the uninsured population, may result in health care expenditures. In turn, higher utilization requires more careful examination. While the rate of surgery may be an imperfect proxy for cost, mandated coverage could result in increased health care spending by increasing the availability of medical services.

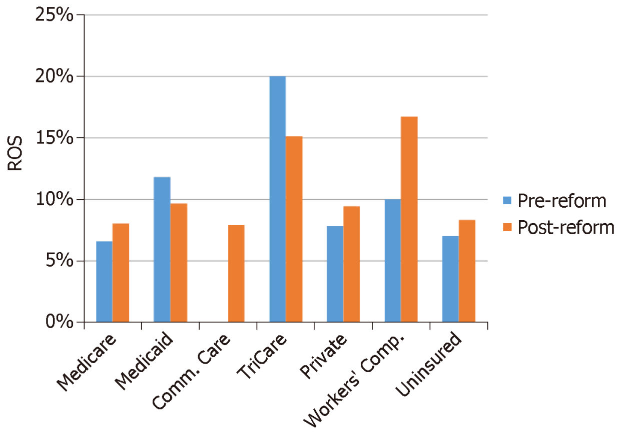

Figure 4 No significant difference in rate of elective knee surgery when compared by insurance sub-type. ROS: Rate of elective knee surgery.

ARTICLE HIGHLIGHTS

Research background

Our study is timely given the recent federal ruling against the Affordable Care Act (ACA), specifically the mandate requiring people to buy insurance. The ACA increased the number of insured Americans through the development of subsidized healthcare plans and health insurance exchanges. Healthcare reform was enacted in Massachusetts, where a similar mandate was put into place years before the ACA was passed. We use this opportunity to describe differences in rates of surgery before and after the implementation of the mandate to purchase insurance after healthcare reform.

Research motivation

We answer the key question of whether healthcare reform and the individual mandate increases the rate of knee surgery. Healthcare cost and healthcare reform are the key questions facing the medical field today. How physicians can deliver quality care without exorbitant costs is of interest to many around the world. This hypothesis generating study provides strong impetus to further examine the effects of healthcare reform on other health services.

Research objectives

The main objective was to determine if healthcare reform had an effect on the rate of knee surgery in the state of Massachusetts. The significance of realizing this research is a greater impetus to study healthcare reform and how it may reflect healthcare costs going forward. This is of great interest to every nation in the world.

Research methods

A retrospective review was performed within the department of orthopedics at a tertiary-care, academic medical center in Massachusetts. The departmental billing database was queried to identify all International Classification of Diseases, Ninth Revision, Clinical Modification codes related to the knee. These ten diagnosis codes were then used to identify all new patients seen by three surgeons in pre-reform (2005-2006) and post-reform (2007-2010) periods (n = 10420). The rate of surgery was defined as the number of patients who underwent surgery divided by the total number of unique patients in that cohort. For each insurance type at both points in time, the rate of elective knee surgery (ROS) was calculated. The ROS was compared using a Pearson-type χ^2 test with Yate's continuity correction for the entire cohort, each group (uninsured *vs* government insurance *vs* private insurance *vs* Workers' Compensation) and the seven types of insurance (uninsured *vs* Commonwealth Care *vs* Medicare *vs* Medicaid *vs* TriCare *vs* private insurance *vs* Workers' Compensation) pre-reform and post-reform. A two-tailed p-value less than or equal to 0.05 was considered significant.

Research results

Comparing the overall rate of surgery during the pre- and post-reform periods, there was a significant increase in the ROS following mandated coverage. This finding suggests that with increased insurance coverage (near-universal), patients enjoy increased access to medical services, and, in turn, there may be a higher ROS for musculoskeletal problems. Because the ROS increased in the post-reform period, it is possible that mandated coverage in Massachusetts leads to rising costs in a time when national health care spending has leveled off for the first time in over a decade. Given the limitations of our study, a study to better examine the relationship between healthcare reform and costs should be considered.

Research conclusions

Healthcare reform and a mandate to purchase health insurance increase the rate of knee surgery.

It suggests that having a mandate to buy insurance will lead to increased healthcare costs as patients who now have insurance will utilize more care. Healthcare reform and the individual mandate lead to high rates of knee surgery. As above, healthcare reform and the individual mandate lead to high rates of knee surgery. Healthcare costs increase as more people obtain insurance. The main difference in our study was that we controlled for surgeon number. Other studies can be confounded increasing or decreasing number of providers. We were able to analyze rates of surgery across three surgeons before and after healthcare reform, keeping one of the largest confounders constant. As noted above, healthcare reform and a mandate to purchase health insurance increases the rate of knee surgery. Rates of healthcare utilization are higher in places that have a greater proportion of insured patients as they utilize more healthcare services.

Research perspectives

Healthcare reform should be pursued carefully as policies to increase access may also increase costs which may not be desired. A study to examine how other procedures and healthcare service utilization changed with healthcare reform. A similar study can be done for other types of procedures assuming appropriate sample size and ability to collect key information such as rates of procedure done before and after healthcare reform. It would be interesting to do in Massachusetts but also on a national level.

REFERENCES

1 **AAOS**. Burden of Musculoskeletal Diseases in the United States: Prevalence, Societal and Economic Cost. Amer Academy of Orthopaedic, 2008. Available from: https://www.boneandjointburden.org/docs/The%20Burden%20of%20Musculoskeletal%20Diseases%20in%20the%20United%20States%20(BMUS)%202nd%20Edition%20(2011).pdf

2 **Time**. A Judge Ruled Obamacare is Unconstitutional, Here's How it Could Impact Your Health Insurance. Dec 18, 2018. Available from: http://time.com/5482004/affordable-care-act-court-ruling/

3 **Goodnough A**, Pear R. Texas Judge Strikes Down Obama's Affordable Care Act as Unconstitutional. Dec 14, 2018. Available from: https://www.nytimes.com/2018/12/14/health/obamacare-unconstitutional-texas-judge.html

4 **Brinker MR**, O'Connor DP, Pierce P, Spears JW. Payer type has little effect on operative rate and surgeons' work intensity. *Clin Orthop Relat Res* 2006; **451**: 257-262 [PMID: 16906062 DOI: 10.1097/01.blo.0000229308.90265.96]

5 **Gundle KR**, McGlaston TJ, Ramappa AJ. Effect of insurance status on the rate of surgery following a meniscal tear. *J Bone Joint Surg Am* 2010; **92**: 2452-2456 [PMID: 20962196 DOI: 10.2106/JBJS.I.01369]

6 **McGlaston TJ**, Kim DW, Schrodel P, Deangelis JP, Ramappa AJ. Few insurance-based differences in upper extremity elective surgery rates after healthcare reform. *Clin Orthop Relat Res* 2012; **470**: 1917-1924 [PMID: 22451335 DOI: 10.1007/s11999-012-2305-8]

7 **Ryu AJ**, Gibson TB, McKellar MR, Chernew ME. The slowdown in health care spending in 2009-11 reflected factors other than the weak economy and thus may persist. *Health Aff (Millwood)* 2013; **32**: 835-840 [PMID: 23650315 DOI: 10.1377/hlthaff.2012.1297]

8 **Bigby J**. Controlling health care costs in Massachusetts after health care reform: there is no silver bullet. *Arch Intern Med* 2009; **169**: 1833-1835 [PMID: 19901133 DOI: 10.1001/archinternmed.2009.335]

9 **Long SK**, Stockley K, Dahlen H. Massachusetts health reforms: uninsurance remains low, self-reported health status improves as state prepares to tackle costs. *Health Aff (Millwood)* 2012; **31**: 444-451 [PMID: 22282572 DOI: 10.1377/hlthaff.2011.0653]

10 **Kaiser Family Foundation**. Massachusetts Health Care Reform: Six Years Later. 2012. Available from: https://www.kff.org/health-costs/issue-brief/massachusetts-health-care-reform-six-years-later/

11 **Cutler DM**, Sahni NR. If slow rate of health care spending growth persists, projections may be off by $770 billion. *Health Aff (Millwood)* 2013; **32**: 841-850 [PMID: 23650316 DOI: 10.1377/hlthaff.2012.0289]

P- Reviewer: Angoules A, Elgafy H, Emara KM, Ohishi T, Papachristou G

S- Editor: Ji FF **L- Editor:** A **E- Editor:** Wu YXJ

World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 February 18; 10(2): 90-100

DOI: 10.5312/wjo.v10.i2.90

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Retrospective Study

Return to sport after lower limb arthroplasty - why not for all?

Shivan S Jassim, Jenni Tahmassebi, Fares S Haddad, Angus Robertson

ORCID number: Shivan S Jassim (0000-0002-7855-3743); Jenni Tahmassebi (0000-0002-3953-4566); Fares S Haddad (0000-0003-0311-2211); Angus Robertson (0000-0001-5922-5130).

Author contributions: Jassim SS contributed to writing manuscript, idea for paper; Tahmassebi J contributed to data collection; Robertson A contributed to review of manuscript; Haddad FS contributed to idea for paper and review of manuscript.

Institutional review board statement: Ethical approval for this study was granted by Cardiff Metropolitan University Review Board.

Conflict-of-interest statement: All authors have no conflicts of interest within this study and have signed a statement confirming this.

Manuscript source: Unsolicited manuscript

Received: November 6, 2018
Peer-review started: November 10,

Shivan S Jassim, Trauma and Orthopaedics, Royal London Hospital, London E1 1BB, United Kingdom

Jenni Tahmassebi, Fares S Haddad, Trauma and Orthopaedics, University College London Hospital, London NW1 2BU, United Kingdom

Angus Robertson, Trauma and Orthopaedics, Cardiff and Vale NHS Trust, Cardiff CF64 2XX, United Kingdom

Corresponding author: Shivan S Jassim, MBBS, MSc, Surgeon, Trauma and Orthopaedic Registrar, Trauma and Orthopaedics, Royal London Hospital, Whitechapel Road, London E1 1BB, United Kingdom. shivan.jassim@doctors.org.uk
Telephone: +44-20-73777000

Abstract

BACKGROUND
Total hip and knee replacements are being performed in increasing numbers in progressively younger patients with higher activity demands. Many such patients have expectations of returning to athletic activity post-operatively yet are not always able to do so and the reasons behind this have not been extensively examined. We hypothesise that any reasons for a failure to return to athletic activity post-operatively are multi-factorial.

AIM
To quantify the return to athletic activity following lower limb joint arthroplasty and understand qualitative reasons for altered activity participation.

METHODS
A single centre, single surgeon retrospective questionnaire for hip and knee arthroplasty patients under age 60 years, minimum two years post-surgery with exclusion criteria of multiple degenerative joint involvement and multiple medical co-morbidities. Outcomes were validated joint-specific (Oxford hip and knee) and lifestyle questionnaires [short form 12 (SF-12) and University of California, Los Angeles (UCLA)] and an activity questionnaire assessing ability participation in athletic activity post-operatively. Statistical analysis was performed on the validated outcome data, including comparison between hip and knee replacements. Frequency tables were produced to quantify the different athletic activities participated in by patients.

RESULTS
Responses were received from 64 patients (80% response rate). There was a statistically significant improvement in Oxford hip and knee scores following surgery. SF-12 scores also improved for all patients, but no statistically significant

2018
First decision: December 7, 2018
Revised: January 22, 2019
Accepted: January 26, 2019
Article in press: January 26, 2019
Published online: February 18, 2019

difference was seen between joints (P = 0.88). Mean UCLA scores pre-operatively were 7.67 and at two years post-operatively were 7.69, with no statistically significant change (P = 0.91). All patients reported high satisfaction and improved ability to perform athletic activity at a higher frequency compared to pre-operatively. The most common reasons for changing activity participation were not wanting to stress their joint replacement or instructions by other doctors or the lead surgeon. There was no difference in the responses to the questionnaire based on type of joint replacement (P = 0.995).

CONCLUSION

Patients receiving a joint replacement are able to participate in athletic activity to high levels and are satisfied with their outcomes. Reasons for non-participation are multi-factorial.

Key words: Joint replacement; Athletic activity; Sport; Outcomes

Core tip: Returning to athletic activity is an important goal for many younger patients undergoing hip or knee arthroplasty. Up until now, it is known that, whilst some are able to return to athletic activity, not all patients return to their chosen activity. This qualitative study demonstrates that patients are highly satisfied with their arthroplasty with respect to returning to athletic activity but the reasons for changing their activity of choice varies equally from decisions made by the patient themselves to instructions provided by their surgeon or other medical practitioner.

Citation: Jassim SS, Tahmassebi J, Haddad FS, Robertson A. Return to sport after lower limb arthroplasty - why not for all? *World J Orthop* 2019; 10(2): 90-100
URL: https://www.wjgnet.com/2218-5836/full/v10/i2/90.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i2.90

INTRODUCTION

Total joint replacement (TJR) is an increasingly-performed orthopaedic operation in the United Kingdom[1] and the patient groups having these operations are progressively younger with high activity levels and thus high demands. Sophisticated measures have been developed to more closely reflect health gains associated with TJR beyond mortality and morbidity rates, operative complications and implant survival[2,3]. General function has been shown to improve following TJR but an important and often-neglected consideration are the levels of athletic participation following these operations in younger populations; this has particular relevance given that athletes are at greater risk of developing osteoarthritis of the hip and knee[4-6]. Such patients will have high expectations of continuing to participate in athletic activity following surgery[7].

Relatively few studies have investigated return to sporting activity following TJR. Conflicting opinions have emerged about the suitability of athletic activity following total hip replacement (THR)[8-12] and total knee replacement (TKR)[13,14]. Recent studies analysing the return to sport for both TKR and THR patients were unable to find a difference in rates between the two joints[15,16]. It has, however, been demonstrated that rather than the type of implant received, characteristics such as male sex, lower age, lower BMI and a high pre-operative level of sport participation predicted increased chances of return to athletic activity post-TJR[17].

In addition, TJR patients participating in athletic activities may be at increased risk of acute complications, such as periprosthetic fracture or dislocation; repetitive loading of the implant may pre-dispose to osteolysis and subsequent aseptic loosening[18]. Implant retrieval studies in TKR patients have demonstrated a statistically significant correlation between rates of linear and volumetric wear and University of California, Los Angeles (UCLA) activity scores[19]; similar associations are seen in THR populations[20].

Therefore, although participation in sporting activity is possible post-TJR, it has also been demonstrated that there is a decline in high-impact activities and no studies

2018
First decision: December 7, 2018
Revised: January 22, 2019
Accepted: January 26, 2019
Article in press: January 26, 2019
Published online: February 18, 2019

difference was seen between joints (P = 0.88). Mean UCLA scores pre-operatively were 7.67 and at two years post-operatively were 7.69, with no statistically significant change (P = 0.91). All patients reported high satisfaction and improved ability to perform athletic activity at a higher frequency compared to pre-operatively. The most common reasons for changing activity participation were not wanting to stress their joint replacement or instructions by other doctors or the lead surgeon. There was no difference in the responses to the questionnaire based on type of joint replacement (P = 0.995).

CONCLUSION

Patients receiving a joint replacement are able to participate in athletic activity to high levels and are satisfied with their outcomes. Reasons for non-participation are multi-factorial.

Key words: Joint replacement; Athletic activity; Sport; Outcomes

Core tip: Returning to athletic activity is an important goal for many younger patients undergoing hip or knee arthroplasty. Up until now, it is known that, whilst some are able to return to athletic activity, not all patients return to their chosen activity. This qualitative study demonstrates that patients are highly satisfied with their arthroplasty with respect to returning to athletic activity but the reasons for changing their activity of choice varies equally from decisions made by the patient themselves to instructions provided by their surgeon or other medical practitioner.

Citation: Jassim SS, Tahmassebi J, Haddad FS, Robertson A. Return to sport after lower limb arthroplasty - why not for all? *World J Orthop* 2019; 10(2): 90-100
URL: https://www.wjgnet.com/2218-5836/full/v10/i2/90.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i2.90

INTRODUCTION

Total joint replacement (TJR) is an increasingly-performed orthopaedic operation in the United Kingdom[1] and the patient groups having these operations are progressively younger with high activity levels and thus high demands. Sophisticated measures have been developed to more closely reflect health gains associated with TJR beyond mortality and morbidity rates, operative complications and implant survival[2,3]. General function has been shown to improve following TJR but an important and often-neglected consideration are the levels of athletic participation following these operations in younger populations; this has particular relevance given that athletes are at greater risk of developing osteoarthritis of the hip and knee[4-6]. Such patients will have high expectations of continuing to participate in athletic activity following surgery[7].

