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

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

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Radiation exposure and reduction in the operating room: Perspectives and future directions in spine surgery

Ankur S Narain, Fady Y Hijji, Kelly H Yom, Krishna T Kudaravalli, Brittany E Haws, Kern Singh

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Abstract

Intraoperative imaging is vital for accurate placement of instrumentation in spine surgery. However, the use of biplanar fluoroscopy and other intraoperative imaging modalities is associated with the risk of significant radiation exposure in the patient, surgeon, and surgical staff. Radiation exposure in the form of ionizing radiation can lead to cellular damage *via* the induction of DNA lesions and the production of reactive oxygen species. These effects often result in cell death or genomic instability, leading to various radiation-associated pathologies including an increased risk of malignancy. In attempts to reduce radiation-associated health risks, radiation safety has become an important topic in the medical field. All practitioners, regardless of practice setting, can practice radiation safety techniques including shielding and distance to reduce radiation exposure. Additionally, optimization of fluoroscopic settings and techniques can be used as an effective method of radiation dose reduction. New imaging modalities and spinal navigation systems have also been developed in an effort to replace conventional fluoroscopy and reduce radiation doses. These modalities include Isocentric Three-Dimensional C-Arms, O-Arms, and intraoperative magnetic resonance imaging. While this influx of new technology has advanced radiation safety within the field of spine surgery, more work is still required to overcome specific limitations involving increased costs and inadequate training.

Key words: Intraoperative imaging; Ionizing radiation; DNA damage; Genomic instability; Shielding; Distance; Dose reduction; Spinal navigation

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Core tip: Intraoperative radiation exposure is a significant concern for patients, surgeons, and operative

room staff during spine surgery. All surgeons should practice general radiation safety techniques including shielding, distance, and fluoroscopic dose reduction. New imaging modalities and spinal navigation systems have also been developed to mitigate radiation exposure risk. These modalities include CT-based techniques such as Isocentric Three-Dimensional C-arms and O-Arms. Intraoperative magnetic resonance imaging has also been adapted from the neurosurgical field and is another developing imaging technique. Further research is required to overcome the limitations of these novel technologies in regards to costs and training requirements.

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INTRODUCTION

The use of instrumentation and other implants is often necessary for orthopaedic surgical intervention. This is especially true in the field of spine surgery, where anterior and posterior instrumentation is frequently utilized to treat degenerative, traumatic, and neoplastic pathologies. Posterior pedicle screws are the most widely used instruments within spine surgery; however, inaccurate positioning of such constructs can lead to significant intraoperative and postoperative adverse events^[1-5]. Specifically, injury to nearby neurovascular structures can occur, which often results in significant patient morbidity and financial burden on the healthcare system.

In order to ensure accurate placement of spinal instrumentation, intraoperative radiographic images are used to guide and confirm implant location. The use of intraoperative imaging is especially important in minimally-invasive procedures, where instrumentation is inserted percutaneously without the direct anatomic visualization afforded in open procedures. Biplanar fluoroscopy was one of the first real-time intraoperative imaging modalities, and remains the dominant technique amongst orthopaedic and spinal practitioners^[6-8]. However, radiation exposure from intraoperative imaging remains a significant concern for patients, surgeons, and other operative room personnel^[9-13]. In order to mitigate the risk associated with intraoperative radiation exposure, new imaging technologies and personal protective equipment have been developed.

The purpose of this review is to summarize the pathophysiology of intraoperative radiation exposure, discuss effective strategies for intraoperative radiation safety, and to introduce new intraoperative imaging and navigation modalities within the field of spine

surgery.

PATHOPHYSIOLOGY AND EFFECTS OF RADIATION EXPOSURE

During the use of intraoperative imaging, surgical staff and patients are exposed to both direct and scatter radiation. Direct radiation is the radiation absorbed from the beam as it projects from the source. Direct radiation is the predominant source of radiation exposure for the patient and surgeon. Scatter radiation is radiation from the source that is deflected off of a surface, typically the patient in an operative setting. Scatter radiation exposure is the primary form of exposure for operative staff who stand further away from the surgical table. While many different types of radiation exist, the most concerning in regards to the development of pathology is ionizing radiation. Ionizing radiation from intraoperative imaging leads to cellular damage through the induction of direct or indirect DNA lesions and production of reactive oxygen species^[14,15]. The ensuing cellular stress response can lead to cell death *via* replicative or apoptotic mechanisms^[14]. Conversely, if cell death does not occur, the risk of neoplastic proliferation may be increased due to the persistence and replication of cells with DNA lesions and subsequent genomic instability^[15].

The pathologic effects of ionizing radiation exposure can further be described as either deterministic or stochastic. Deterministic effects are short-term responses observed only after a certain threshold radiation exposure has been reached. These effects are subsequently worsened with any additional exposure past that threshold^[16]. Examples of pathology associated with deterministic effects includes hair loss, skin erythema, skin burns, and cataract formation^[17-19]. As the thresholds for deterministic effects are known in many cases, they can be prevented *via* careful monitoring of radiation exposure levels over short time-periods. More worrisome are stochastic effects, in which incidence increases with exposure without any definitive time period or threshold exposure level^[16]. Stochastic effects are most commonly associated with carcinogenesis and teratogenesis^[17,20-23]. For example, Mastrangelo *et al.*^[21] determined that working as an orthopaedic surgeon was a significant risk factor for tumor development in a survey of cancer incidence amongst 316 hospital employees. The authors cautioned that this increased risk was possibly a result of orthopaedic surgeon radiation exposure along with poor work safety practices.

In order to protect against the dangers of excessive radiation exposure, guidelines are available regarding dosage limits both for those exposed in occupational settings and the general public. The primary international organization producing these guidelines is the International Commission on Radiological Protection (ICRP). The dosage limits are expressed in the units of joules per kilogram, otherwise known as a Sievert

(Sv)^[24]. The Sievert is a measure of the stochastic effects of ionizing radiation, and an exposure of 1 Sv is associated with a 5.5% risk of developing cancer^[24]. Under ICRP guidelines, occupational exposure should be limited to a maximum average of 20 mSv per year over a five-year period, with no exposure greater than 50 mSv in a single year^[24]. For the general public, exposure should be limited strictly to a maximum average of 1 mSv per year over a 5-year period^[24]. These limits can be used as reference points for the evaluation of the safety and efficacy of new imaging technologies and radioprotective techniques.

GENERAL STRATEGIES FOR REDUCING RADIATION EXPOSURE IN SPINAL PROCEDURES

Shielding

In attempting to reduce intraoperative radiation exposure, a variety of simple methods should be employed by all practitioners. One of these methods is shielding, which involves the use of physical barriers to absorb a portion of scatter radiation and prevent it from reaching soft tissues. Shielding for operative room personnel is primarily accomplished by the wearing of lead aprons and thyroid shields, which protect radiosensitive areas from the upper body to the gonads^[18,19,23,25-27]. Other less commonly utilized methods of shielding include lead gloves to reduce hand exposure, lead skirts for operative tables, and mobile shielding screens to provide additional protection to operative room personnel^[28-30]. The literature is overwhelmingly supportive of the utility of shielding, with reported reductions in radiation exposure between 42%-96.9%^[19,27,28,30]. For example, Ahn *et al.*^[27], in a study of three surgeons performing percutaneous endoscopic lumbar discectomies, determined that lead aprons and collars reduced radiation exposure to the upper body and thyroid by 94.2% and 96.9%, respectively. Furthermore, the use of lead aprons was estimated to increase the number of total operations before reaching occupational exposure limits by 5088 procedures.

Distance

An additional method to reduce intraoperative radiation exposure is to feasibly maximize the distance between the patient surface and the surgeon or operative room personnel^[18,30]. This principle derives from the fact that radiation intensity follows an inverse square law, decreasing substantially with increasing distance from the radiation or scatter source. As such, with appropriate shielding, scatter radiation may be reduced to 0.1% and 0.025% of the primary radiation at a distance of 3 feet and 6 feet, respectively^[11]. This principle is further illustrated by Lee *et al.*^[18], in an investigation of scatter radiation doses measured during intraoperative C-arm fluoroscopy. In this study, a chest

phantom on a surgical table was exposed to fluoroscopy while a whole-body phantom was placed in varying positions in the operating room to simulate the surgeon and operative room staff. Measured scatter doses to the whole-body phantom decreased with increasing distance up to 100 cm from the chest phantom device. Kruger *et al.*^[30] provided further recommendations for operative room setup, noting that the image intensifier should be placed on the same side of the operative table as the surgeon so as to increase the distance between the radiation source and operative room personnel.

Fluoroscopic dose reduction techniques

Dose reduction techniques are also an important strategy both in reducing radiation exposure and following the "as low as reasonably achievable" (ALARA) principle. One such technique is the use of fluoroscopy in pulsed and low dose modes^[26,29-31]. Pulsed mode refers to a method where power to the radiation source is applied intermittently producing short pulses of radiation, while low-dose mode reduces the peak kilovolts and miliamperes necessary to create the radiation beam^[26]. Goodman *et al.*^[26], in a study of 316 patients undergoing spinal interventional procedures, determined that the combination of pulsed and low-dose modes decreased average radiation exposure time by 56.7%. The authors also suggested that pulsed modes are most effective in reducing radiation exposure when the surgeon is required to be in closest proximity to the patient. Plastaras *et al.*^[29] examined the effect of pulsed fluoroscopy in conjunction with shielding in patients undergoing interventional spine procedures. The combination of the two methods resulted in a 97.3% reduction in effective dose to all operative room staff. Despite the benefit of radiation exposure reduction, pulsed and low-dose modes exhibit potential disadvantages. Of primary concern is reduced image quality, and as such, the adoption of these fluoroscopy modes is dependent on surgeon acumen and comfort^[26].

Other dose reduction techniques include intermittent fluoroscopy and last image hold^[30,32]. Intermittent fluoroscopy refers to applying fluoroscopy only for short time periods, while last image hold displays the last collected image even when fluoroscopy is not being applied^[32]. These methods allow for both reduced total fluoroscopy time and the ability to better plan surgical approaches through image review. Finally, collimation can be utilized to reduce radiation dose. Collimation refers to narrowing the radiation beam over the area of anatomic interest, thus reducing radiation exposure by subjecting less total body area to interaction with radiation^[26,31].

INTRAOPERATIVE THREE-DIMENSIONAL IMAGING AND SPINAL NAVIGATION SYSTEMS

Spinal navigation systems have been developed with

the goals of increasing the accuracy of instrumentation placement and reducing operative radiation exposure. Navigation technologies are comprised of many different components that must act in concert. Typically, an imaging mechanism is used to collect radiographic images that are then imported into a computer workstation that creates a three-dimensional (3D) reconstruction of the anatomy of interest^[33]. This computer system interacts with a specialized optical camera and surgical tools to guide real-time insertion of instrumentation without the need for repetitive collection of fluoroscopic images^[33].

Since its inception, navigation has shifted from utilizing preoperative images to using intraoperative 3D imaging modalities^[34]. These imaging modalities are more frequently used because, unlike with preoperative imaging, they do not require as significant a degree of the time-consuming process of anatomic registration^[17]. Furthermore, intraoperative imaging is a better representation of surgical anatomy than preoperative studies, as preoperative images do not reflect anatomic shifts and variations due to surgical positioning^[35-40]. Multiple intraoperative imaging modalities can be used in conjunction with navigation systems, including computed tomography (CT) and magnetic resonance imaging (MRI) based approaches.

Isocentric 3D C-arm

Isocentric 3D C-arms are CT based systems that collect images from a 190° screening arc^[36,41,42]. Up to 200 fluoroscopic images are collected at equidistant angles which are then utilized by navigation systems to create a 3D reconstruction of the relevant spinal anatomy^[41,43]. In one pass, these modified C-arms can collect images from a 12 cm³ anatomical space^[44]. Furthermore, the surgeon and surgical staff can step outside of the operating room during image acquisition, possibly reducing unnecessary radiation exposure^[45,46].

In regards to radiation exposure, prior investigations have exhibited reduced fluoroscopy time and radiation doses with the use of Isocentric 3D C-arms compared to standard fluoroscopy^[41,45,46]. Kim *et al.*^[45] performed one such study in 18 cadaveric spines undergoing minimally invasive transforaminal lumbar interbody fusion (MIS TLIF). The authors demonstrated that while the navigation group had greater setup time (9.67 min vs 4.78 min), the overall fluoroscopy time was lower compared to the standard fluoroscopy group (28.7 s vs 41.9 s). Radiation exposure, measured in millirems (mREM), was also lower in the navigation group (undetectable vs 12.4 mREM). Furthermore, in a subsequent series of 18 patients undergoing MIS TLIF, the navigation group had lower overall fluoroscopy time (57.1 vs 147.2 s). Smith *et al.*^[46] noted similar findings in an investigation of 4 cadavers in which lumbar pedicle screw placement was attempted. Compared to standard fluoroscopy, isocentric C-arm use was associated with lower total mean radiation exposure to the surgeon's torso (0.33 mREM vs 4.33 mREM). The

advantages of isocentric 3D C-arm use also extend past limiting radiation exposure, as multiple studies have indicated equivalent or superior accuracy of pedicle screw placement when compared to standard fluoroscopic methods^[36,44,46,47].

O-arm

The O-arm (Medtronic, Fridley, Minnesota) is a cone-beam, CT-based intraoperative imaging modality that can produce a 360° scanning arc^[8]. O-arm devices can acquire up to 750 images in a single scan, and these images can be utilized with navigation systems to create 3D anatomical reconstructions^[7,48,49]. The O-arm also is programmed with preset modes that optimize kilovoltage and milliamperage settings for various patient sizes and anatomical regions^[25,48,49]. Similar to the isocentric 3D C-arm, the O-arm can possibly reduce radiation exposure by allowing the surgical staff to exit the operating theatre during image acquisition^[49].

The literature regarding the use of O-arm imaging is mixed in terms of its efficacy in radiation dose reduction. Multiple studies have determined that while O-arm imaging reduces radiation exposure to operative room personnel, it increases the radiation exposure to the patient^[7,17,25,48-50]. Tabaraee *et al.*^[50] demonstrated such findings in a cadaveric study investigating the insertion of 160 pedicle screws under either C-arm or O-arm imaging. In the operative room staff, O-arm imaging led to undetectable levels of radiation exposure while C-arm imaging was associated with an exposure of 60.75 mREM. The opposite correlation was seen in cadavers, where the use of the O-arm modality was associated with higher mean radiation doses compared to the use of conventional C-arm fluoroscopy. Mendelsohn *et al.*^[17] confirmed this association in a matched cohort analysis of 146 patients undergoing posterior pedicle screw insertion. In the 73 patients undergoing a procedure with O-arm imaging, the observed radiation dose in patients was 8.74 times greater than that of the OR staff. Those patients also experienced a higher mean effective dose of radiation (1.09 mSv) compared to published radiation dosages for patients undergoing pedicle screw insertion using standard C-arm fluoroscopy following MIS (0.611 mSv) or open (0.393 mSv) techniques. The results of these studies indicate that any practitioner considering the use of O-arm imaging must weigh the benefit of reduced radiation exposure to operative staff with the limitation of increased radiation exposure to patients.

Intraoperative MRI

Intraoperative MRI is a developing technology in the field of spine surgery that has the potential for significant reductions in intraoperative radiation exposure both for patients and surgical personnel. Intraoperative MRI has been adapted from the field of neurosurgery, and it involves the use of ultra-high field 3T MRI scanners^[51]. Within the spine literature, few studies exist regarding the safety and efficacy of intraoperative MRI. Woodard

et al.^[52], in a case series consisting of both cervical and lumbar procedures, demonstrated that intraoperative MRI could feasibly be used for localization and confirmation of neural decompression. Similarly, Choi *et al.*^[53] conducted a study utilizing intraoperative MRI for surgical site localization and confirmation of decompression in 89 patients undergoing percutaneous endoscopic lumbar discectomy. The authors concluded that intraoperative MRI was successful in detecting inadequate intraoperative decompression, especially in cases of highly migrated or segmented discs. While this initial data is promising, further work is required to definitively determine the efficacy of procedures utilizing intraoperative MRI.

Limitations to the adoption of intraoperative 3D imaging

While the data supporting the use of intraoperative 3D imaging modalities and navigation systems is promising, these techniques have not yet achieved widespread adoption. Estimates of the percentage of spine surgeons who routinely utilize navigation systems are in some instances as low as 11%^[54]. In attempting to identify impediments to adoption, multiple studies have been undertaken to survey the opinions of practitioners in the field of spine surgery^[54,55]. These investigations consistently identify increased cost, lack of adequate training, and increased associated operative times as factors precluding the use of navigation systems^[54,55]. Costs associated with buying and implementing new imaging and guidance technologies can be burdensome, especially to single-physician and small-group practices. Furthermore, concerns regarding inadequate training extend not only to the surgeon, but to members of the entire operative staff who must adjust to an unfamiliar operative workflow with the introduction of new imaging systems. Worries about increased operative time are also logical, especially during the initial phase of navigation system adoption when surgical teams are at the beginning of their learning curve. However, recent studies have noted no significant differences in operative time in navigated and non-navigated procedures^[44,50]. Nonetheless, manufacturers and proponents of new imaging and navigation systems must still work to overcome the disadvantages of cost, training, and the learning curve to ensure greater adoption of this technology within the field of spine surgery.

CONCLUSION

Radiation exposure is a significant concern for patients, surgeons, and operative room staff. Exposure to ionizing radiation from conventional fluoroscopy is associated with a number of pathologies, the most worrisome being the development of malignancy. As such, radiation safety must be a priority in the operative setting. All practitioners, irrespective of their practice setting, can and should employ the safety principles of

shielding, distance, and dose reduction. Furthermore, practitioners should also consider the use of new navigation systems with alternative imaging modalities such as isocentric-3D C-arm, O-arm, or intraoperative MRI. While these systems may be associated with reductions in radiation exposure to operative staff, they also have significant limitations pertaining to cost, training requirements, and operative times. Further work is still required within the field of spine surgery to improve radiation safety and to further increase the adoption of new imaging modalities.

REFERENCES

1. **Amiot LP**, Lang K, Putzier M, Zippel H, Labelle H. Comparative results between conventional and computer-assisted pedicle screw installation in the thoracic, lumbar, and sacral spine. *Spine* (Phila Pa 1976) 2000; **25**: 606-614 [PMID: 10749638]
2. **Di Silvestre M**, Parisini P, Lolli F, Bakaloudis G. Complications of thoracic pedicle screws in scoliosis treatment. *Spine* (Phila Pa 1976) 2007; **32**: 1655-1661 [PMID: 17621214 DOI: 10.1097/BRS.0b013e318074d604]
3. **Gautschi OP**, Schatlo B, Schaller K, Tessitore E. Clinically relevant complications related to pedicle screw placement in thoracolumbar surgery and their management: a literature review of 35,630 pedicle screws. *Neurosurg Focus* 2011; **31**: E8 [PMID: 21961871 DOI: 10.3171/2011.7.FOCUS11168]
4. **Hicks JM**, Singla A, Shen FH, Arlet V. Complications of pedicle screw fixation in scoliosis surgery: a systematic review. *Spine* (Phila Pa 1976) 2010; **35**: E465-E470 [PMID: 20473117 DOI: 10.1097/BRS.0b013e3181d1021a]
5. **Parker SL**, McGirt MJ, Farber SH, Amin AG, Rick AM, Suk I, Bydon A, Sciubba DM, Wolinsky JP, Gokaslan ZL, Witham TF. Accuracy of free-hand pedicle screws in the thoracic and lumbar spine: analysis of 6816 consecutive screws. *Neurosurgery* 2011; **68**: 170-178; discussion 178 [PMID: 21150762 DOI: 10.1227/NEU.0b013e3181dfaf4]
6. **Cho JY**, Chan CK, Lee SH, Lee HY. The accuracy of 3D image navigation with a cutaneously fixed dynamic reference frame in minimally invasive transforaminal lumbar interbody fusion. *Comput Aided Surg* 2012; **17**: 300-309 [PMID: 23098190 DOI: 10.3109/10929088.2012.728625]
7. **Bandela JR**, Jacob RP, Arreola M, Griglock TM, Bova F, Yang M. Use of CT-based intraoperative spinal navigation: management of radiation exposure to operator, staff, and patients. *World Neurosurg* 2013; **79**: 390-394 [PMID: 22120382 DOI: 10.1016/j.wneu.2011.05.019]
8. **Abdullah KG**, Bishop FS, Lubelski D, Steinmetz MP, Benzel EC, Mroz TE. Radiation exposure to the spine surgeon in lumbar and thoracolumbar fusions with the use of an intraoperative computed tomographic 3-dimensional imaging system. *Spine* (Phila Pa 1976) 2012; **37**: E1074-E1078 [PMID: 22472810 DOI: 10.1097/BRS.0b013e31825786d8]
9. **Ul Haque M**, Shufflebarger HL, O'Brien M, Macagno A. Radiation exposure during pedicle screw placement in adolescent idiopathic scoliosis: is fluoroscopy safe? *Spine* (Phila Pa 1976) 2006; **31**: 2516-2520 [PMID: 17023864 DOI: 10.1097/01.brs.0000238675.91612.2f]
10. **Theocharopoulos N**, Perisinakis K, Damilakis J, Papadokostakis G, Hadjipavlou A, Gourtsoyannis N. Occupational exposure from common fluoroscopic projections used in orthopaedic surgery. *J Bone Joint Surg Am* 2003; **85-A**: 1698-1703 [PMID: 12954827]
11. **Singer G**. Occupational radiation exposure to the surgeon. *J Am Acad Orthop Surg* 2005; **13**: 69-76 [PMID: 15712984]
12. **Rampersaud YR**, Foley KT, Shen AC, Williams S, Solomito M. Radiation exposure to the spine surgeon during fluoroscopically assisted pedicle screw insertion. *Spine* (Phila Pa 1976) 2000; **25**: 2637-2645 [PMID: 11034650]