Relatively few studies have investigated return to sporting activity following TJR. Conflicting opinions have emerged about the suitability of athletic activity following total hip replacement (THR)[8-12] and total knee replacement (TKR)[13,14]. Recent studies analysing the return to sport for both TKR and THR patients were unable to find a difference in rates between the two joints[15,16]. It has, however, been demonstrated that rather than the type of implant received, characteristics such as male sex, lower age, lower BMI and a high pre-operative level of sport participation predicted increased chances of return to athletic activity post-TJR[17].

In addition, TJR patients participating in athletic activities may be at increased risk of acute complications, such as periprosthetic fracture or dislocation; repetitive loading of the implant may pre-dispose to osteolysis and subsequent aseptic loosening[18]. Implant retrieval studies in TKR patients have demonstrated a statistically significant correlation between rates of linear and volumetric wear and University of California, Los Angeles (UCLA) activity scores[19]; similar associations are seen in THR populations[20].

Therefore, although participation in sporting activity is possible post-TJR, it has also been demonstrated that there is a decline in high-impact activities and no studies have explicitly considered specific reasons for the failure of patients to continue with such high-impact activity following TJR. Understanding this is key so that patients considering TJR can be well informed regarding their post-operative prognosis for sporting participation. The aim of this study is to investigate the activity levels and rate of return to athletic activity post arthroplasty and identify qualitative reasons for changes in activity participation.

MATERIALS AND METHODS

A single centre, single surgeon, retrospective questionnaire study was designed. Ethical board approval was received. From the personal database of the lead surgeon (FSH), a list of patients who have received either THR or TKR was obtained with at least 2 years' follow-up. Patients were excluded if they were over the age of 65 years, had an American Society of Anaesthesiologists (ASA) grade of greater than 2 or another joint replacement in situ in order to control for factors that are known to reduce participation in sports post arthroplasty and confound results[17].

Questionnaires

Participation in sports after arthroplasty was determined with the use of self-administered validated activity and lifestyle questionnaires and a subjective activity-related questionnaire. The Oxford Knee and Hip Scores (OKS, OHS)[21] were used to assess the joint-specific functional abilities of the patients. The short form 12 (SF-12) was used to assess the general lifestyle of the patient and has also been validated following TJR[22]. The UCLA activity scale was used to determine participation in functional activity related to sports and correlates most closely with other functional activity scores in comparison to the Tegner score[23]. Patients were asked to complete one UCLA score for the time just prior to their operation and one for their current activity levels. A questionnaire was designed to specifically assess patients' participation levels in sporting activity and reasons behind a lack of participation of sports (if any) (Appendix 1). All patients under the care of the lead surgeon have their OKS/OHS and SF-12 scores collected at the time of surgery as routine practice; these scores were used as their baseline measurements.

Data collection

A total of 80 suitable patients were selected from the database. All patients were contacted by telephone to gain consent for participation. Instructions for completing questionnaires were given with a further option for contact after receipt of the questionnaire to discuss any points for clarification. All patients agreeing to participate received the above questionnaires either via email or via post with a stamped-return envelope. After two weeks, 52 questionnaires were received. The remainder received a telephone call as a reminder and 8 further responses were received. Two weeks following this, the remaining non-responding patients received a telephone call as a reminder. The final number of questionnaires received was 64, giving a total 80% response rate. Upon collection of all data, the scores were entered into a secure database. The sample mean and standard deviation was calculated for the OHS, OKS, SF-12 and UCLA scores. Frequency tables were made for the responses to the sports activity questionnaire.

Statistical analysis

Descriptive statistical testing was done using XLSTAT software version 7 (Addinsoft, New York, United States) and separate analysis was performed for THR and TKR patients. A Shapiro-Wilk calculation demonstrated the scores were normally distributed and a paired t-test was used to compare outcomes within the different joint replacements at baseline and at two years, whilst an independent t-test was used to compare the outcomes of SF-12 and UCLA scores between THR and TKR patients. Chi-squared testing was used to compare the outcomes of the activity questionnaire. A significance level of $P = 0.05$ was set.

RESULTS

A total of 80 questionnaires were sent out to eligible participants and a total of 64 completed forms were received, giving a response rate of 80%. All patients were a minimum of two years since their operation. Their demographics are presented in Table 1.

Table 1 Patient demographics

	THR	TKR	Total
Number of patients	40	24	64
Mean age (SD; range) in years	53.1 (8.4; 33-64)	60 (2.5; 54-64)	55.7 (7.5; 33-64)
Sex M:F	19:21	10:14	29:35
Mean time since operation (SD; range) in years	3.3 (1.1; 2.5-5)	3 (0.9; 2-4.5)	3.1 (0.9; 2-5)

THR: Total hip replacement; TKR: Total knee replacement.

Functional scores

There was an increase between mean baseline and two-year OHS and OKS scores (Table 2), which was statistically significant (P < 0.0001). There was an increase between the mean baseline and two-year SF-12 scores for both the physical and mental portions which was statistically significant (P < 0.0001). The difference between the two joint cohorts demonstrated a higher mean physical score for the TKR cohort but no statistically significant difference between the two joints using an independent t-test at two years post-TJR (P = 0.88) and a higher mean mental score for the TKR cohort at two years post-TJR which was statistically significant (P = 0.005).

The mean baseline UCLA score for the entire cohort was 7.67 (range 6-10). At two years, the mean score was 7.69 (range 6-10) with no statistically significant difference (P = 0.91) between baseline and two year scores. Nine patients had an improvement in their score at 2 years whilst seven patients had a decrease in their score; 48 patients had the same score. Within the joints, there was an increase in the mean UCLA score in THR patients (7.78 to 7.93) and a decrease in TKR patients (7.5 to 7.29). Neither of these results was statistically significant (P = 0.47 for THR cohort and P = 0.17 for TKR cohort). The difference between the two joint cohorts is shown in Table 2, demonstrating that THR patients had a higher mean 2 year UCLA score than the TKR cohort; this was found to be statistically significant (P = 0.03). There were no dislocations and no revisions for fracture, infection or instability amongst the patients.

Sports activity questionnaire

The responses to the questionnaire are displayed in Figures 1-6 and Table 3. There were no statistically significant differences in the responses based on the type of TJR for satisfaction with their TJR (P = 0.997), likelihood of recommending a TJR (P = 0.644), importance of athletic activity post-TJR (P = 0.768), frequency of performing athletic activity post-TJR (P = 0.834) and ability to perform athletic activity post-TJR (P = 0.645)

When asked the reasons for non-participation in their chosen athletic activity, 17 patients felt they had no limitations to performing their chosen activity. The most common reasons listed for non-participation were "I don't want to stress my joint replacement" (17 patients), "A physiotherapist/other doctor/other health professional has told me not to do the activity any more" (11 patients) and "My surgeon has told me not to do the activity anymore" (10 patients). There was no statistically significant difference in the responses based on type of TJR (P = 0.995).

DISCUSSION

The aim of this study was investigate the two-year activity levels and rate of return to athletic activity post arthroplasty and identify qualitative reasons for changes in activity participation. It has been demonstrated that all patients in our cohort returned to athletic activity. Patients are satisfied with their TJR and the ability to perform athletic activity is important. The most common sports to participate in pre-operatively are cycling, golf and running; post-operatively, these tend to be maintained, with tennis and gym also becoming popular. Patients are often able to return to their chosen activity and perform at a similar, if not better, ability in comparison to pre-operative levels. Patients are able to participate in athletic activity at least weekly, if not more frequently. The main reasons for non-participation in athletic activity were because of themselves not wanting to stress their joint replacement or under instruction from the surgeon or other doctor/health professional.

Rates of return to athletic activity

Table 2 Patient outcome scores

	THR	TKR	Total
OHS/OKS			
Mean Baseline score (SD; range)	21.25 (4.8; 13-35)	25.08 (5.8; 14-36)	-
Mean 2-yr post-TJR score (SD; range)	40.68 (3.1; 35-47)	41.67 (4; 33-47)	-
SF-12			
Mean Baseline Physical score (SD; range)	35.9 (6.3; 22.2-49.8)	37 (9.7; 15.4-51.9)	36.29 (7.7; 15.4-51.9)
Mean 2-yr Physical post-TJR score (SD; range)	46.1 (6.4; 29.2-60.3)	46.4 (9.5; 29.3-61.8)	46.19 (7.6; 29.2-61.8)
Mean Baseline Mental score (SD; range)	48.4 (7.9; 24.1-68.9)	54.3 (8.3; 34.1-68.7)	50.52 (8.5; 24.1-68.9)
Mean 2-yr Mental post-TJR score (SD; range)	55.2 (6.7; 33.4-69)	57.7 (7.9; 37.3-69.3)	54.16 (7.5; 33.4-69.3)
UCLA scores			
Mean Baseline score (SD; range)	7.78 (1.2; 6-10)	7.5 (1.1; 6-10)	7.67 (1.2; 6-10)
Mean 2-yr post-TJR score (SD; range)	7.93 (1.2; 6-10)	7.29 (0.9; 6-9)	7.69 (1; 6-10)

THR: Total hip replacement; TKR: Total knee replacement; TJR: Total joint replacement; UCLA: University of California, Los Angeles; OHS/OKS: Oxford Knee and Hip Scores.

In our cohort 100% of patients returned to athletic activity. This compares favourably with studies reporting a range of rates of return to sport between 54%[24] and 98%[25]. A higher rate of return to athletic activity has been observed with later studies and may reflect a more relaxed attitude of surgeons to what their patients may be permitted to do after surgery based on a greater body of evidence.

Changes between types of activity

The range of sports described by our patients is fairly typical of other studies and comparatively, our cohort maintains a higher level of performance. Only seven of the cohort had a lower UCLA score at two years in comparison to their baseline score. In these cases, there was no consistent reasoning given for a change in their activity participation. The relatively younger age of our study, combined with the absence of other joint problems can explain our cohort's overall maintenance of high impact activities. In addition, the questionnaire may not have accurately reflected a flux in the types of activity performed: some patients may have tried to persist with their higher-impact activity for a period after their operation before trying and settling for a lower-impact activity. Similarly, there may be some patients who have started lower-impact activities after their operation but may eventually start and sustain higher-impact activities. Therefore, the post-operative UCLA scores may alter with further follow-up.

Outcome scores for UCLA

Our study had a mean post-operative UCLA score of 7.69, comparing favourably with other studies[26,27]. Some have reported higher UCLA scores: Jackson *et al*[28] demonstrated a mean UCLA score of 8.3 at 8.7 years post-TKR in 93 patients. Here, the main target population involved golf, which automatically gives a UCLA score of 8. Girard *et al*[25] demonstrated a mean UCLA score of 9.1 at 3.7 years post-HRA in 50 patients. Here, there was a lower mean patient age of 51.5 years in comparison to 55.7 in our study; it can be argued that the lower age in addition to our mixed cohort of types of arthroplasty may have influenced the mean score.

Differences between joints

In our study, the mean two-year SF-12 physical and mental scores were higher for our TKR cohort than our THR cohort; these differences were not statistically significant for the physical portion but were significant for the mental portion of the questionnaire. Given the lack of differences between the joints in other aspects of the questionnaires, we cannot find a meaningful reason for this. The mean two-year UCLA scores were higher for THR patients compared to TKR patients (7.93 *vs* 7.29). This was not found to be statistically significant. All but seven patients either increased or maintained their baseline UCLA score. Amongst the cohort with a lower 2-year UCLA score, there were five THR patients and two TKR patients. When comparing the two joint cohorts, we did not see any statistically significant differences for any of the parameters in the sports activity questionnaire. These findings have replicated one of the larger recent studies in this area that did not find any differences in UCLA scores or other functional outcomes between TKR and THR patients[17].

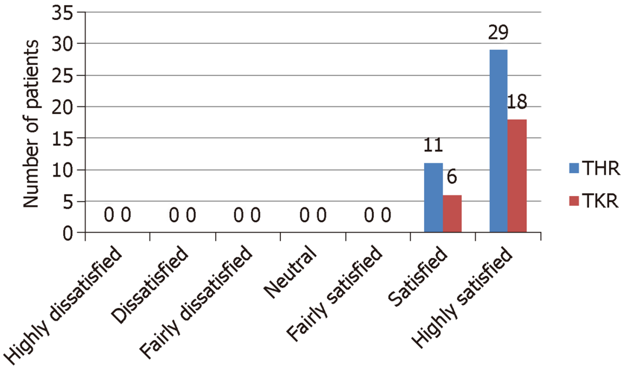

Figure 1 Overall, how satisfied are you with your joint replacement? THR: Total hip replacement; TKR: Total knee replacement.

Reasons involving changes in activity

Prior to this study, the literature did not hold many answers regarding the reasons for non-participation in activity post-surgery. Huch *et al*[9] reported that of the patients that reduced their athletic activity after TJR, almost half mentioned "precaution" and just over a quarter referenced pains in other joints. However, it was not clear as to the source of the basis of this precaution – whether it was from the patients themselves or as directed by their operating surgeon.

Similarly, there has been no clear consensus on the rationality of this "precaution" from patients, *i.e.*, why do patients not want to test their new joint. It is suggested that reducing the intensity of such activities may prolong the lifespan of the replaced joint; however, no studies to date have explicitly linked high activity rates with an increased rate of implant revision and there have been no prospective studies to delineate guidelines for safe and appropriate activities for patients with a joint replacement.

Klein *et al*[29] took consensus from a leading body of surgeons on safe activities for patients with a joint replacement. Given some of the differences between the activities they deemed acceptable and those that are regularly performed post-TJR, this may represent a greater tolerance from surgeons towards granting their patients the ability to a greater number of activities. This may be secondary to improved confidence in surgical technique and biomaterial advances that conferred a longer implant lifespan. With an increasing number of studies on athletic activity after joint replacement available, it can be suggested that this evidence may be used to draft a more up-to-date consensus on the types of activity that patients should be able to perform.

This study has several strengths. It uses validated outcome scores allowing direct comparison with other studies. The mean outcome scores are comparable with other studies, demonstrating that our patient cohort can be considered as fairly typical of other cohorts and the conclusions on reasons for non-participation may be applied to the larger arthroplasty population with similar demographics. As patient selection has been restricted to those under the age of 60 years who have a low ASA grade and do not have multiple painful joints, this study has minimised factors known to significantly reduce participation in athletic activity post-TJR and given more insight into other factors that may reduce participation. Finally, to our knowledge, there are no other studies that have presented such detailed reasons for non-participation in athletic activity post-TJR, thus we present new information that can be used in advising surgeons, other allied healthcare professionals and their patients on capabilities in performing suitable athletic activities.

The limitations of this study are that it has a relatively small number of patients and short follow-up time. However, this study has a larger patient number and longer follow-up than other published studies. Our response rate was 80%, although this is not dissimilar to the rates of other postal questionnaire studies and we do not feel that the conclusions of the study would have been significantly altered with more responses. The study is retrospective in nature, thus the responses may be prone to recall bias on the part of the patients. Many similar studies are also retrospective in nature; therefore we do not believe the validity of our findings is reduced. Finally, in finding the qualitative reasons for non-participation in athletic activity post-TJR, non-validated activity questionnaires were used. However, in order to gain specific reasons for changes in participation levels, a questionnaire designed to directly assess this was felt to be more suitable as the available validated questionnaires did not cover the desired information requested. In addition, several of the papers mentioned

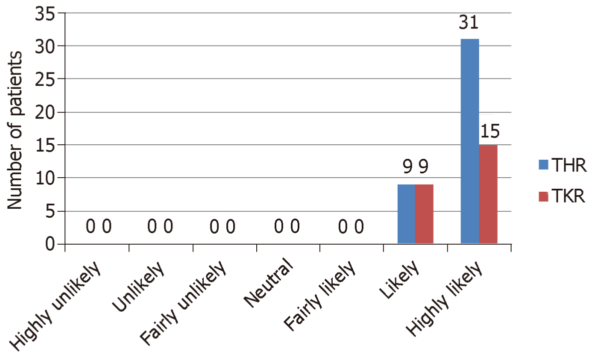

Figure 2 How likely are you to recommend having a joint replacement to others who are in need of one? THR: Total hip replacement; TKR: Total knee replacement.

in this study have also used non-validated questionnaires in drawing their conclusions and therefore this paper is therefore comparable in drawing its own conclusions alongside these other studies.