- 13 **Bindal RK**, Glaze S, Ognoskie M, Tunner V, Malone R, Ghosh S. Surgeon and patient radiation exposure in minimally invasive transforaminal lumbar interbody fusion. *J Neurosurg Spine* 2008; **9**: 570-573 [PMID: 19035750 DOI: 10.3171/SPI.2008.4.08182]
- 14 **Vozenin-Brotons MC**. Tissue toxicity induced by ionizing radiation to the normal intestine: understanding the pathophysiological mechanisms to improve the medical management. *World J Gastroenterol* 2007; **13**: 3031-3032 [PMID: 17589916 DOI: 10.3748/wjg.v13.i22.3031]
- 15 **Morgan WF**, Day JP, Kaplan MI, McGhee EM, Limoli CL. Genomic instability induced by ionizing radiation. *Radiat Res* 1996; **146**: 247-258 [PMID: 8752302]
- 16 **Christensen DM**, Iddins CJ, Sugarman SL. Ionizing radiation injuries and illnesses. *Emerg Med Clin North Am* 2014; **32**: 245-265 [PMID: 24275177 DOI: 10.1016/j.emc.2013.10.002]
- 17 **Mendelsohn D**, Strelzow J, Dea N, Ford NL, Batke J, Pennington A, Yang K, Ailon T, Boyd M, Dvorak M, Kwon B, Paquette S, Fisher C, Street J. Patient and surgeon radiation exposure during spinal instrumentation using intraoperative computed tomography-based navigation. *Spine J* 2016; **16**: 343-354 [PMID: 26686604 DOI: 10.1016/j.spinee.2015.11.020]
- 18 **Lee K**, Lee KM, Park MS, Lee B, Kwon DG, Chung CY. Measurements of surgeons' exposure to ionizing radiation dose during intraoperative use of C-arm fluoroscopy. *Spine (Phila Pa 1976)* 2012; **37**: 1240-1244 [PMID: 22198350 DOI: 10.1097/BRS.0b013e31824589d5]
- 19 **Fitoussi NT**, Efsthathopoulos EP, Delis HB, Kottou S, Kelekis AD, Panayiotakis GS. Patient and staff dosimetry in vertebroplasty. *Spine (Phila Pa 1976)* 2006; **31**: E884-E889; discussion E890 [PMID: 17077725 DOI: 10.1097/01.brs.0000244586.02151.18]
- 20 **Perisinakis K**, Theocharopoulos N, Damilakis J, Katonis P, Papadokostakis G, Hadjipavlou A, Gourtsoyannis N. Estimation of patient dose and associated radiogenic risks from fluoroscopically guided pedicle screw insertion. *Spine (Phila Pa 1976)* 2004; **29**: 1555-1560 [PMID: 15247578]
- 21 **Mastrangelo G**, Fedeli U, Fadda E, Giovanazzi A, Scozzato L, Saia B. Increased cancer risk among surgeons in an orthopaedic hospital. *Occup Med (Lond)* 2005; **55**: 498-500 [PMID: 16140840 DOI: 10.1093/occmed/kqi048]
- 22 **Giordano BD**, Baumhauer JF, Morgan TL, Rehtine GR. Cervical spine imaging using mini--C-arm fluoroscopy: patient and surgeon exposure to direct and scatter radiation. *J Spinal Disord Tech* 2009; **22**: 399-403 [PMID: 19652564 DOI: 10.1097/BSD.0b013e3181847559]
- 23 **Dewey P**, Incoll I. Evaluation of thyroid shields for reduction of radiation exposure to orthopaedic surgeons. *Aust N Z J Surg* 1998; **68**: 635-636 [PMID: 9737257]
- 24 The 2007 Recommendations of the International Commission on Radiological Protection. ICRP publication 103. *Ann ICRP* 2007; **37**: 1-332 [PMID: 18082557 DOI: 10.1016/j.icrp.2007.10.003]
- 25 **Nottmeier EW**, Pirris SM, Edwards S, Kimes S, Bowman C, Nelson KL. Operating room radiation exposure in cone beam computed tomography-based, image-guided spinal surgery: clinical article. *J Neurosurg Spine* 2013; **19**: 226-231 [PMID: 23725398 DOI: 10.3171/2013.4.SPINE.12719]
- 26 **Goodman BS**, Carnel CT, Mallempati S, Agarwal P. Reduction in average fluoroscopic exposure times for interventional spinal procedures through the use of pulsed and low-dose image settings. *Am J Phys Med Rehabil* 2011; **90**: 908-912 [PMID: 21952213 DOI: 10.1097/PHM.0b013e318228c9dd]
- 27 **Ahn Y**, Kim CH, Lee JH, Lee SH, Kim JS. Radiation exposure to the surgeon during percutaneous endoscopic lumbar discectomy: a prospective study. *Spine (Phila Pa 1976)* 2013; **38**: 617-625 [PMID: 23026867 DOI: 10.1097/BRS.0b013e318275ca58]
- 28 **Synowitz M**, Kiwit J. Surgeon's radiation exposure during percutaneous vertebroplasty. *J Neurosurg Spine* 2006; **4**: 106-109 [PMID: 16506476 DOI: 10.3171/spi.2006.4.2.106]
- 29 **Plastaras C**, Appasamy M, Sayeed Y, McLaughlin C, Charles J, Joshi A, Macron D, Pukenas B. Fluoroscopy procedure and equipment changes to reduce staff radiation exposure in the interventional spine suite. *Pain Physician* 2013; **16**: E731-E738 [PMID: 24284854]
- 30 **Kruger R**, Faciszewski T. Radiation dose reduction to medical staff during vertebroplasty: a review of techniques and methods to mitigate occupational dose. *Spine (Phila Pa 1976)* 2003; **28**: 1608-1613 [PMID: 12865853]
- 31 **Artner J**, Lattig F, Reichel H, Cakir B. Effective radiation dose reduction in computed tomography-guided spinal injections: a prospective, comparative study with technical considerations. *Orthop Rev (Pavia)* 2012; **4**: e24 [PMID: 22802992 DOI: 10.4081/or.2012.e24]
- 32 **Mahesh M**. Fluoroscopy: patient radiation exposure issues. *RadioGraphics* 2001; **21**: 1033-1045 [PMID: 11452079 DOI: 10.1148/radiographics.21.4.g01j1271033]
- 33 **Holly LT**. Image-guided spinal surgery. *Int J Med Robot* 2006; **2**: 7-15 [PMID: 17520608 DOI: 10.1002/ics.69]
- 34 **Gebhard F**, Weidner A, Liener UC, Stöckle U, Arand M. Navigation at the spine. *Injury* 2004; **35** Suppl 1: S-A35-S-A45 [PMID: 15183702]
- 35 **Nottmeier EW**, Seemer W, Young PM. Placement of thoracolumbar pedicle screws using three-dimensional image guidance: experience in a large patient cohort. *J Neurosurg Spine* 2009; **10**: 33-39 [PMID: 19119930 DOI: 10.3171/2008.10.SP108383]
- 36 **Nakashima H**, Sato K, Ando T, Inoh H, Nakamura H. Comparison of the percutaneous screw placement precision of isocentric C-arm 3-dimensional fluoroscopy-navigated pedicle screw implantation and conventional fluoroscopy method with minimally invasive surgery. *J Spinal Disord Tech* 2009; **22**: 468-472 [PMID: 20075808 DOI: 10.1097/BSD.0b013e31819877c8]
- 37 **Holly LT**, Foley KT. Three-dimensional fluoroscopy-guided percutaneous thoracolumbar pedicle screw placement. Technical note. *J Neurosurg* 2003; **99**: 324-329 [PMID: 14563154]
- 38 **Ebmeier K**, Giest K, Kalf R. Intraoperative computerized tomography for improved accuracy of spinal navigation in pedicle screw placement of the thoracic spine. *Acta Neurochir Suppl* 2003; **85**: 105-113 [PMID: 12570145]
- 39 **Bledsoe JM**, Fenton D, Fogelson JL, Nottmeier EW. Accuracy of upper thoracic pedicle screw placement using three-dimensional image guidance. *Spine J* 2009; **9**: 817-821 [PMID: 19664966 DOI: 10.1016/j.spinee.2009.06.014]
- 40 **Beck M**, Mittlmeier T, Gierer P, Harms C, Gradl G. Benefit and accuracy of intraoperative 3D-imaging after pedicle screw placement: a prospective study in stabilizing thoracolumbar fractures. *Eur Spine J* 2009; **18**: 1469-1477 [PMID: 19513764 DOI: 10.1007/s00586-009-1050-5]
- 41 **Hott JS**, Papadopoulos SM, Theodore N, Dickman CA, Sonntag VK. Intraoperative Iso-C C-arm navigation in cervical spinal surgery: review of the first 52 cases. *Spine (Phila Pa 1976)* 2004; **29**: 2856-2860 [PMID: 15599290]
- 42 **Klingler JH**, Sircar R, Scheiwe C, Kogias E, Krüger MT, Scholz C, Hubbe U. Comparative Study of C-Arms for Intraoperative 3-Dimensional Imaging and Navigation in Minimally Invasive Spine Surgery Part II - Radiation Exposure. *Clin Spine Surg* 2016 Jun 28; Epub ahead of print [PMID: 25353198]
- 43 **Klingler JH**, Sircar R, Scheiwe C, Kogias E, Volz F, Krüger MT, Hubbe U. Comparative Study of C-Arms for Intraoperative 3-Dimensional Imaging and Navigation in Minimally Invasive Spine Surgery Part I - Applicability and Image Quality. *Clin Spine Surg* 2016 Jun 28; Epub ahead of print [PMID: 25353196]
- 44 **Rajasekaran S**, Vidyadhara S, Ramesh P, Shetty AP. Randomized clinical study to compare the accuracy of navigated and non-navigated thoracic pedicle screws in deformity correction surgeries. *Spine (Phila Pa 1976)* 2007; **32**: E56-E64 [PMID: 17224800 DOI: 10.1097/01.brs.0000252094.64857.ab]
- 45 **Kim CW**, Lee YP, Taylor W, Oygur A, Kim WK. Use of navigation-assisted fluoroscopy to decrease radiation exposure during minimally invasive spine surgery. *Spine J* 2007; **8**: 584-590 [PMID: 18586198 DOI: 10.1016/j.spinee.2006.12.012]
- 46 **Smith HE**, Welsch MD, Sasso RC, Vaccaro AR. Comparison of radiation exposure in lumbar pedicle screw placement

- with fluoroscopy vs computer-assisted image guidance with intraoperative three-dimensional imaging. *J Spinal Cord Med* 2008; **31**: 532-537 [PMID: 19086710]
- 47 **Martirosyan NL**, Kalb S, Cavalcanti DD, Lochhead RA, Uschold TD, Loh A, Theodore N. Comparative analysis of isocentric 3-dimensional C-arm fluoroscopy and biplanar fluoroscopy for anterior screw fixation in odontoid fractures. *J Spinal Disord Tech* 2013; **26**: 189-193 [PMID: 22158300 DOI: 10.1097/BSD.0b013e31823f62e7]
 - 48 **Lange J**, Karellas A, Street J, Eck JC, Lapinsky A, Connolly PJ, Dipaola CP. Estimating the effective radiation dose imparted to patients by intraoperative cone-beam computed tomography in thoracolumbar spinal surgery. *Spine (Phila Pa 1976)* 2013; **38**: E306-E312 [PMID: 23238490 DOI: 10.1097/BRS.0b013e318281d70b]
 - 49 **Pitteloud N**, Gamulin A, Barea C, Damet J, Racloz G, Sans-Merce M. Radiation exposure using the O-arm(®) surgical imaging system. *Eur Spine J* 2017; **26**: 651-657 [PMID: 27652675]
 - 50 **Tabarace E**, Gibson AG, Karahalios DG, Potts EA, Mobasser JP, Burch S. Intraoperative cone beam-computed tomography with navigation (O-ARM) versus conventional fluoroscopy (C-ARM): a cadaveric study comparing accuracy, efficiency, and safety for spinal instrumentation. *Spine (Phila Pa 1976)* 2013; **38**: 1953-1958 [PMID: 23883830]
 - 51 **Jolesz FA**. Intraoperative imaging in neurosurgery: where will the future take us? *Acta Neurochir Suppl* 2011; **109**: 21-25 [PMID: 20960316 DOI: 10.1007/978-3-211-99651-5_4]
 - 52 **Woodard EJ**, Leon SP, Moriarty TM, Quinones A, Zamani AA, Jolesz FA. Initial experience with intraoperative magnetic resonance imaging in spine surgery. *Spine (Phila Pa 1976)* 2001; **26**: 410-417 [PMID: 11224889]
 - 53 **Choi G**, Modi HN, Prada N, Ahn TJ, Myung SH, Gang MS, Lee SH. Clinical results of XMR-assisted percutaneous transforaminal endoscopic lumbar discectomy. *J Orthop Surg Res* 2013; **8**: 14 [PMID: 23705685]
 - 54 **Härtl R**, Lam KS, Wang J, Korge A, Kandziora F, Audigé L. Worldwide survey on the use of navigation in spine surgery. *World Neurosurg* 2013; **79**: 162-172 [PMID: 22469525 DOI: 10.1016/j.wneu.2012.03.011]
 - 55 **Choo AD**, Regev G, Garfin SR, Kim CW. Surgeons' perceptions of spinal navigation: analysis of key factors affecting the lack of adoption of spinal navigation technology. *SAS J* 2008; **2**: 189-194 [PMID: 25802621 DOI: 10.1016/S1935-9810(08)70038-0]

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Use of recombinant human bone morphogenetic protein-2 in spine surgery

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Abstract

Bone morphogenetic proteins are osteoinductive factors which have gained popularity in orthopaedic

surgery and especially in spine surgery. The use of recombinant human bone morphogenetic protein-2 has been officially approved by the United States Food and Drug Administration only for single level anterior lumbar interbody fusion, nevertheless it is widely used by many surgeons with off-label indications. Despite advantages in bone formation, its use still remains a controversial issue and several complications have been described by authors who oppose their wide use.

Key words: Recombinant human bone morphogenetic protein-2; Spine; Fusion; Bone graft; Yale University Open Data project

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Core tip: The use of recombinant human bone morphogenetic protein-2 is widely used in spine surgery not only in approved indications but also in off-label indications. Despite its ability to promote fusion there are many reported disadvantages. That's why the Yale University Open Data project aims to serve both the patients but also the companies which fund the vast majority of research in medical products.

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INTRODUCTION

During the last 10 years, the use of bone morphogenetic proteins (BMPs) has become very popular in orthopaedic surgery. BMPs are osteoinductive factors which are capable of inhibiting chondrocyte differentiation independently and they are recognized

as important regulators of growth, differentiation, and morphogenesis during embryology^[1,2]. They are members of the superfamily of transforming growth factor- β (TGF- β) and play an important role in the development and regeneration of various tissues including bone, cartilage, and tendons^[3,4]. Urist^[5] in 1965 described first these factors with the term "bone autoinduction principle". During the last two decades BMPs gradually gained popularity in bone healing and especially in spinal fusion enhancement. BMPs are released by platelets and osteogenic cells and their main role is to stimulate cellular proliferation, angiogenesis, osteoblast differentiation, and direct bone matrix formation^[6]. More than 20 different types of BMPs have been identified since Urist^[7] described their properties and all of them have significant osteogenic properties. From all types of BMPs, BMP-2 has been found to be the most osteoinductive and its efficacy to generate an osseous fusion mass has been well established in several preclinical spine models^[8].

In spine surgery, autogenous bone grafting is often used to stimulate fusion. Due to the insufficiency of traditional techniques of bone grafting in long spinal fusions or spinal fusions in adverse metabolic conditions, bone graft substitutes, such as recombinant human bone morphogenetic protein-2 (rhBMP-2), have been introduced in the clinical practice^[9].

INDICATIONS

RhBMP-2 in spinal surgery was first studied clinically in anterior lumbar interbody fusion (ALIF) and was compared with iliac crest bone graft^[10]. The fusion rate of rhBMP-2 group was 94.5% whereas the fusion rate in the group where iliac crest bone graft was used was 88.7%. More studies supporting the effectiveness of rhBMP-2 in spine fusion followed, which resulted in the approval of rhBMP-2 by the United States Food and Drug Administration (FDA) for single-level ALIF within specific threaded cages in skeletally mature patients. In a meta-analysis in 2014 the authors report that rhBMP-2 in lumbar spine fusion can increase the fusion rate^[11], while reduce the reoperation rate and operating time. Additionally, it does not increase the complication rate, the amount of blood loss, and the hospital stay.

OFF-LABEL USE

Although rhBMP-2 has been approved by the FDA for a single narrow method of spinal fusion, over the last 10 years, numerous articles on BMP-2 have documented its use for a far wider range of spinal applications. Since its approval, rhBMP-2 has gained popularity as an effective bone-graft substitute as it obviates the need for autologous bone graft harvesting and eliminates associated complications and donor site morbidity^[12,13]. Many surgeons, began the off-label use of the product in all spinal regions^[14-17], after which new complications associated with the use of rhBMP-2

emerged, including among others severe soft-tissue swelling following anterior cervical discectomy and fusion, heterotopic bone formation, and vertebral body osteolysis in the thoracic and lumbar spine^[18-20]. Ong *et al.*^[21] reported that the 85% of all surgeries in which rhBMP-2 was used were for "off-label" applications. These off-label indications included posterior lumbar interbody infusion, transforaminal lumbar interbody infusion, posterior lumbar fusion, anterior cervical discectomy and fusion (ACDF), and more recently, lateral lumbar interbody fusion^[22].

Rihn *et al.*^[23], in 2009 published their study about the use of rhBMP-2 in single-level transforaminal lumbar interbody fusion. They showed high rate of fusion and improvement of symptoms. Nevertheless, its use was associated with complications that raise concern including a high rate of postoperative radiculitis. One year later, Oliveira *et al.*^[24] presented their results using rhBMP-2 in standalone lateral lumbar interbody fusion. Following a 24-mo follow-up, the authors concluded that single level disc degenerative disease can be successfully treated with standalone lateral lumbar interbody fusion using rhBMP-2 providing except of pain relief significant cost reduction. Complications included cage subsidence, heterotopic bone formation, persistent stenosis, and adjacent level degeneration.

According to a current retrospective cohort study^[25], during the last years a decrease in the off-label use of BMP-2 in spinal fusions and particularly in cervical spine fusions was noticed. The authors noted that although there was a tendency of decreased odds from 2009 to 2012, a higher resource utilization and odds for complications remained in patients in whom BMP-2 was used.

ADVANTAGES

One of the main advantages of the use of rhBMP-2 in spinal fusion is the elimination of adverse events that have been associated with iliac crest bone graft harvesting despite the improvement of bone-harvesting techniques. These complications include pain, hematoma formation, sacral fracture, and infection^[8].

In spine surgery, the rhBMP-2 fusion rate is usually compared with the iliac crest bone graft fusion rate. In the first prospective randomized controlled trial in 2000 Boden *et al.*^[26] supported that arthrodesis occurred more reliably in patients treated with rhBMP-2 filled cages than in controls treated with autogenous bone graft. In general, the fusion rate with the use of rhBMP-2 ranges from 94.5% to 100%, whereas with the use of iliac crest bone graft the fusion rate ranges from 88.7% to 100%. The main complaint in the group of patients treated with iliac crest bone graft was the pain at the donor site. It was also suggested that there is more blood loss with the use of iliac crest bone graft, as well as more operating time. Moreover, in some specific cases, such as in women with osteoporosis, it was speculated that the osteoinductive ability of

rhBMP-2 was more efficient when compared to iliac crest bone graft^[10,17].

In 2009, Dawson *et al.*^[27] combined rhBMP-2 on an absorbable collagen sponge with a ceramic-granule bulking agent in patients undergoing single level posterolateral lumbar fusion. The group of patients who received this combination was compared with a control group of patients who were treated with autogenous iliac crest bone graft. The authors concluded that the combination of the absorbable collagen sponge soaked with rhBMP-2 and ceramic granules provided not only improved clinical results, but also higher radiographic fusion rates when compared to the control group of patients.

The cost should also be taken seriously into consideration. In 2008, Glassman *et al.*^[28] compared the perioperative costs for patients treated with rhBMP-2 or iliac crest bone graft. Surprisingly, the mean cost for the 3 mo perioperative period was \$ 33860 in the rhBMP-2 group and \$ 37227 in the iliac crest bone graft group. A decreased physician fee was also noticed in the rhBMP-2 group (\$ 5082 and \$ 5316, respectively).

Taking all these into consideration, someone can assume that there is no difference between the rhBMP-2 and the iliac crest bone graft in terms of obtaining a solid spinal fusion. Nevertheless, it seems that the rhBMP-2 can achieve an "easier" and faster fusion with no donor site morbidity.

COMPLICATIONS

The first studies presenting the results of rhBMP-2 in spine surgery, reported no adverse events directly related to BMP-2 usage^[7]. It has to be mentioned though that all these studies were industry supported.

More recently, authors started to present disadvantages for the use of BMPs especially in its off-label indications. Epstein^[29] in 2013 presented several complications associated with the off-label use of rhBMP-2 including heterotopic ossification, postoperative seroma/hematoma formation, increased infection rate, arachnoiditis, dysphagia following ACDF, retrograde ejaculation after ALIF, increased neurologic deficits, and cancer. Neurologic deficits following lateral lumbar interbody fusion with the supplementary use of rhBMP-2 were also recorded in another study where 919 treated levels were reviewed^[30]. Immediately after surgery, sensory and motor deficits were identified in 38% of the patients treated with rhBMP-2 and in 23.9% of the patients fused with cancellous allograft or iliac crest bone autograft. At the last follow-up, the percentage of sensory and motor deficits was decreased to 24.1% and 17.3%, respectively. A potential deleterious effect of rhBMP-2 on the lumbosacral plexus was suggested^[22]. Mitchell *et al.*^[31] in an experimental study in 2016, modeled the clinical use of BMP-2 for posterior lumbar fusion. They concluded that the implantation of rhBMP-2 on the lumbar spine may trigger neuroinflammatory responses in the dorsal

root ganglia.

Certain cancer cell lines have been shown to have BMPs receptors and local administration of these growth factors has led to stimulation of cell growth of cancer lines *in vitro*^[32]. In a comparative study of 463 patients, Carragee *et al.*^[33] concluded that a high dose of 40 mg of rhBMP-2 in lumbar spinal arthrodesis is associated with an increased risk of new cancer. On the other hand, in a current study of Beachler *et al.*^[34] in a large population of elderly United States adults who underwent lumbar arthrodesis, rhBMP-2 was not associated with cancer risk or increased mortality.

The mechanism of rhBMP-2 action that may have led to complications described above has been investigated. Hsu *et al.*^[35] in an experimental study of posterolateral intertransverse lumbar spinal fusion demonstrated that the *in vivo* host response to rhBMP-2 may be associated with circulating proinflammatory and osteoclastic cytokines, such as tumor necrosis factor- α , macrophage inflammatory protein 1- α , and interleukin1- β . Additionally, angiogenesis was found to be stimulated through the induction of vascular endothelial growth factors secretion^[36].

FURTHER RESEARCH

Increased use of rhBMP-2 in spine surgery has raised several controversial conflicts among investigators. During the last years a new promising project has been established, which aims to cope with the issue of unpublished or selectively published clinical evidence^[37,38]. The Yale University Open Data Access (YODA) project aims to serve patients and produce benefits for the companies that fund the vast majority of research in medical products. Lately two systematic reviews on rhBMP-2, which are based on patient-level data were shared through YODA. The agreement between the YODA team and Medtronic (rhBMP-2 company) included two parts. Firstly, two independent research groups were selected through a competitive process to evaluate the quality of the studies and synthesize evidence regarding the effectiveness and safety of rhBMP-2. Secondly, the YODA team made the data available to others for potential scientific questions. In this way all the clinical trial data for this product should have been made available in order to be used by other investigators for further analysis^[39].

These two studies concluded in the same results after analyzing their data. Despite the higher fusion rate that was observed with the use of rhBMP-2, clinical results showed no significant differences between the use of iliac crest bone graft and rhBMP-2. The authors of both studies agreed that a clear safety risk is posed when rhBMP-2 is used in the anterior aspect of the cervical spine^[8]. As far as it concerns the carcinogenicity, one study showed significantly higher rate of cancer in patients who were treated with rhBMP-2, while the other presented statistically insignificant higher incidence of cancer in the rhBMP-2

group. Both teams of investigators reached to the same conclusion: Despite the higher rate of cancer appearance, the overall absolute risk of carcinogenesis due to the use of rhBMP-2 for spinal fusion is generally low^[40].

However, Carragee *et al*^[41] supported that despite access to Medtronic trial data, the YODA project will not be able to resolve many, if not most, fundamental safety and efficacy issues on various current uses because there are inadequate trials available.

CONCLUSION

RhBMP-2, due to its ability to stimulate bone formation may offer an effective alternative method of fusion in spine surgery. The clinical outcomes and fusion rates are comparable with those of iliac crest bone graft. In some challenging situations though, rhBMP-2 may have even better results. Its cost is higher compared with the cost of other bone graft substitutes, but concerning the total cost for a patient who needs multiple surgeries to achieve a solid spinal fusion, it seems that rhBMP-2 may be proved cost effective. RhBMP-2 is very often used in spinal applications that have not been studied and/or approved by the FDA, where their results may be unpredictable. Long-term outcomes from randomized control trials are warranted to further clarify the appropriate dose, carrier, and indications of rhBMP-2.