Future research should build on our knowledge that, at present, is largely based on mid-term retrospective studies. Given the emergence of more sophisticated outcome scoring tools, it should be suggested that prospectively-designed studies with follow-up beyond 10-15 years are necessary, utilising validated outcome questionnaires alongside radiographic analysis tools, such as wear analysis software, to definitively answer questions on implant survival in cases of higher athletic activity. It is important that in addition to these outcomes, all complications associated with performing athletic activity are meticulously reported, along with suspected early revisions. Finally, an up-to-date consensus piece, led by the experts in the field of arthroplasty, could provide information to surgeons, patients and allied health professionals on suitable athletic activities post-TJR. This should be based on the most recent study evidence but should not neglect the experience of the surgeons.

In conclusion, it has been demonstrated that patients are able to return to a high level athletic activity at two years post-TJR with good functional outcome scores. Patients are highly satisfied with their joint replacement and are able to participate in a variety of activities, the most common being golf, running and gym work. Patients feel that their post-operative ability to perform their activities is better than pre-operatively. The main reason for changing their types of activity is because of wanting to protect their joint replacement, although some also cite instructions from their surgeon or other healthcare professional. We would recommend more prospective studies into this area of sports medicine and arthroplasty in addition to an up-to-date consensus piece by the key opinion leaders in this field to provide health professionals on suitable athletic activities post-TJR based on the most recent literature.

Table 3 Participation in activities before and after total joint replacement

Activity	Pre-TJR frequency (patients)	Post-TJR frequency (patients)
Cycling	12	4
Golf	10	11
Running	9	9
Walking	8	6
Dance	6	3
Tennis	5	8
Football	2	2
Gym	2	9
Sky diving	2	0
Yoga	2	2
Judo	1	0
Pilates	1	3
Table tennis	1	0
Rugby	1	0
Scuba diving	1	1
Swimming	1	1
Badminton	0	1
Triathlon	0	2

TJR: Total joint replacement.

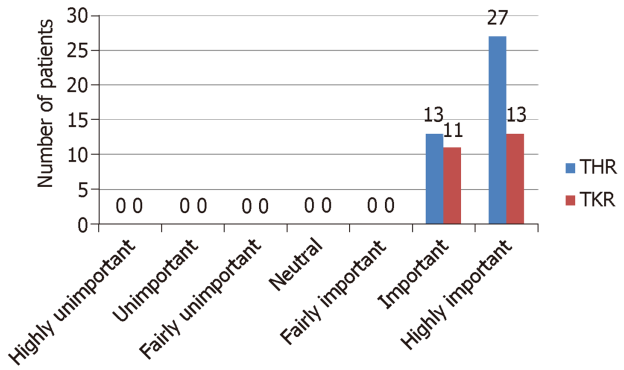

Figure 3 How important is it for you to have been able to continue with your favoured activities following your joint replacement? THR: Total hip replacement; TKR: Total knee replacement.

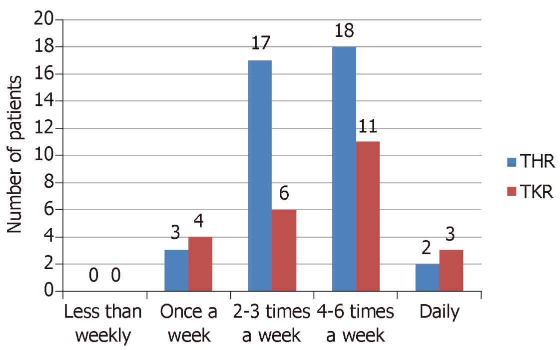

Figure 4 How often are you performing your favoured activities currently? THR: Total hip replacement; TKR: Total knee replacement.

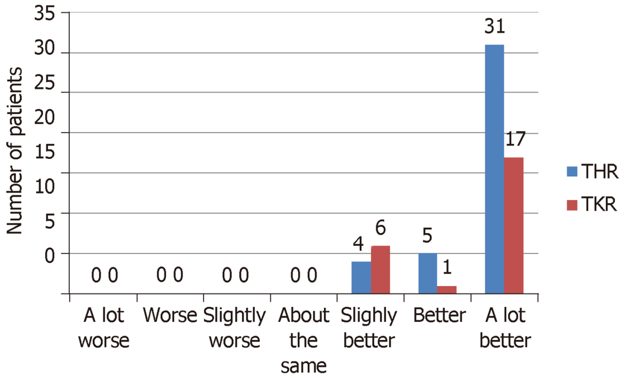

Figure 5 How do you rate your ability in performing your favoured activities now in comparison to the two years before your joint replacement? THR: Total hip replacement; TKR: Total knee replacement.

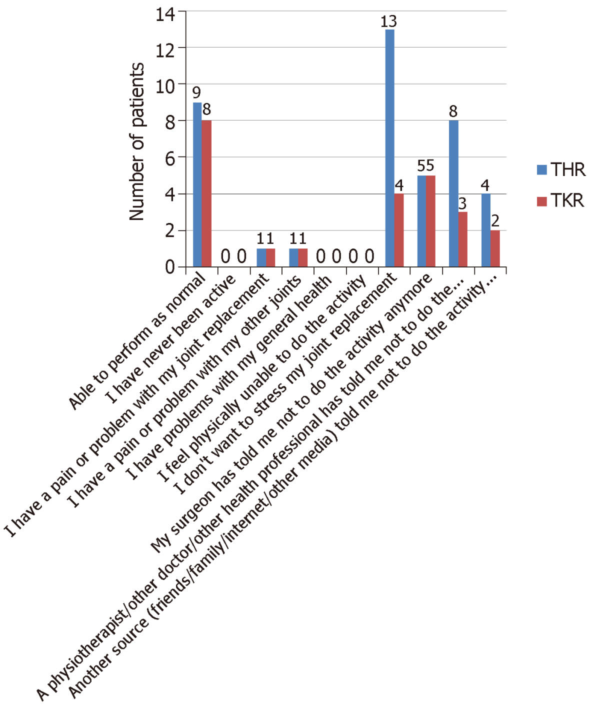

Figure 6 If there are any particular activities that you now no longer perform, what is/are the reason(s) for it? THR: Total hip replacement; TKR: Total knee replacement.

ARTICLE HIGHLIGHTS

Research background

Lower limb arthroplasty is being performed in increasing numbers worldwide on progressively younger patients with few medical co-morbidities. Currently, patients who have stopped participating in athletic activity secondary to their degenerative joint disease may wish to consider returning to their chosen athletic activities. It is not presently clear as to why patients who undergo successful joint arthroplasty do not always return to athletic activity, either under any circumstance or in a different capacity to pre-operatively.

Research motivation

The issues surrounding returning to athletic activity following either hip or knee replacement are explored in this study, specifically the factors behind patients' failure to return to participation in athletic activity post-operatively. Patient expectations being met are key in satisfaction following joint arthroplasty and having information on their ability to perform athletic activity post-operatively is significant information to present the patient with pre-operatively to allow them to make informed choices.

Research objectives

The main objective for this study was to examine the rate of return to athletic activity post lower limb arthroplasty and determine the qualitative reasons for any failure to return to athletic activity. These objectives were met as part of the study, demonstrating that questionnaire studies of this type can deliver qualitative responses as well as quantitative scores, from which meaningful conclusions can be drawn.

Research methods

This was a single centre, single surgeon retrospective questionnaire study with descriptive statistical analysis performed to interpret the results; these methods are frequently employed in questionnaire studies of this nature.

Research results

This study demonstrated that patients can return to athletic activity following joint replacement to a satisfactory level. Reasons for non-participation in athletic activity include (in equal proportions) the patient not wanting to stress their joint replacement or instruction from either the lead surgeon or other doctor/health professional. Hip and knee replacements had similar outcomes and return to athletic activity rates. Problems remaining to be solved are the lack of explicit links between athletic activity and accelerated implant loosening; should such a link be established, it will affect the advice provided by health care professionals regarding the suitability of performing athletic activity post joint replacement.

Research conclusions

The study found there are multiple factors behind a failure to return to athletic activity, including a patient wish to preserve their joint, instructions from the operating surgeon and instructions from another health care professional, including physiotherapists and general practitioners. There is no one single reason why people, with no other co-morbidities or painful joints, do not return to full athletic activity. People who are athletically active before joint replacement have a desire to return to activity post-operatively and are able to do so to a satisfactory level, with no significant differences between hip and knee replacements. The study offers original insight in that there are now qualitative reasons behind a failure to return to normal athletic activity. Future hypotheses that could be tested are that, given the vast ability of patients to perform activity to a high level post-operatively, restrictions on activity may be unnecessary and potentially relaxed given the ability of patients in this study. In addition to a prospective study investigating the conclusions further, a consensus piece could be developed to provide information to patients, surgeons and allied health professionals about suitable athletic activities post joint arthroplasty, based both on recent evidence but not neglecting the experience of the surgeons. The variety of qualitative reasons for non-participation in athletic activities represents a new area in this field. This study confirmed that patients are satisfied with their athletic capabilities following joint arthroplasty. This study may influence the decision making for patients wishing to undergo arthroplasty but also wanting to return to sport

Research perspectives

This study demonstrated that qualitative research has a role in outcome data alongside validated outcome questionnaires. Future research should involve prospective studies with 10-15 year outcomes. The methodology should include validated outcome questionnaires for athletic activity alongside radiographic analysis to assess for implant loosening and assess implant survival in athletically active populations post arthroplasty.

REFERENCES

1 **National Joint Registry**. Available from: http://www.njrcentre.org.uk/

2 **Ethgen O**, Bruyère O, Richy F, Dardennes C, Reginster JY. Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature. *J Bone Joint Surg Am* 2004; **86-A**: 963-974 [PMID: 15118039 DOI: 10.1016/j.injury.2003.09.007]

3 **Rissanen P**, Aro S, Slätis P, Sintonen H, Paavolainen P. Health and quality of life before and after hip or knee arthroplasty. *J Arthroplasty* 1995; **10**: 169-175 [PMID: 7798097 DOI: 10.1016/S0883-5403(05)80123-8]

4 **Elleuch MH**, Guermazi M, Mezghanni M, Ghroubi S, Fki H, Mefteh S, Baklouti S, Sellami S. Knee osteoarthritis in 50 former top-level soccer players: a comparative study. *Ann Readapt Med Phys* 2008; **51**: 174-178 [PMID: 18374445 DOI: 10.1016/j.annrmp.2008.01.003]

5 **Kujala UM**, Kaprio J, Sarna S. Osteoarthritis of weight bearing joints of lower limbs in former élite male athletes. *BMJ* 1994; **308**: 231-234 [PMID: 8111258 DOI: 10.1136/bmj.308.6923.231]

6 **Spector TD**, Harris PA, Hart DJ, Cicuttini FM, Nandra D, Etherington J, Wolman RL, Doyle DV. Risk of osteoarthritis associated with long-term weight-bearing sports: a radiologic survey of the hips and knees in female ex-athletes and population controls. *Arthritis Rheum* 1996; **39**: 988-995 [PMID: 8651993 DOI: 10.1002/art.1780390616]

7 **Noble PC**, Conditt MA, Cook KF, Mathis KB. The John Insall Award: Patient expectations affect satisfaction with total knee arthroplasty. *Clin Orthop Relat Res* 2006; **452**: 35-43 [PMID: 16967035 DOI: 10.1097/01.blo.0000238825.63648.1e]

8 **Cornell CN**, Ranawat CS. Survivorship analysis of total hip replacements. Results in a series of active patients who were less than fifty-five years old. *J Bone Joint Surg Am* 1986; **68**: 1430-1434 [PMID: 3782214 DOI: 10.1007/BF00819639]

9 **Huch K**, Müller KA, Stürmer T, Brenner H, Puhl W, Günther KP. Sports activities 5 years after total knee or hip arthroplasty: the Ulm Osteoarthritis Study. *Ann Rheum Dis* 2005; **64**: 1715-1720 [PMID: 15843453 DOI: 10.1136/ard.2004.033266]

10 **Kilgus DJ**, Dorey FJ, Finerman GA, Amstutz HC. Patient activity, sports participation, and impact loading on the durability of cemented total hip replacements. *Clin Orthop Relat Res* 1991; **269**: 25-31 [PMID: 1864047 DOI: 10.1097/00003086-199108000-00005]
11 **Schmidutz F**, Grote S, Pietschmann M, Weber P, Mazoochian F, Fottner A, Jansson V. Sports activity after short-stem hip arthroplasty. *Am J Sports Med* 2012; **40**: 425-432 [PMID: 21993977 DOI: 10.1177/0363546511424386]
12 **Visuri T**, Honkanen R. Total hip replacement: its influence on spontaneous recreation exercise habits. *Arch Phys Med Rehabil* 1980; **61**: 325-328 [PMID: 7396685 DOI: 10.1080/713857566]
13 **Bradbury N**, Borton D, Spoo G, Cross MJ. Participation in sports after total knee replacement. *Am J Sports Med* 1998; **26**: 530-535 [PMID: 9689373 DOI: 10.1177/03635465980260041001]
14 **Chatterji U**, Ashworth MJ, Lewis PL, Dobson PJ. Effect of total knee arthroplasty on recreational and sporting activity. *ANZ J Surg* 2005; **75**: 405-408 [PMID: 15943726 DOI: 10.1111/j.1445-2197.2005.03400.x]
15 **Bauman S**, Williams D, Petruccelli D, Elliott W, de Beer J. Physical activity after total joint replacement: a cross-sectional survey. *Clin J Sport Med* 2007; **17**: 104-108 [PMID: 17414477 DOI: 10.1097/JSM.0b013e3180379b6a]
16 **Wylde V**, Blom A, Dieppe P, Hewlett S, Learmonth I. Return to sport after joint replacement. *J Bone Joint Surg Br* 2008; **90**: 920-923 [PMID: 18591603 DOI: 10.1302/0301-620X.90B7.20614]
17 **Williams DH**, Greidanus NV, Masri BA, Duncan CP, Garbuz DS. Predictors of participation in sports after hip and knee arthroplasty. *Clin Orthop Relat Res* 2012; **470**: 555-561 [PMID: 22125250 DOI: 10.1007/s11999-011-2198-y]
18 **Golant A**, Christoforou DC, Slover JD, Zuckerman JD. Athletic participation after hip and knee arthroplasty. *Bull NYU Hosp Jt Dis* 2010; **68**: 76-83 [PMID: 20632981]
19 **Lavernia CJ**, Sierra RJ, Hungerford DS, Krackow K. Activity level and wear in total knee arthroplasty: a study of autopsy retrieved specimens. *J Arthroplasty* 2001; **16**: 446-453 [PMID: 11402406 DOI: 10.1054/arth.2001.23509]
20 **Ollivier M**, Frey S, Parratte S, Flecher X, Argenson JN. Does impact sport activity influence total hip arthroplasty durability? *Clin Orthop Relat Res* 2012; **470**: 3060-3066 [PMID: 22535588 DOI: 10.1007/s11999-012-2362-z]
21 **Pynsent PB**, Adams DJ, Disney SP. The Oxford hip and knee outcome questionnaires for arthroplasty. *J Bone Joint Surg Br* 2005; **87**: 241-248 [PMID: 15736751 DOI: 10.1302/0301-620X.87B2.15095]
22 **Paulsen A**, Pedersen AB, Overgaard S, Roos EM. Feasibility of 4 patient-reported outcome measures in a registry setting. *Acta Orthop* 2012; **83**: 321-327 [PMID: 22900909 DOI: 10.3109/17453674.2012.702390]
23 **Naal FD**, Impellizzeri FM, Leunig M. Which is the best activity rating scale for patients undergoing total joint arthroplasty? *Clin Orthop Relat Res* 2009; **467**: 958-965 [PMID: 18587624 DOI: 10.1007/s11999-008-0358-5]
24 **Ritter MA**, Meding JB. Total hip arthroplasty. Can the patient play sports again? *Orthopedics* 1987; **10**: 1447-1452 [PMID: 3684792]
25 **Girard J**, Miletic B, Deny A, Migaud H, Fouilleron N. Can patients return to high-impact physical activities after hip resurfacing? A prospective study. *Int Orthop* 2013; **37**: 1019-1024 [PMID: 23456016 DOI: 10.1007/s00264-013-1834-4]
26 **Fisher N**, Agarwal M, Reuben SF, Johnson DS, Turner PG. Sporting and physical activity following Oxford medial unicompartmental knee arthroplasty. *Knee* 2006; **13**: 296-300 [PMID: 16809040 DOI: 10.1016/j.knee.2006.03.004]
27 **Sechriest VF 2nd**, Kyle RF, Marek DJ, Spates JD, Saleh KJ, Kuskowski M. Activity level in young patients with primary total hip arthroplasty: a 5-year minimum follow-up. *J Arthroplasty* 2007; **22**: 39-47 [PMID: 17197307 DOI: 10.1016/j.arth.2006.02.083]
28 **Jackson JD**, Smith J, Shah JP, Wisniewski SJ, Dahm DL. Golf after total knee arthroplasty: do patients return to walking the course? *Am J Sports Med* 2009; **37**: 2201-2204 [PMID: 19684299 DOI: 10.1177/0363546509339009]
29 **Klein GR**, Levine BR, Hozack WJ, Strauss EJ, D'Antonio JA, Macaulay W, Di Cesare PE. Return to athletic activity after total hip arthroplasty. Consensus guidelines based on a survey of the Hip Society and American Association of Hip and Knee Surgeons. *J Arthroplasty* 2007; **22**: 171-175 [PMID: 17275629 DOI: 10.1016/j.arth.2006.09.001]

P- Reviewer: Tripathy SK, Wyatt MC
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Wu YXJ

WJO World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 February 18; 10(2): 101-114

DOI: 10.5312/wjo.v10.i2.101

ISSN 2218-5836 (online)

SYSTEMATIC REVIEW

Return to sport following scaphoid fractures: A systematic review and meta-analysis

Joaquim S Goffin, Quintin Liao, Gregory AJ Robertson

ORCID number: Joaquim S Goffin (0000-0003-4532-1855); Quintin Liao (0000-0001-9078-0722); Greg AJ Robertson (0000-0002-9152-7144).

Author contributions: Goffin JS, Liao Q and Robertson GAJ conceived the methodology for the manuscript, performed the literature search and analysis for the study, and wrote the manuscript.

Conflict-of-interest statement: All authors have no conflicts of interest to report.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

Manuscript source: Invited manuscript

Received: September 12, 2018
Peer-review started: September 12, 2018

Joaquim S Goffin, Department of Orthopaedic and Trauma Surgery, Ninewells Hospital, Dundee DD2 1SY, United Kingdom

Quintin Liao, Department of Orthopaedic and Trauma Surgery, Forth Valley Royal Hospital, Larbert FK5 4WR, United Kingdom

Gregory AJ Robertson, Edinburgh Orthopaedic Trauma Unit, Royal Infirmary of Edinburgh, Scotland EH16 4SA, United Kingdom

Corresponding author: 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
Telephone: +44-131-2423545
Fax: +44-131-2423541

Abstract

BACKGROUND
Scaphoid fracture is the most commonly fractured carpal bone in the athletic patient, accounting for over 85% of all sport-related carpal bone fractures, and is particularly common in sports involving high impact injuries to the wrist. The management of such injuries comprises both conservative and surgical techniques, as guided by fracture location and type. Athletes demonstrate a unique challenge with regards to the management of scaphoid fractures due to their requirement to return to sport, as soon as able.

AIM
To review systemically all studies recording return to sport following scaphoid fractures, to collate information on return rates to sport (RRS) and mean return times (RTS) to sport and to determine differences in sporting outcome for the various treatment methods.

METHODS
A systematic search of MEDLINE, EMBASE, CINAHAL, Cochrane, Google Scholar, Physiotherapy Evidence Database, SPORTDiscus, Web of Science and Scopus was performed in August 2018 using the keywords "scaphoid", "fracture", "acute", "carpal", "athletes", "sports", "non-operative", "conservative", "operative" and "return to sport". All studies that recorded RRS and RTS following scaphoid fractures were included. RTS was recorded as the length of time from commencement of either primary conservative management or primary surgical procedure to return to sport.

First decision: October 5, 2018
Revised: November 3, 2018
Accepted: January 10, 2019
Article in press: January 10, 2019
Published online: February 18, 2019

RESULTS
Eleven studies were included: Two randomised controlled trials, six retrospective cohort studies and three case series. Seven studies reported on conservative management (n = 77), and eight studies reported on surgical management (n = 83). For conservative management, RRS was 90% (69/77), and the mean RTS was 9.6 wk. Three studies allowed to return to sport in cast [RRS 89% (25/28); RTS 1.9 wk], and four studies required completion of cast treatment prior to returning to sport [RRS 90% (44/49); RTS 13.9 wk]. Four studies recorded fracture union data: Union rate 85% (47/55); mean time to union 14.0 wk. For surgical management, RRS was 98% (81/83), and RTS was 7.3 wk. Three studies reported on Percutaneous Screw Fixation [RRS 97% (32/33); RTS 6.5 wk], and five studies reported on Open Reduction Internal Fixation [RRS 98% (49/50); RTS 7.9 wk]. Six studies recorded fracture union data: Union rate 97% (69/71); mean time to union 9.8 wk. On meta-analysis, RRS (RR = 1.09; 95% confidence interval (CI): 1.00-1.18; P < 0.045), RTS (MD 2.3 wk; 95%CI: 0.79-3.87; P < 0.002), union rates (RR = 1.14; 95%CI: 1.01-1.28; P < 0.030) and mean times to union (MD 4.2 wk; 95%CI: 3.94-4.36; P < 0.001) were all significantly better for the surgical cohort compared to the conservative cohort.

CONCLUSION
Surgical management of scaphoid fractures can provide significantly improved RRS and RTS to sport compared to conservative management. Both treatments, however, remain acceptable options, and athletes should be fully informed of the benefits and risks of both prior to deciding treatment plans. Immediate return to sport in a cast should be avoided due to the significant risk of non-union.

Key words: Acute; Fracture; Scaphoid; Carpal; Return; Sport; Rate; Time

Core tip: We recorded returned rates (RRS) and return times (RTS) to sport following acute scaphoid fractures. Eleven studies were included. Seven studies reported on conservative treatment (n = 77); eight studies reported on surgical treatment (n = 83). For conservative management, RRS was 90% (69/77), and RTS was 9.6 wk. For surgical management, RRS was 98% (81/83), and RTS was 7.3 wk. On meta-analysis, RRS (P < 0.045) and RTS (P < 0.002) were significantly better for surgical management compared to conservative management. Surgical management of acute scaphoid fractures can provide significantly improved RRS and RTS compared to conservative management.

Citation: Goffin JS, Liao Q, Robertson GAJ. Return to sport following scaphoid fractures: A systematic review and meta-analysis. *World J Orthop* 2019; 10(2): 101-114
URL: https://www.wjgnet.com/2218-5836/full/v10/i2/101.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i2.101

INTRODUCTION

The scaphoid is the most commonly fractured carpal bone in the athletic patient, occurring a rate of 0.06 per 1000 population and accounting for over 85% of all sport-related carpal bone fractures[1]. These fractures usually arise from a fall onto a hyperextended wrist, resulting in longitudinal loading of the scaphoid and a subsequent failure of the dorsal cortex on compression[2]. The scaphoid is at particular risk from sports involving high impact injuries to the wrist, such as football, rugby and basketball[1].

Clinicians should have a high index of suspicion in athletes presenting with post-traumatic pain on the radial aspect of the wrist or in the anatomical snuffbox region[3]. Sensitive examination findings include tenderness in the anatomical snuffbox, scaphoid tubercle and pain on longitudinal compression of the thumb[4]. Clinically, this fracture can be difficult to diagnose and may not become visible until repeated scaphoid view radiographs are obtained[3]. When negative, the second line imaging is either magnetic resonance imaging or computed tomography scan: This is particularly valuable when considering return to sport in affected athletes[5,6].

These fractures can be divided according to their location (proximal third; waist or middle third; distal third), fracture displacement (undisplaced or minimally displaced; displaced) and fracture stability[3]. The Herbert Classification is the most common classification, which groups scaphoid fractures into stable (A) and unstable fractures (B)[7]. Stable fracture patterns include those of the scaphoid tubercle (A1) and incomplete fractures through the scaphoid waist (A2). Unstable fracture patterns include distal oblique fractures (B1), complete waist fractures (B2), proximal pole fractures (B3), transscaphoid perilunate dislocation (B4) and comminuted fractures (B5)[7].

Management of these injuries is based on the location and nature of the fracture[3]. Undisplaced stable fractures (A1 and A2) are routinely treated conservatively with a scaphoid or forearm cast for 8 wk to 12 wk, until the fracture unites[3,8]. Due to the risk of non-union and avascular necrosis, displaced fractures are treated surgically with open reduction and internal fixation[3]. Occasionally, displaced distal fractures of the scaphoid tubercle, which are symptomatic, can be treated with surgical excision[3]. The treatment of undisplaced unstable fractures remains controversial: Some clinicians advise conservative management with a scaphoid or forearm cast for 8 to 12 wk; while others recommend surgical management with internal screw fixation (often feasible through a percutaneous approach)[3,9]. Previous studies have demonstrated an earlier return to sport when comparing surgical to conservative management for undisplaced unstable fractures of the scaphoid waist: However, treatment practises of these injuries still remain varied among clinicians[9-11]. Athletes demonstrate a unique challenge with regards to the management of such fractures due to their requirement to return to sport as quickly as possible[12].

The aim of this review was to assess systemically all studies recording return to sport following scaphoid fractures, allowing collation of information on return rates to sport (RRS) and mean return times to sport (RTS), and determining differences in sporting outcome for the various treatment methods.

MATERIALS AND METHODS

Literature search

The authors performed a systematic literature review in August 2018 using the listed databases: CINAHAL, Cochrane Collaboration Database, EMBASE, Google Scholar, Medline (PubMed), Physiotherapy Evidence Database, Scopus and Web of Science and SPORTDiscus. The search was limited to peer-reviewed articles in the English language that reported on rates and times of return to sports following acute scaphoid fractures. The key terms used for the search in each database included “scaphoid”, “fracture”, “acute”, “carpal”, “sports”, “athletes”, “non-operative”, “conservative”, “operative” and “return to sport”. All available studies were included for review with no restrictions on publication year.

All three authors performed an independent review of the retrieved titles and the subsequently selected abstracts, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines[13]. Table 1 records the inclusion and exclusion criteria as per the PRISMA guidelines. Abstracts, anecdotal articles, case reports, review articles, animal, cadaver and *in vitro* studies were all excluded from the review unless they contained relevant clinical information. The full-text article was downloaded when exclusion could not be established from review of the abstract alone. The reference lists of the retrieved articles were also assessed to identify further studies for inclusion. Disagreements in study selection for inclusion in this review were to be resolved through consensus discussion between the three authors: There were, however, no major disagreements. Figure 1 summarises the selection process for the review, as per the PRISMA guidelines.

The following data were extracted from the included studies: general patient demographics; mechanism of injury; fracture location; conservative and surgical management methods; return rates and return times to sport; return rate to pre-injury level of sport; rate of fracture union; time to fracture union and complications. The primary outcome measures were RRS and RTS. Secondary outcome measures included rates of return to pre-injury level of sport, fracture union rate, time to fracture union and complications following treatment. Return to pre-injury level of sport was defined as the ability of the athlete to return to their previous level of play (*i.e.*, to the same competitive standard as pre-injury).

For conservatively-managed patients, RTS was recorded as the time length from commencement of conservative management to return to sport. For surgically managed patients, RTS was recorded as the time length from the primary surgical

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Acute scaphoid fractures	Scaphoid Fracture Delayed Union or Non-Union
Elite or recreational athletes	No sporting outcome data reported
Return rates to sporting activity reported	Paediatric fractures (age under 15)
Time to return to sporting activity reported	Concomitant upper or lower limb fractures
Two or more fractures reported	Reviews, case reports, abstracts or anecdotal articles
Peer-reviewed journals	Animal, cadaver or in vitro studies
English language	

procedure to return to sport.

When a patient was unable to return to sport from the primary treatment technique, requiring conversion to a secondary treatment, this was recorded as a non-return to sport.

Quality assessment

The modified Coleman methodology score (CMS) was employed to determine the quality of the included studies[14]: This has been used in a number of similar reviews[15-20]. The studies were scored by all three authors: the inter-observer reliability of the scoring process was 0.92 (95% confidence interval (CI): 0.90–0.94).

Statistical analysis

Meta-analysis comparisons were performed on cohorts for the following variables: RRS, RTS, rate of fracture union and time to fracture union. These were processed using RevMan Version 5.3 (The Cochrane Group). To assess comparisons between dichotomous data, risk ratios (RRs) with a random effects model were utilised. To assess comparisons between continuous data, mean differences (MDs) with a random effects model were utilised. The I^2 statistic was used to analyse the heterogeneity of the included studies: This was significant when I^2 was greater than 50%. The significance level was identified as $P < 0.05$.

RESULTS

Search

The process of study selection is reported in Figure 1. In total, 46 unique abstracts and 11 unique articles were assessed. The search strategy yielded 11 relevant publications, published from 1979 to 2014, with data available on clinical and functional outcomes of patients who returned to sports activity after sustaining an acute scaphoid fracture[9,10,21-29]. There were two randomised controlled trials[9,10], six retrospective cohort studies[21-26] and three case series[27-29].

Table 2 summarises the characteristics of the articles included in this review. The table contains information on study location, patient demographics including gender and age, fracture type/location, management methods, sporting activities reported and level of sport.

Patient demographics

Of the 170 fractures, 131 (77%) occurred in male patients, 13 (8%) in female patients and 26 (15%) failed to specify gender. Of the 170 fractures recorded, follow-up data were achieved for 160 (94.1%). The mean age at the time of injury ranged from 17.3 years[24] to 31.0 years[10]. The most common recorded sports were American football, soccer, baseball and basketball (Table 2).

Fracture location and classification

Four studies described fracture configuration using a formal fracture classification[9,10,24,25]: all four used the Herbert Classification[9,10,21-25]. Three studies recorded fracture location without using a formal classification[21-23]. Four studies failed to report on fracture location[26-29].

The reported fracture types comprised waist/middle third (n = 68), proximal third (n = 9), distal third (n = 6), Herbert A2 (n = 3), Herbert B1 (n = 1), Herbert B2 (n = 66) and Herbert B3 (n = 1). There was no avulsion fracture recorded in the studies.

Study design

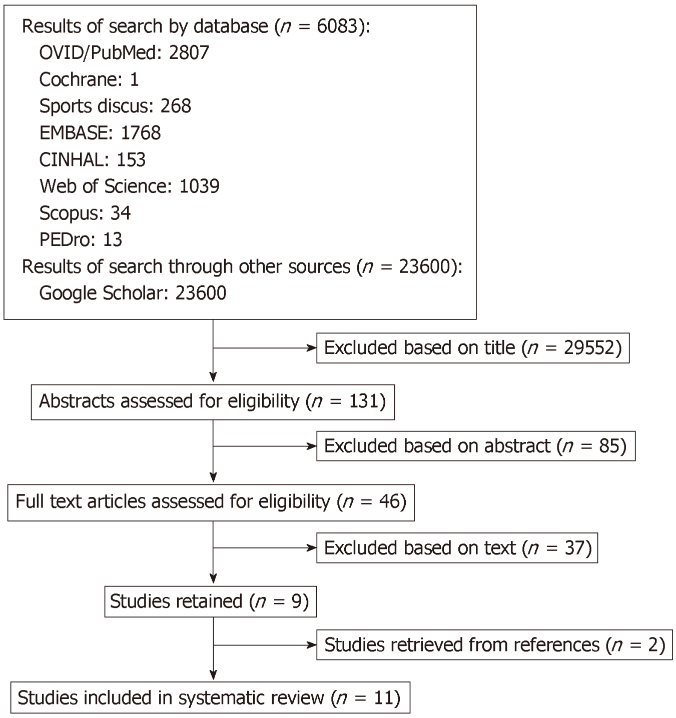

Figure 1 Selection of articles for inclusion in the review in accordance with the PRISMA protocol[13]. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses.

The CMS for all the studies was 59.5 (range 42-82) (Table 3)[9,10,21-29]. The CMS was 58.6 for the studies reporting on conservative management (range 42-82) (Table 3)[9,10,21,22,26,27,29]. The CMS was 62.9 for the studies reporting on surgical management (range 44-82) (Table 3)[9,10,22-26,28].

Management

Of 160 fractures available for follow up, 77 were managed conservatively, and 83 were managed surgically. Of those managed conservatively, 28 were allowed to return to sport in cast, while 49 were only allowed to return to sport following cast treatment. Of those managed surgically, 50 were treated with open reduction and internal fixation (ORIF), and 33 were treated with percutaneous surgical fixation (PSF).

Conservative management

Seventy-seven of the scaphoid fractures were managed conservatively[9,10,21,22,26,27,29], of which 28 were allowed to return to sport in cast[21,22,27], and 49 were only allowed to return to sport following cast treatment[9,10,26,29].

The recorded forms of cast immobilisation included short arm thumb spica cast with the wrist in a neutral position[21], colles casts without thumb immobilisation[9] and below elbow plaster casts[10]. Two of the studies provided the patient with a specific silastic[21] or orthoplast[22] "playing" cast, which was used during sporting activities[22].