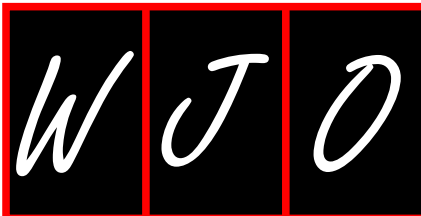
REFERENCES

- 1 **Gkiatas I**, Lykissas M, Kostas-Agnantis I, Korompilias A, Batsitatos A, Beris A. Factors affecting bone growth. *Am J Orthop* (Belle Mead NJ) 2015; **44**: 61-67 [PMID: 25658073]
- 2 **Reddi AH**. Bone morphogenetic proteins: from basic science to clinical applications. *J Bone Joint Surg Am* 2001; **83-A** Suppl 1: S1-S6 [PMID: 11263660 DOI: 10.2106/00004623-200100001-0001]
- 3 **Yamada M**, Akeda K, Asanuma K, Thonar EJ, An HS, Uchida A, Masuda K. Effect of osteogenic protein-1 on the matrix metabolism of bovine tendon cells. *J Orthop Res* 2008; **26**: 42-48 [PMID: 17676621 DOI: 10.1002/jor.20474]
- 4 **Helm GA**, Alden TD, Sheehan JP, Kallmes D. Bone morphogenetic proteins and bone morphogenetic protein gene therapy in neurological surgery: a review. *Neurosurgery* 2000; **46**: 1213-1222 [PMID: 10807254 DOI: 10.1097/00006123-200005000-00038]
- 5 **Urist MR**. Bone: formation by autoinduction. 1965. *Clin Orthop Relat Res* 2002; **(395)**: 4-10 [PMID: 11937861 DOI: 10.1097/00003086-200202000-00002]
- 6 **Valdes MA**, Thakur NA, Namdari S, Ciombor DM, Palumbo M. Recombinant bone morphogenetic protein-2 in orthopaedic surgery: a review. *Arch Orthop Trauma Surg* 2009; **129**: 1651-1657 [PMID: 19280204 DOI: 10.1007/s00402-009-0850-8]
- 7 **Even J**, Eskander M, Kang J. Bone morphogenetic protein in spine surgery: current and future uses. *J Am Acad Orthop Surg* 2012; **20**: 547-552 [PMID: 22941797 DOI: 10.5435/JAAOS-20-09-547]
- 8 **Hsu WK**. Recombinant Human Bone Morphogenetic Protein-2 in Spine Surgery. *JBJS Rev* 2014; **2**: pii: 01874474-201402060-00004 [PMID: 27500718 DOI: 10.2106/JBJS.RVW.M.00107]
- 9 **Carragee EJ**, Hurwitz EL, Weiner BK. A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned. *Spine J* 2011; **11**: 471-491 [PMID: 21729796 DOI: 10.1016/j.spinee.2011.04.023]
- 10 **Burkus JK**, Gornet MF, Dickman CA, Zdeblick TA. Anterior lumbar interbody fusion using rhBMP-2 with tapered interbody cages. *J Spinal Disord Tech* 2002; **15**: 337-349 [PMID: 12394656 DOI: 10.1097/00024720-200210000-00001]
- 11 **Zhang H**, Wang F, Ding L, Zhang Z, Sun D, Feng X, An J, Zhu Y. A meta analysis of lumbar spinal fusion surgery using bone morphogenetic proteins and autologous iliac crest bone graft. *PLoS One* 2014; **9**: e97049 [PMID: 24886911 DOI: 10.1371/journal.pone.0097049]
- 12 **Mummaneni PV**, Pan J, Haid RW, Rodts GE. Contribution of recombinant human bone morphogenetic protein-2 to the rapid creation of interbody fusion when used in transforaminal lumbar interbody fusion: a preliminary report. Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2004. *J Neurosurg Spine* 2004; **1**: 19-23 [PMID: 15291015 DOI: 10.3171/spi.2004.1.1.0019]
- 13 **Villavicencio AT**, Burneikiene S, Nelson EL, Bulsara KR, Favors M, Thramann J. Safety of transforaminal lumbar interbody fusion and intervertebral recombinant human bone morphogenetic protein-2. *J Neurosurg Spine* 2005; **3**: 436-443 [PMID: 16381205 DOI: 10.3171/spi.2005.3.6.0436]
- 14 **Glassman SD**, Carreon L, Djurasovic M, Campbell MJ, Puno RM, Johnson JR, Dimar JR. Posterolateral lumbar spine fusion with INFUSE bone graft. *Spine J* 2007; **7**: 44-49 [PMID: 17197332 DOI: 10.1016/j.spinee.2006.06.381]
- 15 **Glassman SD**, Dimar JR, Burkus K, Hardacker JW, Pryor PW, Boden SD, Carreon LY. The efficacy of rhBMP-2 for posterolateral lumbar fusion in smokers. *Spine* (Phila Pa 1976) 2007; **32**: 1693-1698 [PMID: 17621221 DOI: 10.1097/BRS.0b013e318074c366]
- 16 **Boden SD**, Kang J, Sandhu H, Heller JG. Use of recombinant human bone morphogenetic protein-2 to achieve posterolateral lumbar spine fusion in humans: a prospective, randomized clinical pilot trial: 2002 Volvo Award in clinical studies. *Spine* (Phila Pa 1976) 2002; **27**: 2662-2673 [PMID: 12461392 DOI: 10.1097/00007632-200212010-00005]
- 17 **Baskin DS**, Ryan P, Sonntag V, Westmark R, Widmayer MA. A prospective, randomized, controlled cervical fusion study using recombinant human bone morphogenetic protein-2 with the CORNERSTONE-SR allograft ring and the ATLANTIS anterior cervical plate. *Spine* (Phila Pa 1976) 2003; **28**: 1219-1224; discussion 1225 [PMID: 12811263 DOI: 10.1097/01.BRS.0000065486.22141.CA]
- 18 **Shields LB**, Raque GH, Glassman SD, Campbell M, Vitaz T, Harpring J, Shields CB. Adverse effects associated with high-dose recombinant human bone morphogenetic protein-2 use in anterior cervical spine fusion. *Spine* (Phila Pa 1976) 2006; **31**: 542-547 [PMID: 16508549 DOI: 10.1097/01.brs.0000201424.27509.72]
- 19 **Smucker JD**, Rhee JM, Singh K, Yoon ST, Heller JG. Increased swelling complications associated with off-label usage of rhBMP-2 in the anterior cervical spine. *Spine* (Phila Pa 1976) 2006; **31**: 2813-2819 [PMID: 17108835 DOI: 10.1097/01.brs.0000245863.52371.c2]
- 20 **Dmitriev AE**, Castner S, Lehman RA, Ling GS, Symes AJ. Alterations in recovery from spinal cord injury in rats treated with recombinant human bone morphogenetic protein-2 for posterolateral arthrodesis. *J Bone Joint Surg Am* 2011; **93**: 1488-1499 [PMID: 22204004 DOI: 10.2106/JBJS.J.00904]
- 21 **Ong KL**, Villarraga ML, Lau E, Carreon LY, Kurtz SM, Glassman SD. Off-label use of bone morphogenetic proteins in the United States using administrative data. *Spine* (Phila Pa 1976) 2010; **35**: 1794-1800 [PMID: 20700081 DOI: 10.1097/BRS.0b013e3181ecf6e4]
- 22 **Lykissas MG**, Aichmair A, Sama AA, Hughes AP, Lebl DR, Cammisia FP, Girardi FP. Nerve injury and recovery after lateral lumbar interbody fusion with and without bone morphogenetic protein-2 augmentation: a cohort-controlled study. *Spine J* 2014; **4**: 217-224 [PMID: 242269858 DOI: 10.1016/j.spinee.2013.06.109]
- 23 **Rihn JA**, Makda J, Hong J, Patel R, Hilibrand AS, Anderson DG, Vaccaro AR, Albert TJ. The use of RhBMP-2 in single-level transforaminal lumbar interbody fusion: a clinical and radiographic analysis. *Eur Spine J* 2009; **18**: 1629-1636 [PMID: 19475434 DOI: 10.1007/s00586-009-1046-1]

- 24 **Oliveira L**, Marchi L, Coutinho E, Abdala N, Pimenta L. The use of rh-bmp2 in standalone extreme lateral interbody fusion (Xliff®): clinical and radiological results after 24 months follow-up. *World Spinal Column J* 2010; **1**: 19-25
- 25 **Poeran J**, Opperer M, Rasul R, Mazumdar M, Girardi FP, Hughes AP, Memtsoudis SG, Vougioukas V. Change in Off-Label Use of Bone Morphogenetic Protein in Spine Surgery and Associations with Adverse Outcome. *Global Spine J* 2016; **6**: 650-659 [PMID: 27781184 DOI: 10.1055/s-0036-1571284]
- 26 **Boden SD**, Zdeblick TA, Sandhu HS, Heim SE. The use of rhBMP-2 in interbody fusion cages. Definitive evidence of osteoinduction in humans: a preliminary report. *Spine (Phila Pa 1976)* 2000; **25**: 376-381 [PMID: 10703113 DOI: 10.1097/00007632-200002010-00020]
- 27 **Dawson E**, Bae HW, Burkus JK, Stambough JL, Glassman SD. Recombinant human bone morphogenetic protein-2 on an absorbable collagen sponge with an osteoconductive bulking agent in posterolateral arthrodesis with instrumentation. A prospective randomized trial. *J Bone Joint Surg Am* 2009; **91**: 1604-1613 [PMID: 19571082 DOI: 10.2106/JBJS.G.01157]
- 28 **Glassman SD**, Carreon LY, Campbell MJ, Johnson JR, Puno RM, Djurasovic M, Dimar JR. The perioperative cost of Infuse bone graft in posterolateral lumbar spine fusion. *Spine J* 2008; **8**: 443-448 [PMID: 17526436 DOI: 10.1016/j.spinee.2007.03.004]
- 29 **Epstein NE**. Complications due to the use of BMP/INFUSE in spine surgery: The evidence continues to mount. *Surg Neurol Int* 2013; **4**: S343-S352 [PMID: 23878769 DOI: 10.4103/2152-7806.114813]
- 30 **Lykissas MG**, Aichmair A, Hughes AP, Sama AA, Lebl DR, Taher F, Du JY, Cammisia FP, Girardi FP. Nerve injury after lateral lumbar interbody fusion: a review of 919 treated levels with identification of risk factors. *Spine J* 2014; **14**: 749-758 [PMID: 24012428 DOI: 10.1016/j.spinee.2013.06.066]
- 31 **Mitchell K**, Shah JP, Dalgard CL, Tsytsikova LV, Tipton AC, Dmitriev AE, Symes AJ. Bone morphogenetic protein-2-mediated pain and inflammation in a rat model of posterolateral arthrodesis. *BMC Neurosci* 2016; **17**: 80 [PMID: 27905881 DOI: 10.1186/s12868-016-0314-3]
- 32 **Feeley BT**, Gamradt SC, Hsu WK, Liu N, Krenke L, Robbins P, Huard J, Lieberman JR. Influence of BMPs on the formation of osteoblastic lesions in metastatic prostate cancer. *J Bone Miner Res* 2005; **20**: 2189-2199 [PMID: 16294272 DOI: 10.1359/JBMR.050802]
- 33 **Carragee EJ**, Chu G, Rohatgi R, Hurwitz EL, Weiner BK, Yoon ST, Comer G, Kopjar B. Cancer risk after use of recombinant bone morphogenetic protein-2 for spinal arthrodesis. *J Bone Joint Surg Am* 2013; **95**: 1537-1545 [PMID: 24005193 DOI: 10.2106/JBJS.L.01483]
- 34 **Beachler DC**, Yanik EL, Martin BI, Pfeiffer RM, Mirza SK, Deyo RA, Engels EA. Bone Morphogenetic Protein Use and Cancer Risk Among Patients Undergoing Lumbar Arthrodesis: A Case-Cohort Study Using the SEER-Medicare Database. *J Bone Joint Surg Am* 2016; **98**: 1064-1072 [PMID: 27385679 DOI: 10.2106/JBJS.15.01106]
- 35 **Hsu WK**, Polavarapu M, Riaz R, Larson AC, Diegmueeller JJ, Ghodasra JH, Hsu EL. Characterizing the host response to rhBMP-2 in a rat spinal arthrodesis model. *Spine (Phila Pa 1976)* 2013; **38**: E691-E698 [PMID: 23429681 DOI: 10.1097/BRS.0b013e3-1828cb977]
- 36 **Deckers MM**, van Bezooijen RL, van der Horst G, Hoogendam J, van Der Bent C, Papapoulos SE, Löwik CW. Bone morphogenetic proteins stimulate angiogenesis through osteoblast-derived vascular endothelial growth factor A. *Endocrinology* 2002; **143**: 1545-1553 [PMID: 11897714 DOI: 10.1210/endo.143.4.8719]
- 37 **Krumholz HM**. Open science and data sharing in clinical research: basing informed decisions on the totality of the evidence. *Circ Cardiovasc Qual Outcomes* 2012; **5**: 141-142 [PMID: 22438459 DOI: 10.1161/CIRCOUTCOMES.112.965848]
- 38 **Ross JS**, Lehman R, Gross CP. The importance of clinical trial data sharing: toward more open science. *Circ Cardiovasc Qual Outcomes* 2012; **5**: 238-240 [PMID: 22438465 DOI: 10.1161/CIRCOUTCOMES.112.965798]
- 39 **Krumholz HM**, Ross JS, Gross CP, Emanuel EJ, Hodshon B, Ritchie JD, Low JB, Lehman R. A historic moment for open science: the Yale University Open Data Access project and medtronic. *Ann Intern Med* 2013; **158**: 910-911 [PMID: 23778908 DOI: 10.7326/0003-4819-158-12-201306180-00009]
- 40 **Fu R**, Selph S, McDonagh M, Peterson K, Tiwari A, Chou R, Helfand M. Effectiveness and harms of recombinant human bone morphogenetic protein-2 in spine fusion: a systematic review and meta-analysis. *Ann Intern Med* 2013; **158**: 890-902 [PMID: 23778906 DOI: 10.7326/0003-4819-158-12-201306180-00006]
- 41 **Carragee EJ**, Baker RM, Benzel EC, Bigos SJ, Cheng I, Corbin TP, Deyo RA, Hurwitz EL, Jarvik JG, Kang JD, Lurie JD, Mroz TE, Oner FC, Peul WC, Rainville J, Ratliff JK, Rihn JA, Rothman DJ, Schoene ML, Spengler DM, Weiner BK. A biologic without guidelines: the YODA project and the future of bone morphogenetic protein-2 research. *Spine J* 2012; **12**: 877-880 [PMID: 23199819 DOI: 10.1016/j.spinee.2012.11.002]

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Basic Study

Possibilities for arthroscopic treatment of the ageing sternoclavicular joint

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Conflict-of-interest statement: None. Each author certifies that he has no commercial associations (*e.g.*, consultancies, stock ownership, equity interest, patent/licensing arrangements, *etc.*) that might pose a conflict of interest in connection with the submitted article.

Data sharing statement: No additional data are available.

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Abstract

AIM

To investigate if there are typical degenerative changes in the ageing sternoclavicular joint (SCJ), potentially accessible for arthroscopic intervention.

METHODS

Both SCJs were obtained from 39 human cadavers (mean age: 79 years, range: 59-96, 13 F/26 M). Each frozen specimen was divided frontally with a band saw, so that both SCJs were opened in the same section through the center of the discs. After thawing of the specimens, the condition of the discs was evaluated by probing and visual inspection. The articular cartilages were graded according to Outerbridge, and disc attachments were probed. Cranio-caudal heights of the joint cartilages were measured. Superior motion of the clavicle with inferior movement of the lateral clavicle was measured.