For the studies that allowed return in cast, the mean duration of immobilisation ranged from 3 mo to 6 mo[21,22,27]. For the studies that did not allow return in cast, the mean duration of immobilisation was 10 wk maximum[9,10,26,29].

Surgical management

Eighty-three of the scaphoid fractures were managed surgically[9,10,22-26,28]; the reported surgical techniques included ORIF (n = 50)[22-25,28] and PSF (n = 33)[9,10,26].

PSF was performed in three studies[9,10,26], of which two reported on surgical technique and post-operative rehabilitation[9,10]. Both studies performed the technique through a minimal incision over the distal pole of the scaphoid and used a cannulated scaphoid screw for fixation[9,10]. Post-operatively, Adolfsson *et al*[10] immobilised patients for 3 wk full time in a below elbow plaster splint, then 3 wk part time with a removable plastic splint during sports or vigorous activities; McQueen *et al*[9] used no immobilisation post-operatively, encouraging patient to mobilise as able. McQueen *et al*[9] advocated referral to physiotherapy post-operatively if clinically indicated.

ORIF was performed in five studies[22-25,28], of which four reported on surgical technique and post-operative rehabilitation[22-25]. Three studies used a volar (Russe-

Table 2 Characteristics of the included studies

Ref.	Study location	*n*	Fracture type/ location	Gender (count)	Mean age	Study design	Treatment	Sport activity	Level of sport
Adolfsson *et al*[10] (2001)	Linkoping & Lund, Sweden	5	Waist (5)	N/A	31 (15-75)	RCT	PSF (3); Conservative (2)	Soccer (3); Swimming (1); Squash (1)	National level
Bedi *et al*[25] (2007)	Ann Arbor, Michigan, United States	6	B2 (6)	N/A	25 (16-62)	RCS	ORIF (6)	Sport (6)	Collegiate/ Professional
Ellsasser and Stein[27] (1979)	St. Louis, Missouri, United States	2	-	M: 2	N/A	CS	Conservative (2); Returned immediately	American football (2)	Professional
Huene[28] (1979)	Fresno, California, United States	4	-	N/A	N/A	CS	ORIF (4)	Sport (4)	N/A
McQueen *et al*[9] (2008)	Edinburgh, United Kingdom	55	B1 (1); B2 (54)	M: 50 F: 10	29.4 (17-65)	RCT	PSF (28); Conservative (27)	N/A	N/A
Muramatsu *et al*[24] (2002)	Yamaguchi, Japan	10	A2 (3); B2 (6); B3 (1)	M: 10	17.3 (13-22)	RCS	ORIF (10)	Badminton (1); Baseball (2); Basketball (2); Boxing (2); Handball (1); Judo (2); Rugby (1); Soccer (16); Tennis (1); Track (2)	N/A
Rettig *et al*[22] (1994)	Indianapolis, Indiana, United States	30	MT (30)	M: 25 F: 5	18.3	RCS	ORIF (18); Conservative (12); Returned immediately	Sport (30)	N/A
Rettig and Kollias[23] (1996)	Indianapolis, Indiana, United States	12	MT (10) PT (2)	M: 11 F: 1	21 (17-31)	RCS	ORIF (12)	Baseball (2); Basketball (8); Archery (2)	N/A
Riester *et al*[21] (1985)	Syracuse, New York, United States	14	MT (11) PT (3)	M: 13 F: 1	N/A	RCS	Conservative (14); Returned immediately	American Football (12); Basketball (1); Soccer (1)	Intercollegiate / High school
Robertson *et al*[26] (2012)	Edinburgh, United Kingdom	20	MT (11); PT (4); DT (5)	M: 20	26.1	RCS	PSF (2); Conservative (18)	Soccer (20)	N/A
Robertson *et al*[29] (2014)	Edinburgh, United Kingdom	2	MT (1); DT (1)	M: 2	21	CS	Conservative (2)	Rugby (2)	N/A

RCT: Randomised controlled trial; RCS: Retrospective cohort study; CS: Case series; ORIF: Open reduction and internal fixation; PSF: Percutaneous surgical fixation; M: Male; F: Female; N/A: No data available; MT: Middle third; PT: Proximal third; DT: Distal third; A2: Stable waist fracture; B1: Unstable distal oblique fracture; B2: Unstable waist fracture; B3: Unstable proximal pole fracture; S: Surgical management; C: Conservative management.

Type) approach to the scaphoid[22-24]; one used a dorsal approach[25]. All studies performed fixation with a scaphoid screw[22-25]. Post-operative immobilisation regimes comprised: a below elbow spica splint for 7 d to 10 d followed by a resting splint as needed[22,23]; below elbow cast immobilisation for 1 wk to 7 wk (mean 4 wk) with duration of cast immobilisation based on the intra-operative findings and the clinical judgement of the responsible surgeon[24]; a below-elbow plaster splint for 2 wk, followed by a removable forearm splint for 2 wk to 4 wk[25]. Formal physiotherapy programmes were described in three studies[22,23,25].

Functional assessment

Three studies used formal validated scoring systems to assess functional outcomes post intervention[9,24,25]. Two studies reported on scaphoid fractures treated with ORIF[24,25]; the other study was a randomised controlled trial comparing conservative *vs* surgical management[9]. The functional scores used included the Disabilities of the Arm, Shoulder and Hand Score[25], the Mayo wrist score[24], the modified Green/O'Brien score[9] and a Visual Analogue Score for Pain[25].

Table 3 Scaphoid fractures - only fractures with follow-up data included (mean values unless otherwise stated).

Ref.	*n*	Mean follow-up	Coleman score	Return Rate	Return rate by treatment modality	Return rate to same level of sport	Return time (range)	Return time (range) by treatment modality	Rate of union	Time to union (range)	Complications by treatment modality
Adolfsson *et al*[10] (2001)	5	-	70	5/5	C: 2/2; S: 3/3	C: 2/2; S: 3/3	8.2 (6-12) wk	C: 11.5 (11-12) wk; S: 6 wk	C: 2/2; S: 3/3	C: N/A; S: N/A	C: Persistent radial border wrist pain (1); S: Nil
Bedi *et al*[25] (2007)	6	98 (12-272) wk	64	5/6	S: 5/6	S: 5/6	N/A	S: N/A	S: N/A	S: N/A	S: Non-union (6%) ; Scar sensitivity (6%)
Ellsasser & Stein[27] (1979)	2	-	42	2/2	C: 2/2	C: 2/2	0 wk	C: 0 wk	S: N/A	S: N/A	C: Nil
Huene[28] (1979)	4	-	48	4/4	S: 4/4	S: 4/4	7 (6-8) wk	S: 7 (6-8) wk	S: N/A	S: N/A	S: SRNN (40%)
McQueen *et al*[9] (2008)	55	1 yr	82	53/55	C: 26/27; S: 27/28	C: 26/27; S: 27/28	10.9 (2-26) wk	C: 15.5 (6-26) wk; S: 6.4 (2-20) wk	C: 23/27; S: 27/28	C: 13.9 (8-36) wk; S: 9.2 (8-18) wk	C: Non-union (4); Malunion (3); AVN (2); CRPS (1); Radioscaphoid OA(1); S: Peri-operative breakage of the cannulated screwdriver (2) Symptomatic metalwork (1); Non-union (1)
Muramatsu *et al*[24] (2002)	10	-	66	10/10	S: 10/10	n/a	10.7 (6-13) wk	S: 10.7 (6-13) wk	S: 10/10	S: 9.2 (6–16) wk	S: nil
Rettig *et al*[22] (1994)	30	C: 48.7 (9-136) wk; S: 49.3 (5-164) wk	63	29/30 (96.7%)	C: 11/12; S: 18/18	n/a	6.6 (0-21) wk	C: 4.3 (0-10) wk; S: 8 (3-21) wk	C: 11/12; S: 18/18	C: 14.2 (8-26) wk; S: 11.2 (4-24) wk	C: Non-union (1); S: nil
Rettig & Kollias[23] (1996)	12	2.9 yr	66	12/12 (100%)	S: 12/12	S: 12/12	5.8 (1-10) wk	S: 5.8 (1-10) wk	S: 11/12	S: 9.8 (6-18) wk	S: Non-union (1)
Riester *et al*[21] (1985)	14	47 mo (3.9 yr)	65	12/14	C: 12/14 (85.7%)	C: 12/14	0 wk	C: 0 (0-0) wk	C: 11/14	C: N/A	C: Non-union (3) (of which 2 patients required surgical intervention)
Robertson *et al*[26] (2012)	20	30 (24-36) mo	44	16/20	C: 14/181; S: 2/2	C: 13/181; S: 2/2	12.2 (6-24) wk	C: 12.7 (6-24) wk; S: 8.5 (8-9) wk	C: N/A; S: N/A	C: N/A; S: N/A	C: Non-union (3) (all 3 patient required delayed conversion to surgical fixation); S: Nil

Robertson *et al*[29] (2014)	2	40 (34-46) mo	44	2/2	C: 2/2	C 2/2	4 (4-4) wk	C: 4 (4-4) wk	C: N/A	C: N/A	C: Nil

[1]Three fractures initially treated conservatively developed non-union and required conversion to surgical treatment. 2 of these returned to soccer post-surgery. N/A: No data available; S: Surgical management; C: Conservative management; SRNN: Superficial radial nerve neuropraxia; AVN: Avascular necrosis; CRPS: Complex regional pain syndrome; OA: Osteoarthritis.

Return rates to sport

Conservative management: The RRS for conservatively-managed scaphoid fractures are provided in Table 4 and Figure 2A. RRS to pre-injury level of sport for each conservative management method are provided in Table 4 and Figure 2B.

For the "conservative" synthesis cohort, the RRS was 90% (69/77). For patients who returned to sport in a cast, the RRS was 89% (25/28). For patients who returned to sports after cast removal, the RRS was 90% (44/49).

Surgical management: The RRS for scaphoid fractures managed surgically are provided in Table 4 and Figure 2A. Return rates to pre-injury level of sport for each surgical management method are provided in Table 4 and Figure 2B.

For the "surgical" synthesis cohort, the RRS was 98% (81/83). For patients treated with ORIF, the RRS was 98% (49/50). For patients treated with PSF, the RRS was 97% (32/33).

On meta-analysis, when comparing the "conservative" synthesis cohort to the "surgical" synthesis cohort, the difference in RRS was significant (RR = 1.09; 95%CI: 1.00-1.18; $P < 0.045$: $I^2 = 0\%$, $P = 0.78$).

Return times to sport

Conservative management: The RTS for the conservatively-managed scaphoid fractures are provided in Table 4 and Figure 3. For the "conservative" synthesis cohort, the mean RTS was 9.6 (0-16) wk. For patients who returned to sport in a cast, the mean RTS was 1.9 (0-4) wk. For patients who returned to sports after cast removal, the mean RTS was 13.9 (4-16) wk.

Surgical management: The RTS for surgically managed scaphoid fractures are provided in Table 4 and Figure 3. For the "surgical" synthesis cohort, the mean RTS was 7.3 (6-11) wk. For patients treated with ORIF, the mean RTS was 7.9 (6-11) wk. For patient treated with PSF, the mean RTS was 6.5 (6-9) wk.

On meta-analysis, comparing the "conservative" synthesis cohort to the "surgical" synthesis cohort, the difference in the mean RTS was significant (MD 2.3 wk; 95%CI: 0.79-3.87; $P < 0.002$).

Fracture union

Conservative management: Four studies reporting on conservatively managed fractures recorded data on fracture union[9,10,21,22]. The union rate for this cohort was 85% (47/55), and the mean time to union was 14.0 (14-14) wk. For patients who returned to sport in a cast, the union rate was 85% (22/26), and the mean time to union was 14.2 wk[21,22]. For patients who returned to sports after cast removal, the union rate was 86% (25/29), and the mean time to union was 13.9 wk[9,10].

Surgical management: Five studies reporting on surgically managed fractures recorded data on fracture union[9,10,22-24]. The union rate for this cohort was 97% (69/71), and the mean time to union was 9.8 (9-11) wk. For patients treated with ORIF, the union rate was 98% (39/40), and the mean time to union was 10.3 (9-11) wk[22-24]. For patients treated with PSF, the union rate was 97% (30/31), and the mean time to union was 9.2 (9-9) wk[9,10].

On meta-analysis, comparing the "conservative" cohort to the "surgical" cohort, the difference in union rates (RR = 1.14; 95%CI 1.01-1.28; $P < 0.030$: $I^2 = 0\%$, $P = 0.99$) and mean union times (MD 4.2 wk; 95%CI 3.94-4.36; $P < 0.001$) were both significantly better for the 'surgical' cohort (Table 4).

Complications

Conservative management: Two of the three studies, which comprised conservatively-managed patients who returned to sport immediately in cast, reported complications[21,22]. These comprised non-union (8%-21%)[21,22] and delayed surgical intervention for non-union (14%)[21] (Table 3).

Three of the four studies, which comprised conservatively-managed patients who returned to sport after cast treatment, reported complications[9,10,26]. These comprised non-union (15%-17%)[9,26], delayed surgical intervention for non-union (17%)[26],

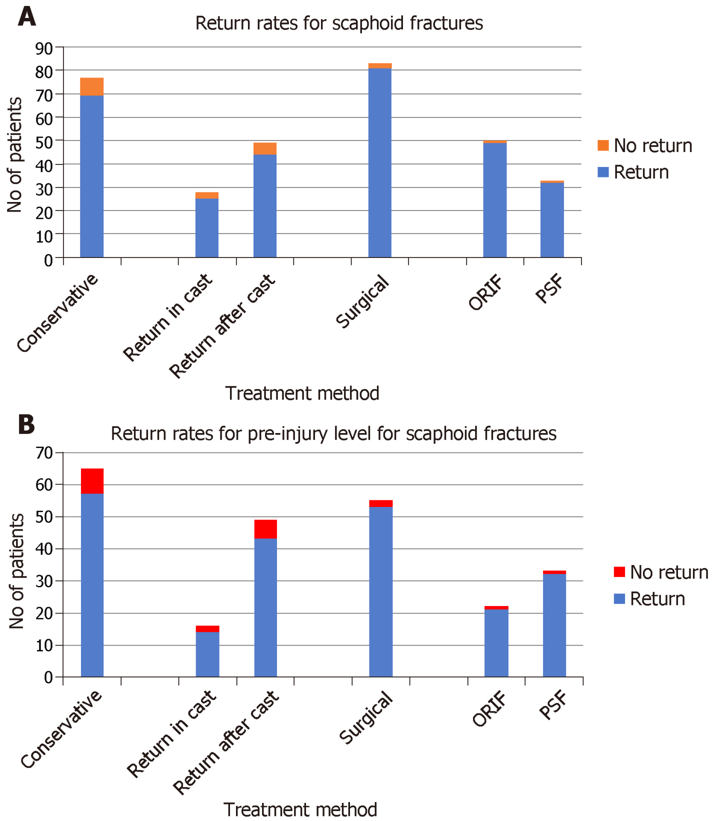

Figure 2 Return rates to sport following scaphoid fractures (A) and return rates to pre-injury level of sport following scaphoid fractures (B). ORIF: Open reduction and internal fixation; PSF: Percutaneous surgical fixation.

avascular necrosis (7%)[9], complex regional pain syndrome (4%)[9], malunion (11%)[9], radioscaphoid osteoarthritis (4%)[9] and persistent radial border wrist pain (50%)[10] (Table 3).

Surgical management: One of the three studies, reporting on patients treated with PSF, reported complications[9]. These comprised peri-operative breakage of the cannulated screwdriver (7%)[9], symptomatic metalwork (4%)[9] and non-union (4%)[9] (Table 3).

Three of the five studies, reporting on patients treated with ORIF, reported complications[23,25,28]. These comprised non-union (8%)[23]; scar sensitivity(6%)[25] and superficial radial nerve neuropraxia (40%)[28].

DISCUSSION

The management of scaphoid fractures remains a challenge in the athletic population. The findings from our review demonstrate that surgical management offers the best outcome regarding RRS and RTS post treatment. Not only does conservative management result in significantly lower RRS and RTS, it also demonstrates a substantial rate of fracture non-union, which can further impair athletes in their recovery from this injury.

In this review, the methodological quality of studies was lower than that of previous similar systematic reviews looking at return to sports following various fracture types, with a mean CMS of 59.5[16-20]. Thus, despite the inclusion of two randomised controlled trials in this study[9,10], this demonstrates a need for further high-quality research in this area including level one studies.

The management of scaphoid fractures is dependent on the location and the nature of the fracture. Of the recorded fracture types in the review, scaphoid waist fractures (waist, middle third, Herbert B2, Herbert A2) comprised the significant majority, representing 89% of these. All fractures types recorded in the review were, however, amenable to either surgical or conservative treatment as acute management: and these were therefore considered suitable for synthesis into the sub-cohorts accordingly.

From this review, the authors found that conservative management offered an RRS

Table 4 Summary of the return rates to sport and return times to sport by treatment modality

Mode of treatment	*n*	Return rates to sport	Mean return times to sport	Return rate to pre-injury level of sport	Union rate	Mean time to union
All[9,10,21-29]	160	150/160 (94%)[9,10,21-29]	8.4 wk[9,10,21-24,26-29]	110/120 (92%)[9,10,21,23,25-29]	116/126 (92%)[9,10,21-24]	11.3 wk[9,22-24]
Conservative[9,10,21,22,26,27,29]	77	69/77 (90%)[9,10,21,22,26,27,29]	9.6 wk[9,10,21,22,26,27,29]	57/65 (88%)[9,10,26,29]	47/55 (85%)[9,10,21,22]	14.0 wk[9,22]
Conservative - return in cast[21,22,27]	28	25/28 (89%)[21,22,27]	1.9 wk[21,22,27]	14/16 (88%)[21,27]	22/26 (85%)[21,22]	14.2 wk[22]
Conservative - return after cast[9,10,26,29]	49	44/49 (90%)[9,10,26,29]	13.9 wk[9,10,26,29]	43/49 (88%)[9,10,26,29]	25/29 (86%)[9,10]	13.9 wk[9]
Surgical[9,10,22-26,28]	83	81/83 (98%)[9,10,22-26,28]	7.3 wk[9,10,22-24,26,28]	53/55 (96%)[9,10,23,25,26,28]	69/71 (97%)[9,10,22-24]	9.8 wk[9,22-24]
ORIF[22-25,28]	50	49/50 (98%)[22-25,28]	7.9 wk[22-24,28]	21/22 (95%)[23,25,28]	39/40 (98%)[22-24]	10.3 wk[22-24]
PSF[9,10,26]	33	32/33 (97%)[9,10,26]	6.5 wk[9,10,26]	32/33 (97%)[9,10,26]	30/31 (97%)[9,10]	9.2 wk[9]

of 90% (88% return rate to pre-injury level of sport) with a mean RTS of 9.6 wk. While this can be considered satisfactory, as compared to figures reported from other fracture types, the return rates and return times were significantly lower compared to those reported from surgical management. With this, the rate of non-union from the conservatively-managed cohort was 15%, which again was significantly higher than that for the surgically managed cohort (3%)

To note, with the conservatively-managed cohort, there were three studies that advocated immediate return to sport following the injury, using cast or splint immobilisation[21,22,27]. This group demonstrated a non-union rate of 15%, which is likely the result of excessive movement at the fracture site secondary to early return to sporting activities. All three studies were published over 30 years ago[21,22,27], and such practice is currently not recommended for this reason[3]. Given that this provided return times of 0 wk for their patients, this considerably skews the "return time" data for the conservatively-managed patients. When the return times for the "conservative" cohort are analysed in consideration of this, the mean RTS for the patients who returned to sport following cast treatment was 13.9 wk. This is considerably longer than that recorded by the "surgical" cohort (7.3 wk) and so provides further recommendation towards surgical management of these injuries.

Thus, while conservative management can provide acceptable results in terms of RRS and RTS, athletes should be appropriately informed of the likely increased return time, decreased return rate and increased non-union rate associated with this treatment, in comparison to surgical management. Given the comparably high non-union rate associated with return to sport in cast, it is currently not recommended to allow patients to return to sports during cast immobilisation.

On analysis of the data from the "surgical" cohort, the authors found that this treatment provided an RRS of 98% (96% return rate to pre-injury level of sport) and a mean RTS of 7.3 wk: both these figures were significantly less than those from the "conservative" cohort. The union rate was also significantly higher for the "surgical" cohort (97%) compared to the "conservative" cohort (85%). ORIF and PSF provided similar RRS (98% and 97% respectively): however, PSF provided a marginally improved mean RTS (6.5 wk *vs* 7.9 wk). This is likely accounted for by the reduced tissue dissection, reduced duration of post-operative immobilisation and the simpler fracture patterns amenable to PSF when compared to ORIF[9,10,22-26,28]. However, despite this, both treatment methods offered similar union rates (98% *vs* 97%), providing evidence of the substantial benefit that surgical stabilisation and compression can provide to bone healing with this injury[9,10,22-26,28]. Our findings correlate with a similar systematic review, comparing conservative to surgical management of scaphoid waist fractures, which demonstrated earlier return to work and faster time to union with surgical management[30].

Given the substantial benefits in RRS, RTS and union rates for surgical management as compared to conservative management, surgical management should be the recommended option for treatment of these injuries in the athlete[31]. However, given that conservative management remains a reasonable option, any treatment recommendation must include a full discussion regarding the benefits and risk of both surgical and conservative management, particularly detailing the risk of surgical

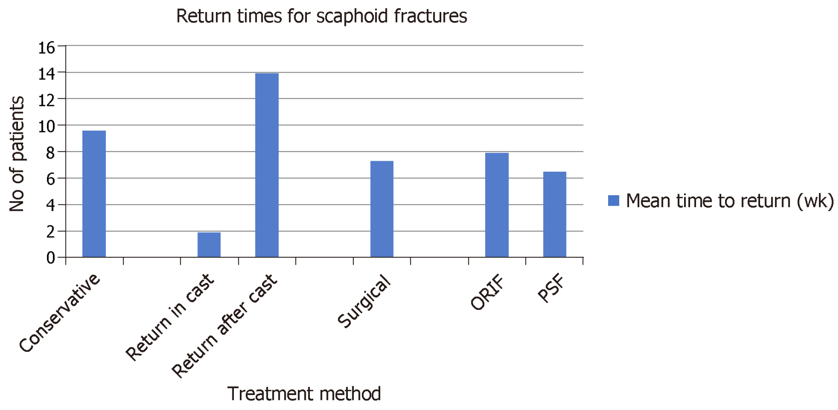

Figure 3 Return times to sport following scaphoid fractures. ORIF: Open reduction and internal fixation; PSF: Percutaneous surgical fixation.

complications (surgical site infection, metalwork-related symptoms, neuro-vascular injury and wound problems) when describing surgical management[32,33].

To note, there were a number of different immobilisation techniques and regimes used in the included studies [9,10,21,25]. A clear benefit of surgical stabilisation is that it reduces the requirement for post-operative immobilisation, facilitating an accelerated return to sporting activities[9,10,22-26,28]. However, on comparing studies within the conservative and surgical cohorts, significant variations were noted within each treatment group. Within the surgical cohort, post-operative immobilisation post ORIF ranged from 1 wk to 7 wk, with a variety of below elbow spica splints, casts and plaster splints employed[22-25,28]. Of the studies that employed PSF, one did not require post-operative immobilisation[9], while another required splinting up 6 wk post-operatively[10]. Within the conservative cohort, the methods of immobilisation included a short arm thumb spica cast with the wrist in a neutral position[21], colles' cast without thumb immobilisation[9] and below elbow plaster casts[10], while the mean duration of immobilisation ranged from 10 wk to 6 mo[9,10,26,29]. Interestingly, the studies that allowed return to sport in a cast had considerably longer immobilisation durations (3 mo to 6 mo)[21,22,27] than the other studies[9,10,26,29]. Given the substantial variety present, it was not possible to analyse the effect of immobilisation methods and duration on sporting outcome. However, such variation clearly demonstrates an area of future research, whereby the optimal methods and duration of immobilisation can be determined for these fractures to improve further RRS and RTS.

The use of formal functional outcomes scores was lower when compared to similar reviews assessing other fracture types[15-20]. Only three of the 11 studies used formal functional assessments to assess patient outcome[9,24,25]. Future prospective studies should aim to utilise validated functional assessment scoring systems in order to assess further the effect of immobilisation and rehabilitation following fractures of the scaphoid in athletes.

Our review has several limitations

The first of these relates to the fact that a number of the earlier studies included in the review had very limited information on patient demographics as well as post-operative care. Although they provided the relevant information regarding RRS and RTS, the lack of additional information limited our ability to perform more detailed analyses, assessing for associated predictive factors of sporting outcome.

Further to this, most of the included studies did not provide detailed information regarding sporting outcomes, often failing to provide information on return to pre-injury level of sport. To accommodate for this, the authors designated three main categories for sporting outcome (return to sport, RTS, return to pre-injury level of sport), allowing clear definitive outcome data to be extracted from each study, thus facilitating direct comparisons to be made on the effect of different treatments from the various studies included.

A further limitation of the review lies in the inclusion of studies from several years previous, which report on treatment methods that are no longer recommended[21,22,27]. Three of the earlier studies allowed patients to return to sports immediately in cast, which positively skewed the RTS for the conservative cohort[21,22,27]: such practice is actively discouraged in current practice given the substantial risk of fracture displacement and non-union[3]. However, the results were appropriately divided into sub-cohorts, demonstrating the effects of such practices on the synthesis data.

The final limitation comprises the variety of fracture locations present within the review. While the significant majority of the recorded fractures were within the scaphoid waist region, a number of studies reported on fractures both within the proximal and distal third regions of the scaphoid. However, all recorded fracture types were suitable for either conservative or surgical management, and so it was considered appropriate to synthesise these accordingly for outcome analyses.

Over 90% of athletes who sustain a scaphoid fracture can expect to return to sport. While conservative management can provide acceptable results regarding RRS and RTS, surgical management can provide athletes with a significantly greater chance of returning to sport and allow them to return to sport significantly quicker. It can also provide them with a significantly higher rate of fracture union. However, given that both treatments remain considerable options, all patients should be comprehensively informed of the benefits and risk of both treatment methods prior to deciding management. In particular, patients should be made aware of the risk of surgical complications, which include surgical site infection, neurovascular injury, metalwork-related symptoms and wound problems. Return to sport during cast immobilisation should be actively discouraged due to the high risk of non-union. Further prospective randomised controlled trials should aim to define better the benefit over surgical over conservative management for treatment of these injuries in athletic patients.

ARTICLE HIGHLIGHTS

Research background

Scaphoid fractures account for over 85% of all sport-related carpal bone fractures and are particularly common in sports involving high impact injuries to the wrist. The management of such injuries comprises both conservative and surgical techniques, as guided by fracture location and type. Athletes demonstrate a unique challenge with regards to the management of scaphoid fractures due to their requirement to return to sport as soon as able.

Research motivation

Scaphoid fractures significantly impact an athlete’s ability to return to sport. This topic should therefore be addressed to understand further the outcome of various treatment options and to optimise the management of these injuries.

Research objectives

To identify the available literature reporting on the sporting outcomes of both conservative and surgical management of scaphoid fractures in the athletic population.

Research methods

A systematic review of the available literature was performed, identifying all articles reporting on return rates to sport (RRS) and return times to sport (RTS) following acute scaphoid fractures. A total of 160 acute scaphoid fractures were included for analysis.

Research results

The RRS for conservative management and for surgical management were 90% and 98%, respectively. The mean RTS was lower in the surgical cohort at 7.3 wk, compared to 9.6 wk in the conservative cohort. Union rate was higher in the surgical cohort at 97% compared to 85% in the conservative cohort. On meta-analysis, surgical management of scaphoid fractures provided significantly better RRS, RTS, union rates and mean times to union as compared to conservative management.

Research conclusions

Most athletes can expect to return to sports following scaphoid fractures, with either conservative or surgical management. Surgical management did however offer improved RRS, RTS and union rates. Both treatment options remain appropriate in the management of scaphoid fractures, and patients should be counselled accordingly prior to treatment decisions. Return to sport in a cast should be discouraged due to the risk of non-union.

Research perspectives

The management of scaphoid fractures remains a challenge in the athletic population. Further well-designed studies should aim to address this topic in order to provide a better understanding of the RRS and RTS following the various treatment methods for acute scaphoid fractures in the athlete.

REFERENCES

1 **Aitken S**, Court-Brown CM. The epidemiology of sports-related fractures of the hand. *Injury* 2008; **39**: 1377-1383 [PMID: 18656191 DOI: 10.1016/j.injury.2008.04.012]

2 **Weber ER**, Chao EY. An experimental approach to the mechanism of scaphoid waist fractures. *J Hand*

Surg Am 1978; **3**: 142-148 [PMID: 556476 DOI: 10.1016/S0363-5023(78)80062-8]

3 **Coutr-Brown C**, McQueen M, Tornetta P. *Trauma. 1st ed*. Philadelphia: Lippincott Williams Wilkins 2006;

4 **Parvizi J**, Wayman J, Kelly P, Moran CG. Combining the clinical signs improves diagnosis of scaphoid fractures. A prospective study with follow-up. *J Hand Surg Br* 1998; **23**: 324-327 [PMID: 9665518 DOI: 10.1016/S0266-7681(98)80050-8]

5 **Ring D**, Lozano-Calderón S. Imaging for suspected scaphoid fracture. *J Hand Surg Am* 2008; **33**: 954-957 [PMID: 18656772 DOI: 10.1016/j.jhsa.2008.04.016]

6 **Winston MJ**, Weiland AJ. Scaphoid fractures in the athlete. *Curr Rev Musculoskelet Med* 2017; **10**: 38-44 [PMID: 28251560 DOI: 10.1007/s12178-017-9382-y]

7 **Herbert TJ**, Fisher WE. Management of the fractured scaphoid using a new bone screw. *J Bone Joint Surg Br* 1984; **66**: 114-123 [PMID: 6693468 DOI: 10.1097/00006534-198678060-00052]

8 **Geoghegan JM**, Woodruff MJ, Bhatia R, Dawson JS, Kerslake RW, Downing ND, Oni JA, Davis TR. Undisplaced scaphoid waist fractures: is 4 weeks' immobilisation in a below-elbow cast sufficient if a week 4 CT scan suggests fracture union? *J Hand Surg Eur Vol* 2009; **34**: 631-637 [PMID: 19959447 DOI: 10.1177/1753193409105189]

9 **McQueen MM**, Gelbke MK, Wakefield A, Will EM, Gaebler C. Percutaneous screw fixation versus conservative treatment for fractures of the waist of the scaphoid: a prospective randomised study. *J Bone Joint Surg Br* 2008; **90**: 66-71 [PMID: 18160502 DOI: 10.1302/0301-620X.90B1.19767]

10 **Adolfsson L**, Lindau T, Arner M. Acutrak screw fixation versus cast immobilisation for undisplaced scaphoid waist fractures. *J Hand Surg Br* 2001; **26**: 192-195 [PMID: 11386765 DOI: 10.1054/jhsb.2001.0558]

11 **Dy CJ**, Khmelnitskaya E, Hearns KA, Carlson MG. Opinions regarding the management of hand and wrist injuries in elite athletes. *Orthopedics* 2013; **36**: 815-819 [PMID: 23746021 DOI: 10.3928/01477447-20130523-30]

12 **Rizzo M**, Shin AY. Treatment of acute scaphoid fractures in the athlete. *Curr Sports Med Rep* 2006; **5**: 242-248 [PMID: 16934205 DOI: 10.1007/s11932-006-0005-4]

13 **Moher D**, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097 [PMID: 19621072 DOI: 10.1371/journal.pmed.1000097]

14 **Coleman BD**, Khan KM, Maffulli N, Cook JL, Wark JD. Studies of surgical outcome after patellar tendinopathy: clinical significance of methodological deficiencies and guidelines for future studies. Victorian Institute of Sport Tendon Study Group. *Scand J Med Sci Sports* 2000; **10**: 2-11 [PMID: 10693606 DOI: 10.1034/j.1600-0838.2000.010001002.x]

15 **Del Buono A**, Smith R, Coco M, Woolley L, Denaro V, Maffulli N. Return to sports after ankle fractures: a systematic review. *Br Med Bull* 2013; **106**: 179-191 [PMID: 23258924 DOI: 10.1093/bmb/lds039]

16 **Robertson GA**, Wood AM. Return to sports after stress fractures of the tibial diaphysis: a systematic review. *Br Med Bull* 2015; **114**: 95-111 [PMID: 25712999 DOI: 10.1093/bmb/ldv006]

17 **Robertson GA**, Wood AM. Return to Sport After Tibial Shaft Fractures: A Systematic Review. *Sports Health* 2016; **8**: 324-330 [PMID: 27340245 DOI: 10.1177/1941738115601425]