RESULTS

Degenerative changes of the discs were common. Only 22 discs (28%) were fully attached and the discs were thickest superiorly. We found a typical pattern: Detachment of the disc inferiorly in connection with thinning, fraying and fragmentation of the inferior part of the disc, and detachment from the anterior and/or posterior capsule. Severe joint cartilage degeneration \geq grade 3 was more common on the clavicular side (73%) than on the sternal side (54%) of the joint. In cadavers

< 70 years 75% had \leq grade 2 changes while this was the case for only 19% aged 90 years or more. There was no difference in cartilage changes when right and left sides were compared, and no difference between sexes. Only one cadaver - a woman aged 60 years - had normal cartilages.

CONCLUSION

Changes in the disc and cartilages can be treated by resection of disc, cartilage, intraarticular osteophytes or medial clavicle end. Reattachment of a degenerated disc is not possible.

Key words: Sternoclavicular; Degenerative; Cartilage; Disc; Arthroscopy

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Core tip: Arthroscopic treatment is an option in patients with symptoms from the ageing sternoclavicular joint (SCJ). However, knowledge of age-related changes is essential for planning of such arthroscopic procedures. In 78 human cadaveric SCJs with a mean age of 79 years (range: 59-96 years) we found that degenerative changes of the discs were common, in particular inferior detachment, and only 28% were fully attached. Severe cartilage degeneration was more common on the clavicular than the sternal side. When there was inferior detachment of the disc, we observed increased supero-medial gliding of the clavicle. We conclude that a torn disc or degenerated articular cartilage might be treated by arthroscopic resection, debridement and clavicle end resection. Reattachment of a degenerated disc is not possible.

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INTRODUCTION

Arthroscopy has opened for specific procedures on the sternoclavicular joint (SCJ), *e.g.*, resection of a torn intraarticular disc. Changes of the joint with age might be expected just like it is seen in the acromioclavicular joint, due to the substantial gliding and rotation in both joints during movement of the arm^[1-3]. Resection of the lateral clavicle end is a common procedure for painful osteoarthritis of the acromioclavicular joint. The prevalence of symptoms from SCJ is unknown, but surgery on the joint is infrequent^[4-6], partly by tradition and perhaps of fear to injure vessels and lungs adjacent to its posterior capsule^[7].

Open resection of the articular disc and capsulorrhaphy in patients with degenerative disease of the

SCJ has been reported successful in 6 patients^[8]. Open resection of the medial clavicular end show good results in treatment for SCJ osteoarthritis^[9,10] when the costoclavicular ligament is kept intact^[10-12]. However, the scar after open surgery can be cosmetically prominent because of the location.

Arthroscopic surgery of the SCJ can be performed through two portals (Figure 1), leaving minor scars, using a 2.7 mm arthroscope and standard instruments (Figure 2). The two portals give access to both compartments of the joint on either side of the articular disc. The depth of the joint is about 1.5 cm, and care should be taken not to exceed this during introduction of the arthroscope, in order not to penetrate the posterior capsule. Once the arthroscope is introduced all structures are usually easy to identify, and resection of the disc, medial clavicle or intraarticular osteophytes, as well as synovectomy and removal of loose bodies can be performed under visual control without risk of penetrating into the mediastinum.

The articular disc of SCJ is superiorly attached to the medial end of the clavicle, inferiorly to the first rib at its junction with the manubrium and to the joint capsule. In older cadavers the disc is incomplete in 29%-56%^[13-16], with a central hole^[13,15,16] or a meniscoid appearance^[14]. During arthroscopy in younger patients (age mean 40 years, range: 16-70, 28 F/11 M) we have often found detachment of the disc from the anterior capsule and marked disintegration of the disc at the inferior part with detachment from manubrium (Figure 3) (unpublished).

These differences in reported changes are confusing in relation to whether there is an anatomic basis for arthroscopic treatment of the disc in the painful ageing SCJ.

Degenerative changes of the articular cartilage are reported to be more severe on the medial clavicle compared to manubrium^[16], which is surprising as the superior part of the clavicular cartilage only articulates when the arm is abducted.

Our aims were to study the anatomy of the SCJ, focusing on the occurrence of conditions that are potentially accessible for surgical intervention. Also, to evaluate if the hyaline cartilages on the clavicle and manubrium are equally affected by age, and if degenerative conditions and detachment of the disc has any influence on medial end clavicular stability.

MATERIALS AND METHODS

From 39 formalin embalmed human cadavers (age mean: 79 years, range: 59-96, 13 F/26 M) we obtained both SCJs. The sternum was cut at level of the second rib, and clavicles and first rib were cut lateral to the costoclavicular ligament. To be able to examine the capsular attachments of the intraarticular disc, each specimen was frozen and divided frontally with a thin band saw, so that both SCJs were opened in the

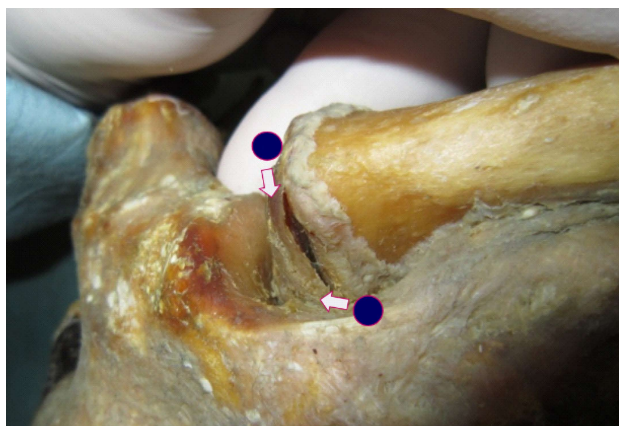


Figure 1 The two standard portals for sternoclavicular arthroscopy.

same section through the center of the disc (Figure 4). Examination of the joints was performed after the specimens had been thawed and stored in 30% ethanol. The cut surfaces were cleaned with a dry cloth. The height of the articular cartilage (cranio-caudal) on the clavicle and manubrium was measured (Figure 5). The attachments of the intraarticular disc to the clavicle and first rib-manubrium junction as well as to the anterior and posterior capsule were probed with a hooked arthroscopic probe (Figure 6). Any detachment was recorded. The disc was probed, and holes, fraying and flap lesions were visually inspected and recorded. The thickest and thinnest parts of the disc were measured with a calipergauge designed especially for this purpose (Figure 7). The cartilage at the medial clavicular end and at manubrium was classified according to Outerbridge^[17] based on visual inspection and probing, and by agreement of two observers. Information about the age and sex of the cadavers was obtained after the measurements had been recorded. There were no signs of previous surgery to any of the SCJs.

Ethical considerations

The study was conducted on deceased who had bequeathed their bodies to science and education at the Department of Cellular and Molecular Medicine (ICMM) at the University of Copenhagen according to Danish legislation (Health Law #546, § 188). The study was approved by the head of the body donation program at ICMM. The study was performed at Department of Cellular and Molecular Medicine (ICMM), University of Copenhagen, Denmark.

Statistical analysis

The data are presented as mean \pm SD. For the statistics, Student's *t* test was used. *P* < 0.05 was considered as statistically significant.

RESULTS

In the 26 males 4 discs were missing on the right side,



Figure 2 Sternoclavicular arthroscopy performed with the patient supine, using a 2.7 mm arthroscope and a 4.0 mm shaver.

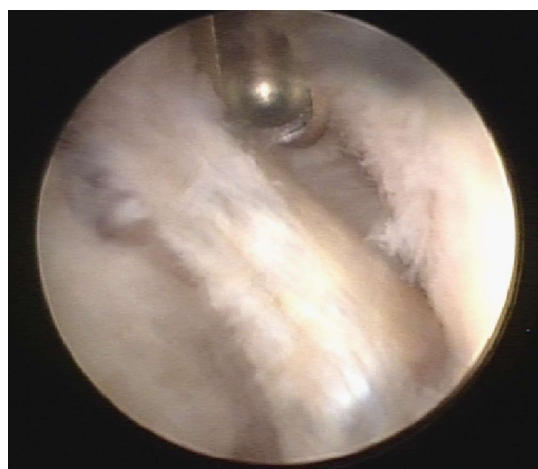


Figure 3 Arthroscopic view of the left sternoclavicular joint showing degenerative changes in the partially resected disc (in the middle) and chondral degeneration of the clavicular cartilage (right side of photo). The shaver is introduced through the superior portal.

1 joint was ankylotic and 21 discs were present, but 4 of these had a central hole. On the left side 4 discs were missing, 22 were present and 3 of these had a central hole.

In the 13 females 3 discs were missing on the right side, 10 were present and 4 of these had a central hole. On the left side 2 discs were missing, 11 were present and 4 of these had a central hole.

Figure 8 visualizes the attachments of the discs, illustrating that the discs were most often detached inferiorly. Only 22 discs (28%) were fully attached.

In nearly all cases the disc was thickest superiorly.

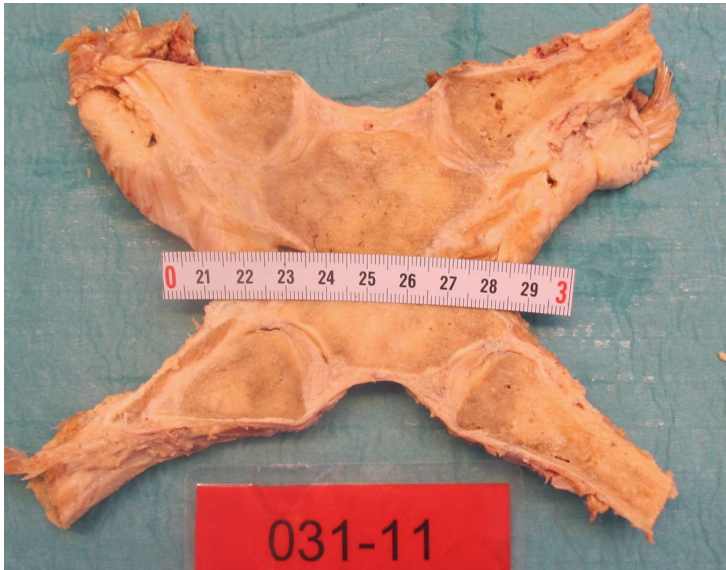


Figure 4 The sternoclavicular joints were divided frontally with a thin band saw so that both sternoclavicular joints were unfolded in the same section through the center of the discs.

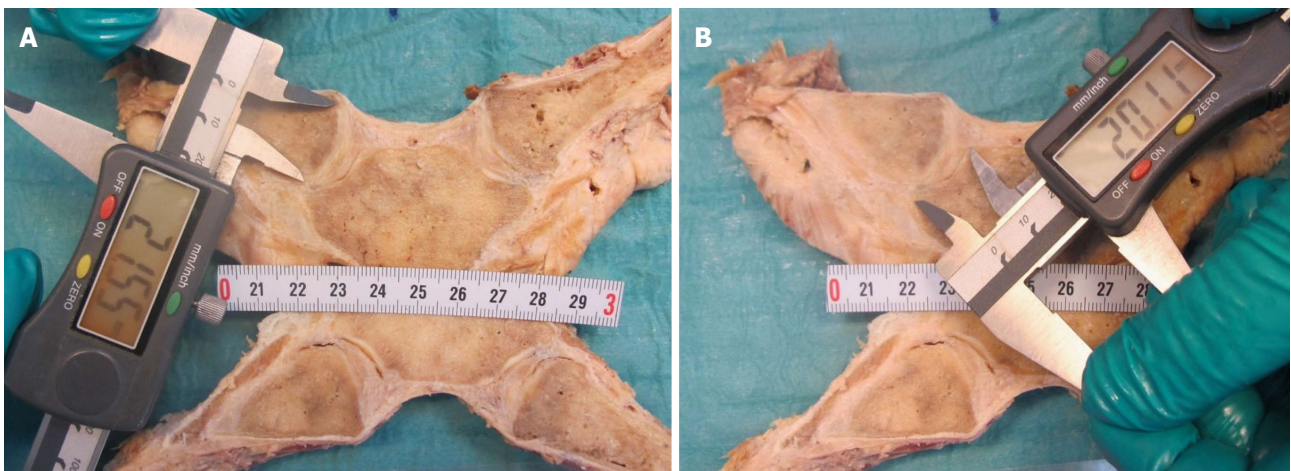


Figure 5 Measurement of the height of the articular cartilages (cranial-caudal) on the clavicle (A) and manubrium (B).