18 **Robertson GA**, Wood AM. Return to sport following clavicle fractures: a systematic review. *Br Med Bull* 2016; **119**: 111-128 [PMID: 27554280 DOI: 10.1093/bmb/ldw029]

19 **Robertson GAJ**, Goffin JS, Wood AM. Return to sport following stress fractures of the great toe sesamoids: a systematic review. *Br Med Bull* 2017; **122**: 135-149 [PMID: 28444129 DOI: 10.1093/bmb/ldx010]

20 **Robertson GAJ**, Wong SJ, Wood AM. Return to sport following tibial plateau fractures: A systematic review. *World J Orthop* 2017; **8**: 574-587 [PMID: 28808629 DOI: 10.5312/wjo.v8.i7.574]

21 **Riester JN**, Baker BE, Mosher JF, Lowe D. A review of scaphoid fracture healing in competitive athletes. *Am J Sports Med* 1985; **13**: 159-161 [PMID: 4014530 DOI: 10.1177/036354658501300303]

22 **Rettig AC**, Weidenbener EJ, Gloyeske R. Alternative management of midthird scaphoid fractures in the athlete. *Am J Sports Med* 1994; **22**: 711-714 [PMID: 7810798 DOI: 10.1177/036354659402200522]

23 **Rettig AC**, Kollias SC. Internal fixation of acute stable scaphoid fractures in the athlete. *Am J Sports Med* 1996; **24**: 182-186 [PMID: 8775117 DOI: 10.1177/036354659602400211]

24 **Muramatsu K**, Doi K, Kuwata N, Kawakami F, Ihara K, Kawai S. Scaphoid fracture in the young athlete--therapeutic outcome of internal fixation using the Herbert screw. *Arch Orthop Trauma Surg* 2002; **122**: 510-513 [PMID: 12483331 DOI: 10.1007/s00402-002-0417-4]

25 **Bedi A**, Jebson PJ, Hayden RJ, Jacobson JA, Martus JE. Internal fixation of acute, nondisplaced scaphoid waist fractures via a limited dorsal approach: an assessment of radiographic and functional outcomes. *J Hand Surg Am* 2007; **32**: 326-333 [PMID: 17336838 DOI: 10.1016/j.jhsa.2007.01.002]

26 **Robertson GA**, Wood AM, Bakker-Dyos J, Aitken SA, Keenan AC, Court-Brown CM. The epidemiology, morbidity, and outcome of soccer-related fractures in a standard population. *Am J Sports Med* 2012; **40**: 1851-1857 [PMID: 22610519 DOI: 10.1177/0363546512448318]

27 **Ellsasser JC**, Stein AH. Management of hand injuries in a professional football team. Review of 15 years of experience with one team. *Am J Sports Med* 1979; **7**: 178-182 [PMID: 464173 DOI: 10.1177/036354657900700308]

28 **Huene DR**. Primary internal fixation of carpal navicular fractures in the athlete. *Am J Sports Med* 1979; **7**: 175-177 [PMID: 464172 DOI: 10.1177/036354657900700307]

29 **Robertson GA**, Wood AM, Heil K, Aitken SA, Court-Brown CM. The epidemiology, morbidity and outcome of fractures in rugby union from a standard population. *Injury* 2014; **45**: 677-683 [PMID: 23830199 DOI: 10.1016/j.injury.2013.06.006]

30 **Modi CS**, Nancoo T, Powers D, Ho K, Boer R, Turner SM. Operative versus nonoperative treatment of acute undisplaced and minimally displaced scaphoid waist fractures--a systematic review. *Injury* 2009; **40**: 268-273 [PMID: 19195652 DOI: 10.1016/j.injury.2008.07.030]

31 **Belsky MR**, Leibman MI, Ruchelsman DE. Scaphoid fracture in the elite athlete. *Hand Clin* 2012; **28**: 269-278, vii [PMID: 22883862 DOI: 10.1016/j.hcl.2012.05.005]

32 **Moatshe G**, Godin JA, Chahla J, Cinque ME, Kennedy NI, Sanchez G, Beaulieu-Jones BR, LaPrade RF, Provencher MT. Clinical and Radiologic Outcomes After Scaphoid Fracture: Injury and Treatment Patterns in National Football League Combine Athletes Between 2009 and 2014. *Arthroscopy* 2017; **33**: 2154-2158 [PMID: 29102567 DOI: 10.1016/j.arthro.2017.08.259]

33 **de Boer BNP**, Doornberg JN, Mallee WH, Buijze GA. Surgical Versus Conservative Treatment for Nondisplaced Scaphoid Waist Fractures. *Buijze GA, Jupiter JB, editors*. Scaphoid Fractures: Evidence-

Based Management. Elsevier 2018; 99-106

P- Reviewer: Lee PN
S- Editor: Ma YJ **L- Editor:** Filipodia **E- Editor:** Wu YXJ

World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 February 18; 10(2): 115-122

DOI: 10.5312/wjo.v10.i2.115

ISSN 2218-5836 (online)

CASE REPORT

Adolescent Lisfranc injury treated with TightRope™: A case report and review of literature

Themistoklis Tzatzairis, Gregory Firth, Lee Parker

ORCID number: Themistoklis Tzatzairis (0000-0002-2324-031X); Gregory Firth (0000-0002-1594-2290); Lee Parker (0000-0002-6968-7950).

Author contributions: All authors have equally contributed in this article; all authors issued final approval for the version to be submitted.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report.

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

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2013), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Manuscript source: Unsolicited manuscript

Themistoklis Tzatzairis, Gregory Firth, Royal London Hospital, Paediatric Orthopaedic Department, Barts NHS Trust, London E1 2AA, Whitechapel, United Kingdom

Lee Parker, Royal London Hospital, Foot and Ankle Orthopaedic department, Barts NHS Trust, London E13 8SL, United Kingdom

Corresponding author: Themistoklis Tzatzairis, MBBS, MSc, Doctor, Senior Clinical Fellow in Paediatric Orthopaedic, Royal London Hospital, Paediatric Orthopaedic Department, Barts NHS Trust, St Augustine with St Philip's Church, Newark Street, London E1 2AA, Whitechapel, United Kingdom. themistoklis.tzatzairis@bartshealth.nhs.uk
Telephone: +44-792-3301467

Abstract

BACKGROUND
Lisfranc injuries are rare and can be easily missed. This injury is extremely rare in children, with limited published data. Different treatment options have been described; one of the options in adults is the "mini" TightRope™ Syndesmosis Device that provides non-rigid fixation with impressive results. However, there is no reference regarding the use of this device in children.

CASE SUMMARY
We describe the case of an 11-year-old girl who sustained a Lisfranc injury of her right foot that was initially missed in the Accident and Emergency department of her local hospital. This case was a ligamentous/periosteal sleeve avulsion type of Lisfranc injury and a percutaneous technique using the "mini" TightRope™ syndesmosis device was used. Clinical and radiological results were excellent at final follow up.

CONCLUSION
The "mini" TightRope™ syndesmosis device is a promising method of fixation for children with certain Lisfranc injuries. This method has many advantages, including the non-rigid type of the fixation and no need for subsequent metalwork removal.

Key words: Lisfranc; Injury; Foot; Tightrope; Paediatric; Case report

Core tip: We describe the case of an 11-year-old girl who sustained a ligamentous/periosteal sleeve avulsion type of Lisfranc injury of her right foot that was

Received: November 27, 2018
Peer-review started: November 27, 2018
First decision: December 30, 2018
Revised: January 14, 2019
Accepted: January 26, 2019
Article in press: January 26, 2019
Published online: February 18, 2019

initially missed in a local Accident and Emergency department. The "mini" TightRope™ syndesmosis device, can be used safely and effectively in children with certain Lisfranc injuries, based on experience in the adult literature.

Citation: Tzatzairis T, Firth G, Parker L. Adolescent Lisfranc injury treated with TightRope™: A case report and review of literature. *World J Orthop* 2019; 10(2): 115-122
URL: https://www.wjgnet.com/2218-5836/full/v10/i2/115.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i2.115

INTRODUCTION

Jacques Lisfranc de St. Martin (1787-1847) was a French surgeon who lived during the Napoleonic Wars. Lisfranc (surgeon and gynaecologist) was founder of a great number of surgical procedures including surgical resection in rectal carcinoma, lithotomy in women and a variety of amputations[1]. In 1815, during the Napoleonic Wars, he encountered a soldier who suffered from gangrene on his foot after having a fall from his horse. This is when his name got, for the first time, affiliated with the terms "Lisfranc joint" and "Lisfranc injury" after performing a tarsometatarsal-level amputation on this soldier. Although, in reality, Lisfranc did not describe the anatomy or the mechanism of injury, nowadays his name has come to mean a dislocation/fracture injury at the tarso-metatarsal joints[2].

Anatomically, the Lisfranc joint complex consists of ligaments and bones that connect the midfoot and forefoot (tarsometatarsal, intermetatarsal and anterior intertarsal joints). Each cuneiform bone articulates with one of the medial metatarsal whereas the lateral two metatarsals articulate with the cuboid. Apart from the trapezoid geometry of the cuneiforms and their "Roman arch" alignment, extra stability is provided by a number of ligaments. The most important is the Lisfranc ligament that connects the lateral aspect of the medial cuneiform with the base of the second metatarsal. The ligament is of vital importance to stability in this part of the foot, as there is no ligamentous connection between the first and the second metatarsal[3].

Many different classification systems have been proposed, with the first one originally been described in 1909 by Quenu and Kuss[4]. That was the first classification system describing the injuries as homolateral, isolated or divergent based on the direction of the displaced metatarsals. Many years later, Hardcastle *et al*[5] categorized these injuries in three different types based on displacement and incongruity. Myerson followed with modification to Hardcastle's system (Table 1)[6]. Despite these multiple classification systems, the treatment method and the clinical outcome do not reliably correlate with any injury type[5,7,8].

Lisfranc injuries are rare (around 0.2% of all fractures) with reported incidence of 1:55000 per year (male:female = 4:1). It occurs more often in athletes and there is a peak at the third decade of life[9]. The rate of delayed diagnosis is up to 24%, most of these being pure ligamentous injuries[10]. In children this injury is extremely rare. There is nothing published regarding the epidemiology of this injury and the largest series in the literature includes only 52 children over a 12-year period. There are no specific guidelines regarding the treatment in children and many options have been described[11].

TightRope™ technique

The TightRope™ syndesmosis device (Arthrex Inc., Naples, FL) was originally made for the injured ankle syndesmosis to provide non-rigid fixation[12]. Its "mini" version has been used to treat syndesmotic injuries, including Lisfranc injuries[13]. The TightRope™ consists of two buttons connected to each other by fiber wire. Tensioning and compression of the Lisfranc joint can be achieved without using any screws at all.

No articles regarding the use of the TightRope™ in children's Lisfranc injury were found. This case report presents the first described case of a Lisfranc injury in a 11-year-old girl treated with the TightRope™ technique.

CASE PRESENTATION

Chief complaints

Table 1 Myerson classification system

Incogruity	Subtype	Description
Type A: Complete	-	Dislocation of M1-M5 in the same direction (either lateral or dorsoplantar)
Type B: Incomplete	B1	Medial dislocation involving only the M1 joint
	B2	Lateral dislocation involving any of the M2-M4
Type C: Incomplete/Complete	C1	Divergent, incomplete dislocation involving M1 and some of the lateral metatarsals
	C2	Divergent, complete dislocation involving M1 and all of the lateral metatarsals

An 11-year-old girl was referred to our clinic by her general practitioner for bilateral patellar instability with symptoms starting 4 mo prior.

History of present illness

However, two weeks before, she had a fall after tripping, and sustained an injury at her right foot. On the day of injury she was admitted to the Accident and Emergency (A and E) department of a different hospital for pain limiting her ability to weight bear on that foot. Although a clinical assessment and an X-ray were performed, the injury was initially missed and due to discomfort and pain she was treated with a walking boot.

Imaging examinations

During the appointment in our clinic, her patella instability was assessed clinically and radiographically. Increased ligamentous laxity with no previous injury or patella dislocation was noted. Her family and past medical history were free. However, her parents mentioned the recent injury on her right foot and described the ongoing symptoms. On examination there was swelling throughout the midfoot with tenderness over the tarsometatarsal joint and she was still unable to bear weight. As a result, apart from the knee X-rays we requested additional X-rays of the right foot (anteroposterior, lateral and oblique view) (Figure 1). The X-ray showed "malalignment of the intermediate cuneiform with the second metatarsal, with a small bone fragment of the adjacent bone, in keeping with a Lisfranc fracture/dislocation".

FINAL DIAGNOSIS

No further laboratory tests were needed but an urgent magnetic resonance imaging scan (MRI) was scheduled that same day to further assess the injury. The MRI revealed: (1) Disruption of the Lisfranc ligament with mild associated displacement of the first and second metatarsals in relation to the medial and intermediate cuneiforms; (2) High T2 marrow signal at the bases of the 1^{st}-4^{th} metatarsals; (3) Free fluid around the tarsal bones; and (4) Sprain of calcaneonavicular ligament (Figure 2). A final diagnosis was made, based on this MRI report of a ligamentous/periosteal avulsion type Lisfranc injury.

TREATMENT

Based on the clinical and radiographical findings and after having a thorough discussion with the parents, the advantages (improve bone/ligament healing, improve symptoms/pain and increase movement/ROM) and the disadvantages (scar, infection, nerve/vessel injury, need for additional procedure, stiffness, anaesthetic risks) of a potential operation were discussed. She was then taken to theatre and under general anaesthetic an examination under anaesthesia revealed instability between the first and second metatarsals with concomitant dorsal subluxation and surgical treatment was decided.

Considering the age of our patient and trying to prevent any articular damage we used the TightRope™ technique under the same anaesthetic. Under c-arm guidance the medial cuneiform and base of second metatarsal were identified. Two small incisions were made, dorsally over the lateral aspect of the 2^{nd} metatarsal base and over the medial aspect of the medial cuneiform. Reduction of the joint was achieved with a bone reduction clamp. A drill hole (2 mm) was made from the medial cuneiform into the second metatarsal (base). The device was guided and pulled through under fluoroscopic guidance. The medial cuneiform and the lateral wall of the 2^{nd} metatarsal base were engaged and the required compression was applied. The

Figure 1 Pre-operative X-ray showing increased distance between 1st and 2nd metatarsals with small bone fragment (inside circle).

reduction was maintained after taking the clamp off (Figure 3). Extra care was taken to be sure that there was no soft tissue between the medial and lateral buttons and bone surface. Post-operatively, the foot was held in a moonboot for 4 wk, with partial weight-bearing with crutches for the first two weeks.

OUTCOME AND FOLLOW-UP

In the 3rd week the patient was reviewed in our clinic. The X-ray demonstrated excellent maintenance of reduction of the Lisfranc joint (2.2 mm distance between 1st and 2nd metatarsals post-operatively, compared to 7.1 mm pre-operatively) and patient's symptoms had improved (Figure 4). At six weeks post-operatively, after 3 sessions of physiotherapy, the patient was able to fully weight bear without symptoms. At 12 wk post-operatively, the X-ray showed preserved reduction of the Lisfranc joint and she remained symptom-free.

DISCUSSION

Lisfranc injuries in adults are rare and known to be easily missed[10]. In the paediatric population the lack of data in the literature suggests that it is even less common or underdiagnosed or a combination of both. There are few studies of Lisfranc injuries in children and thus the treatment strategies are based on the reported results applying to adults. Depending on the mechanism of injury and its result (ligamentous and/or osseous injury), different treatment options have been described including conservative treatment, use of k-wires and/or screws and/or plates[11,14,15]. These methods seem to offer really stable fixation but disadvantages and complications have been reported including screw breakage, reduced range of motion and pain of the affected area, extensive cartilage damage, prolonged immobilization period and need for additional procedures to remove the screws[16-19]. Specifically, a cadaveric study showed that use of a 3.5 mm trans-articular screw can lead on to significant damage of the tarso-metatarsal joint[16]. Dorsal or plantar plating with locking, low-profile plates seem to provide adequate outcomes and stability[16,20]. Recently, the mini-TightRope™ technique was described as an option in the treatment of isolated Lisfranc ligament injuries with promising results. However, further studies are needed to confirm the long-term results[13,21,22].

The TightRope™ construct is made of 2 buttons (one flat 5.5 mm round stainless-steel button and a second oblong 2.6 mm × 8.0 mm stainless-steel button) connected to each other by 4 strands of #2 fibre wire. This structure creates a double pulley system between the two anchored ends which allows for better compression between the two bones. Usually, a two-incision technique is used with the first one being dorsally between the 1st and 2nd metatarsal and the second incision medially to the medial cuneiform. Extra care should be taken to protect the neurovascular bundle lying dorsally. After reducing the fracture/dislocation with a clamp and under fluoroscopic guidance, a drill is made from the medial cuneiform into the second metatarsal base over a guide wire (or retrogradely). The suture passes through this hole and is tightened making sure that the buttons remain flush over the cortex and the reduction is maintained. Further radiographs are obtained to confirm it and anatomic alignment

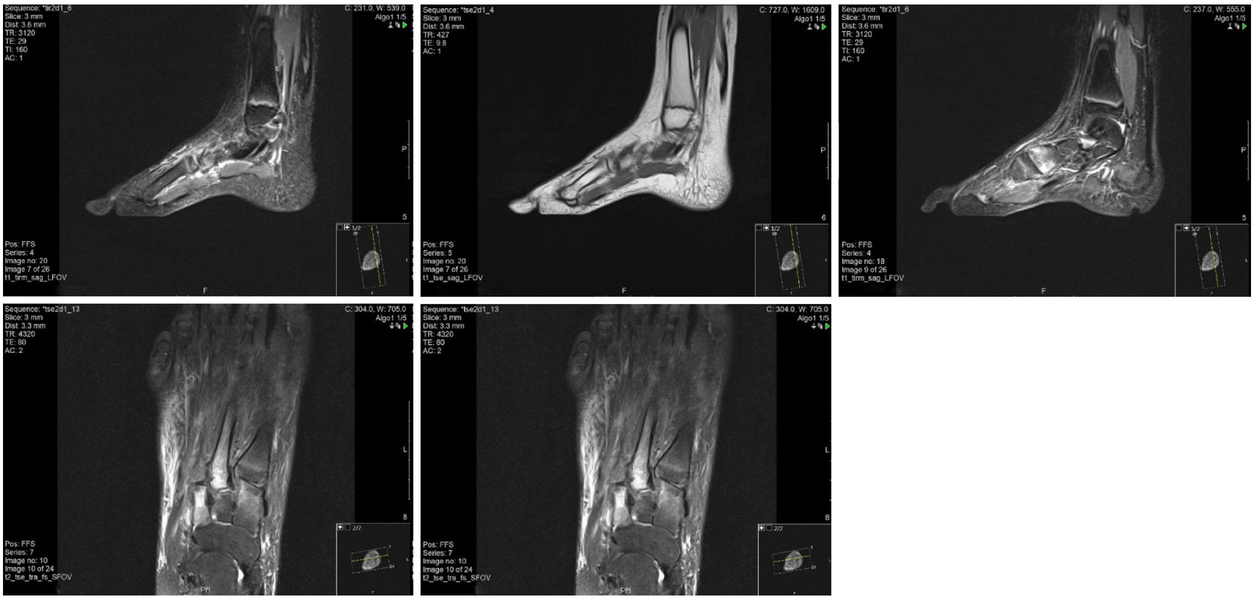

Figure 2 Magnetic resonance imaging image series.

is checked with direct inspection.

Brin *et al*[13] in their case series of adults highlighted the advantages of this method, in addition to the excellent clinical results that were reported. Non-rigid fixation seems to enhance healing, early weight bearing and early mobilization. Additionally, this method has a short learning curve and there is no need for a second operation to remove the metalwork[13].

In 2009, a cadaveric study concluded that the suture-button technique can provide similar results when compared to screw fixation with the advantage of avoiding an additional operation to remove the hardware prior to weight bearing[22]. To the best of our knowledge, this is the first description of a paediatric Lisfranc injury treated with TightRope™. Our case was a ligamentous/periosteal avulsion Lisfranc injury and therefore we opted to follow this method, based on the adult literature[13,22,23].

Although our hospital is a tertiary hospital this kind of injury is rarely seen. From our database search we managed to find only a few cases in the last ten years. Most of them were treated with open reduction and internal fixation (ORIF) with plate and screws. Two cases in which there was no displacement, and mild tenderness, were treated conservatively. No complications were seen, apart from post-operative stiffness in the ORIF "group" and the need for additional procedure to remove the metalwork.

Literature dealing with Lisfranc injuries in adolescents/children are extremely limited (Table 2). Veijola *et al*[14] in their retrospective study included six patients (range 13 to 16 years) treated with ORIF. In all but one case, they achieved anatomical reduction, but most patients claimed discomfort in the injured foot. Hill *et al*[11] reviewed 56 children treated for bony or ligamentous Lisfranc injuries with ORIF or non-operative management. These authors didn't find any correlation between age and type of injury but concluded that a large percentage of patients, even if they had open physes, required surgery. An important limitation was the lack of data on outcomes and follow-up[11]. A case of a 10-year-old girl who sustained a Lisfranc fracture-dislocation in 2013 was presented by Lesko *et al*[24] last year. Injury was fixed with ORIF but now (5 years post-operatively) she has developed functional pain and radiographic evidence of degenerative arthritis. All the other articles found in the literature did not deal with treatment and outcome but discussed the mechanism of injury which was not the focus of this report[15,25,26].

This minimally invasive technique has many advantages: (1) reduced duration of the procedure; (2) non-rigid type of the fixation that allows early mobilization; (3) prevention of cartilage damage; and (4) no need for metalwork removal. The main limitation of this study is that it is just a case report, but we hope that it will open the way for further research using this technique for ligamentous Lisfranc injuries in children.

CONCLUSION

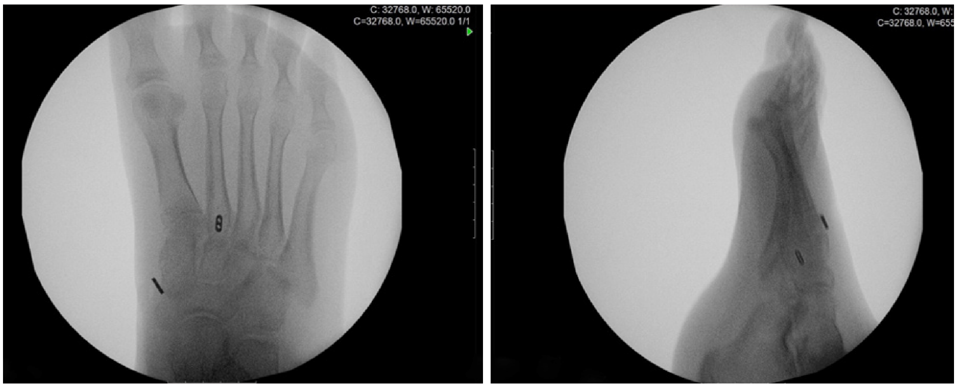

Figure 3 Intra-operative X-ray confirmed maintance of reduction after removal of bone reduction clamp.

The TightRope™ syndesmosis device technique in children with ligamentous Lisfranc injuries is efficacious as it combines the advantages of a percutaneous technique with a less rigid type of fixation and good short-term results. Further research is needed to confirm its routine use in children.

Table 2 Current literature dealing with Lisfranc injury in children/adolescents

Article	Type of study	No. of patients	Type of fixation	Result
Lisfranc Injury in Adolescents (Veijola *et al*[14], 2013)	Retrospective	6	ORIF	Good anatomical reduction, post-operative discomfort
Lisfranc injuries in children and adolescents (Hill *et al*[11], 2017)	Retrospective	56	ORIF (19); Conservatively (37)	Good post-operative results with rare complications (physeal arrest, broken implant)
Midfoot Degenerative Arthritis and Partial Fusion After Pediatric Lisfranc Fracture-Dislocation (Lesko *et al*[24], 2018)	Case report	1	ORIF	Functional pain and radiographic evidence of degenerative arthritis: 5-yr post-operatively
Pediatric Lisfranc injury: "bunk bed" fracture (Johnson[15], 1981)	Retrospective	16	-	Pathogenesis of Lisfranc injury
Plantar-flexion tarsometatarsal joint injuries in children (Buoncristiani *et al*[25], 2001)	Retrospective	8	Conservative	Early degenerative changes can occur and may be responsible for chronic pain and activity limitation
Tarso-metatarsal joint injuries in children (Wiley[26], 1981)	-	-	-	Pathogenesis of Lisfranc injury

ORIF: Open reduction and internal fixation.

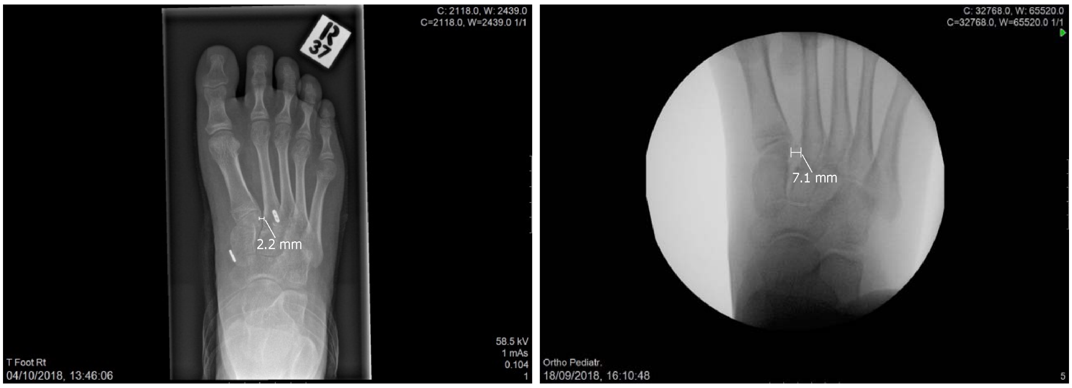

Figure 4 Post-operative x-ray (3rd week) on the left side and pre-operative X-ray on the right side.

REFERENCES

1 M. Lisfranc on Diseased Joints. *Med Chir Rev* 1826; **5**: 296-297 [PMID: 29919637]
2 **Cassebaum WH**. Lisfranc fracture-dislocations. *Clin Orthop Relat Res* 1963; **30**: 116-129 [PMID: 5888997 DOI: 10.1097/00003086-196300300-00014]
3 **de Palma L**, Santucci A, Sabetta SP, Rapali S. Anatomy of the Lisfranc joint complex. *Foot Ankle Int* 1997; **18**: 356-364 [PMID: 9208295 DOI: 10.1177/107110079701800609]
4 **Quenu E**, Küss G. Etude sur les luxations du métatarse (luxations metatarsotarsiennes) du diastasis entre le 1er et le 2e métatarsien. *Rev Chir* 1909; **39**: 1093-1134
5 **Hardcastle PH**, Reschauer R, Kutscha-Lissberg E, Schoffmann W. Injuries to the tarsometatarsal joint. Incidence, classification and treatment. *J Bone Joint Surg Br* 1982; **64**: 349-356 [PMID: 7096403 DOI: 10.1302/0301-620X.64B3.7096403]
6 **Myerson MS**. The diagnosis and treatment of injury to the tarsometatarsal joint complex. *J Bone Joint Surg Br* 1999; **81**: 756-763 [PMID: 10530832 DOI: 10.1302/0301-620X.81B5.0810756]
7 **Myerson MS**, Fisher RT, Burgess AR, Kenzora JE. Fracture dislocations of the tarsometatarsal joints: end results correlated with pathology and treatment. *Foot Ankle* 1986; **6**: 225-242 [PMID: 3710321 DOI: 10.1177/107110078600600504]
8 **Shariff S**, Clark C, Dega R. Lisfranc injury classifications. *The Internet Journal of Orthopedic Surgery* 2008; 11(1)
9 **Buchanan BK**, Donnally III CJ. Dislocation, Lisfranc. 2018 [PMID: 28846306]
10 **Sherief TI**, Mucci B, Greiss M. Lisfranc injury: how frequently does it get missed? And how can we improve? *Injury* 2007; **38**: 856-860 [PMID: 17214988 DOI: 10.1016/j.injury.2006.10.002]
11 **Hill JF**, Heyworth BE, Lierhaus A, Kocher MS, Mahan ST. Lisfranc injuries in children and adolescents. *J*

Pediatr Orthop B 2017; **26**: 159-163 [PMID: 27602913 DOI: 10.1097/BPB.0000000000000380]
12 **Cottom JM**, Hyer CF, Philbin TM, Berlet GC. Treatment of syndesmotic disruptions with the Arthrex Tightrope: a report of 25 cases. *Foot Ankle Int* 2008; **29**: 773-780 [PMID: 18752774 DOI: 10.3113/FAI.2008.0773]
13 **Brin YS**, Nyska M, Kish B. Lisfranc injury repair with the TightRope device: a short-term case series. *Foot Ankle Int* 2010; **31**: 624-627 [PMID: 20663431 DOI: 10.3113/FAI.2010.0624]
14 **Veijola K**, Laine HJ, Pajulo O. Lisfranc injury in adolescents. *Eur J Pediatr Surg* 2013; **23**: 297-303 [PMID: 23172567 DOI: 10.1055/s-0032-1330847]
15 **Johnson GF**. Pediatric Lisfranc injury: "bunk bed" fracture. *AJR Am J Roentgenol* 1981; **137**: 1041-1044 [PMID: 6974997 DOI: 10.2214/ajr.137.5.1041]
16 **Alberta FG**, Aronow MS, Barrero M, Diaz-Doran V, Sullivan RJ, Adams DJ. Ligamentous Lisfranc joint injuries: a biomechanical comparison of dorsal plate and transarticular screw fixation. *Foot Ankle Int* 2005; **26**: 462-473 [PMID: 15960913 DOI: 10.1177/107110070502600607]
17 **Ando A**, Hagiwara Y, Tsuchiya M, Onoda Y, Suda H, Chimoto E, Itoi E. Increased expression of metalloproteinase-8 and -13 on articular cartilage in a rat immobilized knee model. *Tohoku J Exp Med* 2009; **217**: 271-278 [PMID: 19346731 DOI: 10.1620/tjem.217.271]
18 **Kuo RS**, Tejwani NC, Digiovanni CW, Holt SK, Benirschke SK, Hansen ST, Sangeorzan BJ. Outcome after open reduction and internal fixation of Lisfranc joint injuries. *J Bone Joint Surg Am* 2000; **82-A**: 1609-1618 [PMID: 11097452 DOI: 10.2106/00004623-200011000-00015]
19 **Rammelt S**, Schneiders W, Schikore H, Holch M, Heineck J, Zwipp H. Primary open reduction and fixation compared with delayed corrective arthrodesis in the treatment of tarsometatarsal (Lisfranc) fracture dislocation. *J Bone Joint Surg Br* 2008; **90**: 1499-1506 [PMID: 18978273 DOI: 10.1302/0301-620X.90B11.20695]
20 **Marks RM**, Parks BG, Schon LC. Midfoot fusion technique for neuroarthropathic feet: biomechanical analysis and rationale. *Foot Ankle Int* 1998; **19**: 507-510 [PMID: 9728696 DOI: 10.1177/107110079801900801]
21 **Baravarian B**, Geffen D. Lisfranc tightrope. *Foot Ankle Spec* 2009; **2**: 249-250 [PMID: 19825783 DOI: 10.1177/1938640009347169]
22 **Panchbhavi VK**, Vallurupalli S, Yang J, Andersen CR. Screw fixation compared with suture-button fixation of isolated Lisfranc ligament injuries. *J Bone Joint Surg Am* 2009; **91**: 1143-1148 [PMID: 19411463 DOI: 10.2106/JBJS.H.00162]
23 **Regauer M**, Baumbach S, Brumann M, Mutschler W, Polzer H. [Lisfranc dislocation fracture: Dynamic examination under anesthesia and minimally invasive stabilization with mini-TightRope®]. *Unfallchirurg* 2015; **118**: 727-732 [PMID: 25519821 DOI: 10.1007/s00113-014-2685-1]
24 **Lesko G**, Altman K, Hogue G. Midfoot Degenerative Arthritis and Partial Fusion After Pediatric Lisfranc Fracture-Dislocation. *J Am Acad Orthop Surg Glob Res Rev* 2018; **2**: e004 [PMID: 30211381 DOI: 10.5435/JAAOSGlobal-D-17-00004]
25 **Buoncristiani AM**, Manos RE, Mills WJ. Plantar-flexion tarsometatarsal joint injuries in children. *J Pediatr Orthop* 2001; **21**: 324-327 [PMID: 11371814 DOI: 10.1097/01241398-200105000-00012]
26 **Wiley JJ**. Tarso-metatarsal joint injuries in children. *J Pediatr Orthop* 1981; **1**: 255-260 [PMID: 7334103 DOI: 10.1097/01241398-198111000-00003]

P- Reviewer: Hooper GJ, Malik H, Serban ED, von Engelhardt LV
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Wu YXJ

Published By Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com