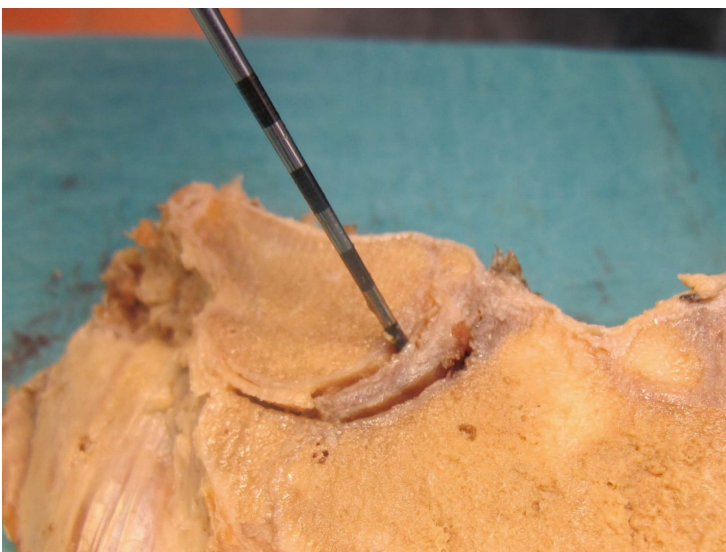


Figure 6 Probing the attachments of the intraarticular disc to the clavicle and first rib-manubrium junction as well as to the anterior and posterior capsule with a hooked arthroscopic probe.

All but one cadaver - a woman aged 60 years - showed degenerative changes of the cartilages. Grade 5 changes (no cartilage) were not seen in any of

the specimens, but one joint was ankylotic (no joint cavity). Severe degeneration \geq grade 3 was seen in 73% on the clavicular side and 54% on the sternal

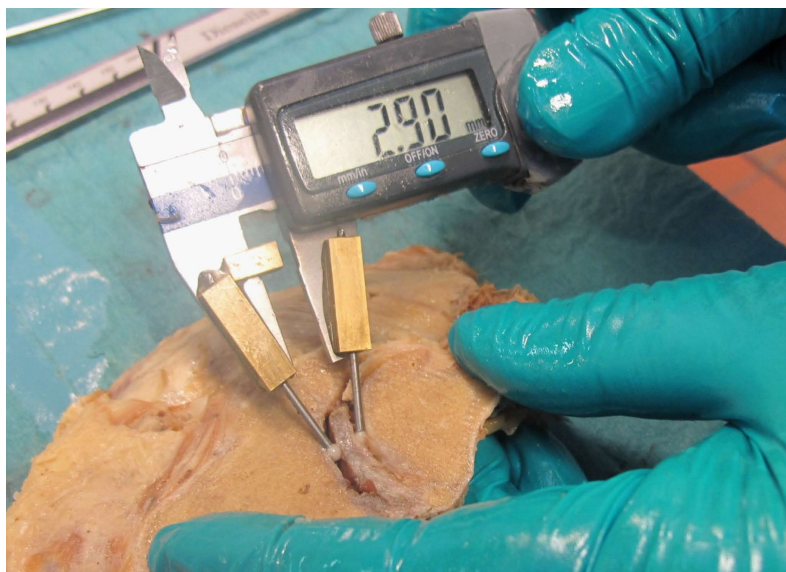


Figure 7 Measurement of the thickest and thinnest parts of the intraarticular discs with a calliper gauge.

side, confirming that degenerative changes are more common on the clavicular side of the joint. In cadavers < 70 years 75% had \leq grade 2 changes, while this was the case for only 19% aged 90 years or more. In the age groups 70-79 and 80-89 years 33%-35% had \leq grade 2 changes. There was no difference in cartilage changes when right and left sides were compared, and no difference between sexes ($P > 0.05$).

We found a typical pattern: Detachment of the disc inferiorly with thinning, fraying and fragmentation of the inferior part of the disc, and detachment from the anterior and/or posterior capsule. Typical examples of changes in the discs are shown in Figure 9.

In the cases with inferior detachment we found a marked increase in supero-medial displacement of the medial clavicular end compared to cases with intact inferior attachment, when a light medially directed push was applied to the lateral clavicle shaft ($P < 0.05$) (Figure 9).

The mean cranio-caudal length \pm 1 SD of the joint cartilages was in male cadavers on the right side 26.0 ± 3.1 mm on the clavicle and 18.1 ± 2.0 mm on the sternum, and on the left side 25.4 ± 2.9 mm and 17.9 ± 2.3 mm, respectively, while in female cadavers on the right side it was 23.5 ± 2.9 mm on the clavicle and 17.2 ± 1.7 mm on the sternum, and on the left side 24.1 ± 3.0 mm and 17.5 ± 2.1 mm, respectively. All data are shown in Table 1.

DISCUSSION

Our main purpose was to evaluate if changes to the intraarticular disc in the ageing SCJ could explain painful mechanical symptoms that are seen in some patients. In light of previous reports we were surprised by the marked changes of the discs observed in the majority of the SCJs. In a large cadaver study^[16] 56% of discs were found to be incomplete, but the defects were described as a central hole and fraying.

In our study the changes were much more general; in particular inferior detachment was a common finding (20/39 right, 16/39 left). This pattern resembles what we have seen in arthroscopic examination of the SCJ in symptomatic patients with degenerative joint disease. An inferiorly detached disc is more likely to produce mechanical symptoms than a central hole as it is unstable and may cause locking during motion of the joint.

We have no information about symptoms, work or sports activity for the donors. Based on the increasing pathology with increasing age, it is likely, that the changes in the disc and cartilages are of degenerative nature. In the specimens with complete inferior detachment of the disc there was supero-medial instability of the medial clavicular end. Motion of the clavicle relative to manubrium is during most activities sliding with no compression^[2]. When the shoulder is depressed the clavicle acts as a lever arm (ratio about 7:1) with the center of rotation (the fulcrum) at its crossing of the first rib (*i.e.*, the site of the costoclavicular ligament), then the sternal end of the clavicle is lifted forcibly upwards. With increased motion of the clavicle, symptoms from an unstable, degenerated disc and degenerated cartilages are likely to increase. A forceful depression of the shoulder, *e.g.*, during lifting a heavy load, applies a substantial load on the interclavicular ligament^[1,15]. It is not known to which extent force is absorbed in the disc during lifting, but the attachment of the disc inferiorly on the manubrium and superiorly on the upper facet of the clavicular joint surface indicates that the disc in this respect may function as a ligament, working in synergy with the interclavicular ligament. Histological examination of the disc has shown the most common collagen fibers to be type I, III and V^[18] which are all strong fibrillar collagens, designed to resist force.

Slackness of the interclavicular ligament with age might result in increased tension on the disc during

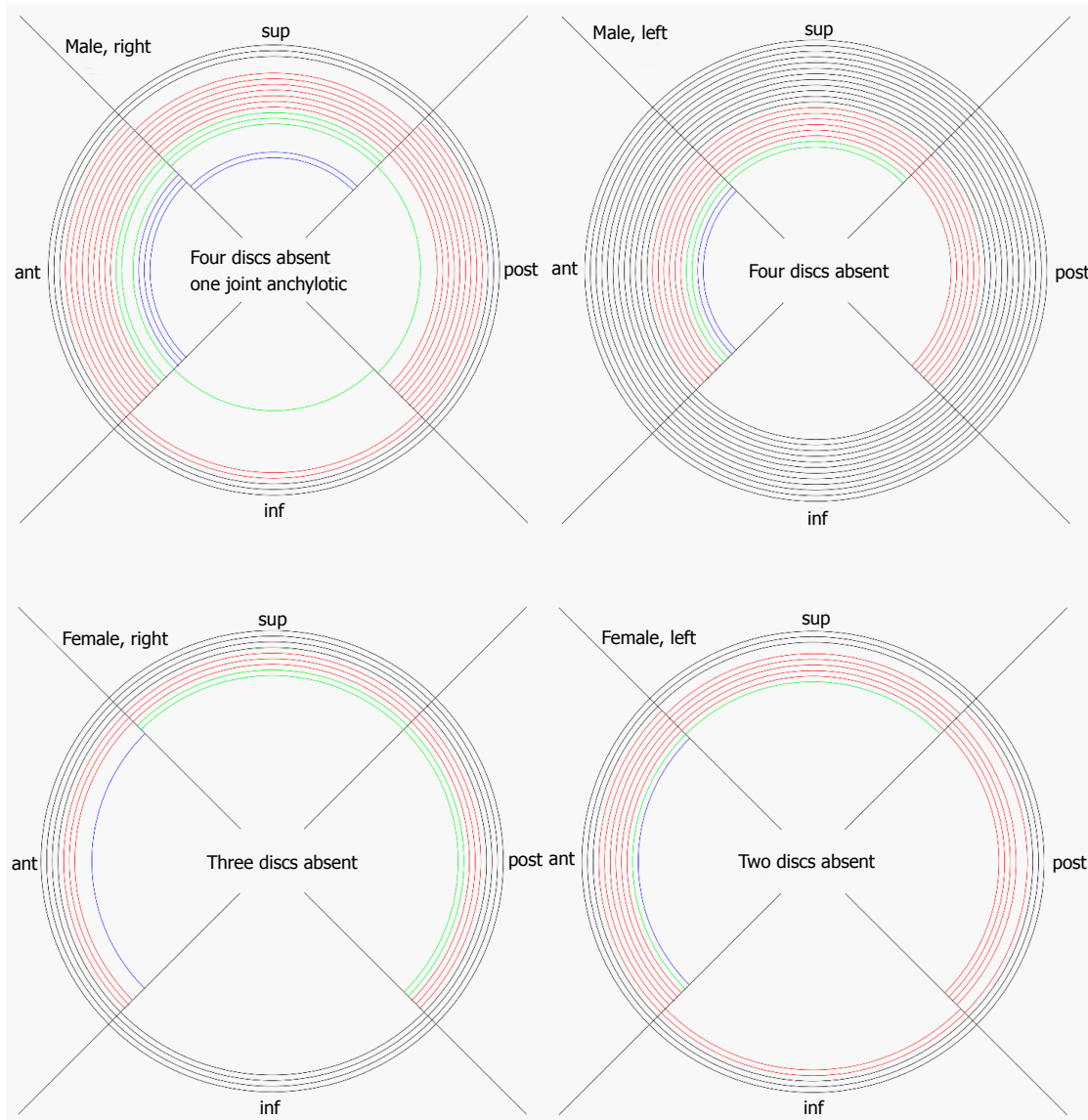


Figure 8 Graphic visualization of the attachments we found of the discs in left (left) and right (right) sternoclavicular joints of males and females. Black lines: Full attachment of all four sectors; red lines: Attachment of three sectors; green lines: Attachment of two sectors; blue lines: Attachment of one sector only. inf: Inferior, sup: Superior; post: Posterior; ant: Anterior.

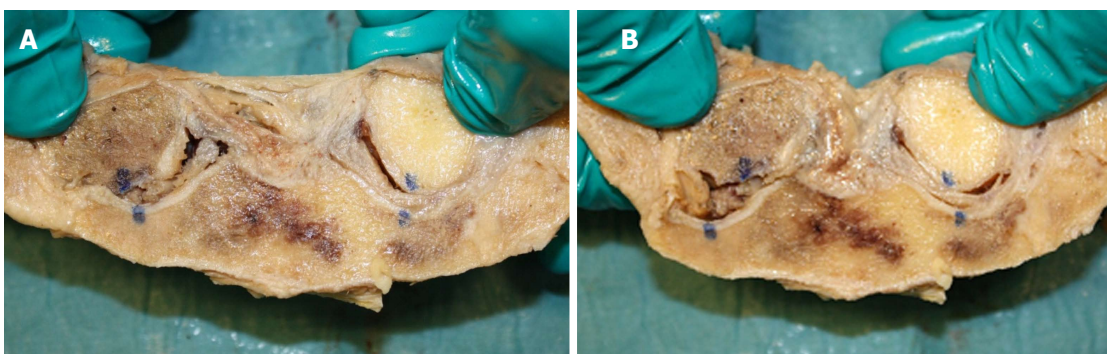


Figure 9 With inferior detachment (the sternoclavicular joint to the left) there was a substantial increase in supero-medial displacement of the medial clavicular end when a light medially directed push was applied to the lateral clavicle shaft (A: Light pull, B: Push). With full attachment of the disc (as seen in the joint to the right) this displacement was much smaller. Blue dots were marked when no external forces were applied to the joints.

lifting, and, in addition to the compressive forces on the inferior part of the disc during motion, this may

be an explanation for the high rate of thinning and detachment of the inferior part of the disc.

Table 1 Characteristics of the cadavers, the articular cartilage and the disc of the sternoclavicular joint

Age (yr)	Sex	Right thinnest/thickest part of disc mm ¹	Left thinnest/thickest part of disc mm ¹	Right attach- ment disc ²	Left attach- ment disc ²	Right cartilage C/S mm	Left cartilage C/S mm	Right cartilage quality C/S ³	Left cartilage quality C/S ³
59	F	2.1 i/3.1 s	2.2 i/4.4 s	1	5	21/15	22/14	2/2	3/3
60	F	0 i/3.9 s	0.5 i/3.9 s	5	1	23/18	25/20	0/0	0/0
65	M	2.3 i/4.3 s	4.4 i/6.4 s	1	1	24/17	26/17	2/1	2/1
65	F	1.7 i/4.8 s	0/2.4	1	5	27/18	24/21	1/1	4/4
66	M	2.2 i/4.3 s	0.9 i/4.2 s	5	1	30/19	26/21	1/1	3/1
71	M	1.2 i/4.5 s	2.2 i/6.3 s	4 + 5	1	32/20	29/21	3/2	2/3
71	M	0.6 i/1.6 s	0.9 i/2.2 s	3	5	21/17	22/13	3/3	3/3
72	F	0 i/1.4 s	0 c/2.6 s	2 + 5	1	25/18	26/19	3/2	3/2
73	M	Absent	Absent	Absent	Absent	31/20	29/21	3/3	3/3
73	M	0/3.2 anterior rim	0/4.0 anterior rim	3 + 4 + 5	3 + 4 + 5	28/18	24/17	3/4	3/4
74	M	2.9 i/3.8 s	2.0 s/3.3 i	2 + 4 + 5	1	29/19	28/17	3/2	3/2
75	F	Absent	2.1 i/2.8 s	Absent	5	19/15	18/14	3/2	1/1
75	M	2.5 i/3.5 s	1.1 i/4.1 s	5	1	25/14	25/18	3/3	2/3
76	M	0/2.2 i (flap)	2.3 i + s/3.8 c	3 + 4	1	27/17	25/17	4/4	2/3
78	M	3.5 i/4.5 s	3.5 i/5.7 s	3	1	27/19	25/22	3/3	3/3
78	M	2.3 i/3.0 s	1.0 i/2.9 s	5	5	26/17	27/18	2/1	2/1
78	M	Absent	0.9 i/3.4 s	Absent	1	25/17	29/19	4/4	3/3
79	M	0 i/0.8 s	0/2.7 s	5	5	21/17	21/17	2/3	3/2
79	M	2.0 i/3.7 s	Absent	5	Absent	29/21	28/20	3/3	2/2
79	M	0.5 i/3.9 s	0.1 i/4.4 s	1	1	24/16	21/16	3/2	4/2
79	M	Ankylosis	2.0 i/5.2 s	Ankylosis	4 + 5	25/20	23/16	Ankylosis	3/3
81	F	1.8 i/3.3 s	0/2.9 s	5	4 + 5	24/17	25/17	2/1	1/1
81	F	Absent	1.2 s/2.7 i	Absent	3	26/20	28/19	4/4	3/2
83	M	1.0 s/2.9 i	3.0 i/3.6 s	5	5	28/21	24/13	4/3	4/2
84	M	2.3 i/5.4 s	3.0 i/4.9 s	5	1	26/20	26/19	3/1	2/1
84	M	1.0 i/1.7 s	1.6 s/1.4 i	1	1	24/16	24/19	3/1	3/1
84	M	Absent	Absent	Absent	Absent	23/20	24/19	3/4	3/3
85	M	2.4 i/2.7 s	1.2 i/3.5 s	3 + 4 + 5	1	22/17	21/16	4/2	4/2
85	F	2.3 i/4.0 s	0/2.2 anterior rim	5	3 + 4 + 5	25/18	24/17	4/2	3/3
86	F	Absent	Absent	Absent	Absent	20/16	20/16	3/4	3/4
89	F	1.0 i/2.7 s	Absent	2 + 5	Absent	22/15	23/16	1/1	3/3
90	F	0.8 i/2.5 s	1.1 s/1.2 i	1	1	29/19	29/21	3/3	2/2
90	M	3.3 i/3.6 s	2.5 i/2.9 s	4 + 5	5	26/18	28/18	4/3	4/3
90	F	0/1.9 anterior rim	1.5 i/2.5 s	3 + 4 + 5	5	23/19	23/17	4/4	4/4
91	F	0 c/3.1 s	1.5 i/0 s	1	4	21/16	26/18	4/3	4/3
92	M	Absent	1.9 s/3.4 i	2 + 4 + 5	5	21/14	20/16	3/4	2/2
93	M	0/0 (absent)	0/3.2 s	Absent	4 + 5	31/18	31/17	3/3	4/4
94	M	1.7 i/3.3 s	Absent	2 + 5	Absent	26/21	27/21	3/2	4/4
96	M	0/2.2 anterior rim	0/3.8 anterior rim	3 + 4 + 5	3 + 4 + 5	26/18	28/17	4/4	4/4

¹i: Inferior; s: Superior. ²1: Full attachment; 2: Detachment anterior; 3: Detachment superior; 4: Detachment posterior; 5: Detachment inferior. ³Outerbridge classification: 0: Normal cartilage; 5: No cartilage. M: Male; F: Female.

In addition, the fact that the cranio-caudal length of the articular surface of the clavicle was about 40% longer than the articular surface on the manubrium, meaning that the upper third of the disc is not subject to compressive or frictional forces in most working situations, may explain why the superior part of the disc is often intact.

It is described that symptomatic SCJs with degenerative changes have an increased size of the clavicular head and a relative anterior subluxation of the clavicle compared to asymptomatic joints^[1], but not a superior subluxation. Even though the intraarticular disc in most of these joints must be expected to be severely changed and unable to prevent the clavicular head from superior motion during lifting, the enlargement of the head, related to the degenerative condition, might pull the interclavicular ligament superiorly, resulting in

a tightening of the ligament. This could explain why the clavicular head in this situation is not subluxating superiorly during depression of the shoulder^[19].

There was an overweight of thinning and detachment of the inferior part of the disc on the right side compared to left and fewer normal discs on the right side. Of 91% are right dominant and some activities are performed with more power by the dominant arm. This increases load on the SCJ, its ligaments and the disc, and may cause additional wear on the right SCJ on top of the degenerative wear that is affecting both sides.

We could confirm earlier findings of more severe changes of the cartilage on the clavicle compared to manubrium^[16]. Therefore, it makes sense to resect the clavicular and not the sternal part of the joint in case of surgery for osteoarthritis of the SCJ.

Arthroscopic surgery of the SCJ is described in a few series^[4-6,20]. Resection of the medial clavicular end is the procedure that has been reported in most of the cases^[4,5,20], and in open^[10] as well as arthroscopic^[4,5,20] series it resulted in marked pain reduction. The indication for this operation is degenerative changes that can be demonstrated by X-rays, MRI or CT-scan. In some cases of pain in the SCJ no such changes can be demonstrated. Our study shows that at least in the elderly population detachment of the articular disc is common. It is not known to which extent these changes in the disc are symptomatic, but detachment can probably lead to pain, locking and swelling, and technically it can be treated by arthroscopic debridement or resection of the disc as well as resection of the medial clavicular end. Pathology of the disc is not visible on X-rays or CT-scan, but can often be demonstrated on T2 weighted MRI-scans (personal experience). Persistent pain, locking and/or swelling of a SCJ without degenerative changes on X-rays or CT-scan might be caused by detachment or fraying of the disc, and an MRI-scan should be considered in these cases. The detachment and thinning of the discs inferiorly as found in our study means that surgical reattachment of the disc is impossible. Contrary, in case of traumatic detachment of otherwise normal discs in younger individuals, reattachment is an option in case of symptoms.

Detachment or destruction of the articular disc in the SCJ is a common finding in the aging population and can result in pain, locking and swelling which might be treated by resection of the torn disc. Degenerative changes of the articular cartilages are more common on the clavicle than on manubrium, and normal cartilage is rarely seen in this age group. Debridement, chondrectomy and medial clavicle resection may be relevant, but reattachment of the disc is not possible because of the marked tissue changes.

ACKNOWLEDGMENTS

We thank Johnny Grant and Lars-Bo Nielsen for preparation of the specimens and Keld Ottosen for preparing the graphic illustration (Figure 8).

COMMENTS

Background

Arthroscopy of the sternoclavicular joint (SCJ) is a recently introduced technique that has opened for more specific procedures on this joint, e.g., resection or reinsertion of a torn disc, synovectomy, chondrectomy and removal of loose bodies. Knowledge of age-related changes is essential for planning of arthroscopic procedures, and previous cadaver studies have shown conflicting results.

Research frontiers

Open surgical procedures on the SCJ leave a scar at a cosmetically problematic location, and visualization of the deep part of the joint is often limited. Arthroscopy makes full inspection of the SCJ possible. The arthroscopic procedure that has previously been reported in the SCJ is clavicle end resection

for osteoarthritis.

Innovations and breakthroughs

This is the first study to describe the SCJ in cadaver specimens prepared without interference with the joint capsule and disc attachment sites. The authors found degenerative changes to disc and joint cartilages to be much more common than previously thought and showing in a typical pattern.

Applications

Arthroscopic resection of disc, cartilages and clavicular end of the SCJ may be applied in cases of pain, locking or swelling that is resistant to non-surgical intervention.

Peer-review

This is very classic study on degenerative SCJ. The study demonstrated the stage of cartilage in SC comprehensively.

REFERENCES

- 1 Bearn JG. Direct observations on the function of the capsule of the sternoclavicular joint in clavicular support. *J Anat* 1967; **101**: 159-170 [PMID: 6047697]
- 2 Ludewig PM, Phadke V, Braman JP, Hassett DR, Cieminski CJ, LaPrade RF. Motion of the shoulder complex during multiplanar humeral elevation. *J Bone Joint Surg Am* 2009; **91**: 378-389 [PMID: 19181982 DOI: 10.2106/JBJS.G.01483]
- 3 Negri JH, Malavolta EA, Assunção JH, Gracitelli ME, Pereira CA, Bolliger Neto R, Croci AT, Ferreira Neto AA. Assessment of the function and resistance of sternoclavicular ligaments: A biomechanical study in cadavers. *Orthop Traumatol Surg Res* 2014; **100**: 727-731 [PMID: 25261174 DOI: 10.1016/j.otsr.2014.07.011]
- 4 Tytherleigh-Strong GM, Getgood AJ, Griffiths DE. Arthroscopic intra-articular disk excision of the sternoclavicular joint. *Am J Sports Med* 2012; **40**: 1172-1175 [PMID: 22459240 DOI: 10.1177/0363546512439286]
- 5 Tytherleigh-Strong G, Griffith D. Arthroscopic excision of the sternoclavicular joint for the treatment of sternoclavicular osteoarthritis. *Arthroscopy* 2013; **29**: 1487-1491 [PMID: 23910004 DOI: 10.1016/j.arthro.2013.05.029]
- 6 Tytherleigh-Strong G. Arthroscopy of the sternoclavicular joint. *Arthrosc Tech* 2013; **2**: e141-e145 [PMID: 23875140 DOI: 10.1016/j.eats.2013.01.005]
- 7 Van Tongel A, Van Hoof T, Pouliart N, Debeer P, D'Herde K, De Wilde L. Arthroscopy of the sternoclavicular joint: an anatomic evaluation of structures at risk. *Surg Radiol Anat* 2014; **36**: 375-381 [PMID: 23995518 DOI: 10.1007/s00276-013-1195-0]
- 8 Aumann U, Brüning W. [Discopathy of the sternoclavicular joint]. *Chirurg* 1980; **51**: 722-726 [PMID: 7471942]
- 9 Pingsmann A, Patsalis T, Michiels I. Resection arthroplasty of the sternoclavicular joint for the treatment of primary degenerative sternoclavicular arthritis. *J Bone Joint Surg Br* 2002; **84**: 513-517 [PMID: 12043770 DOI: 10.1302/0301-620X.84B4.12601]
- 10 Rockwood CA, Groh GI, Wirth MA, Grassi FA. Resection arthroplasty of the sternoclavicular joint. *J Bone Joint Surg Am* 1997; **79**: 387-393 [PMID: 9070528 DOI: 10.2106/00004623-1997-03000-00011]
- 11 Carrera EF, Archetti Neto N, Carvalho RL, Souza MA, Santos JB, Faloppa F. Resection of the medial end of the clavicle: an anatomic study. *J Shoulder Elbow Surg* 2007; **16**: 112-114 [PMID: 17055749 DOI: 10.1016/j.jse.2006.04.010]
- 12 Lee JT, Campbell KJ, Michalski MP, Wilson KJ, Spiegl UJ, Wijedicks CA, Millett PJ. Surgical anatomy of the sternoclavicular joint: a qualitative and quantitative anatomical study. *J Bone Joint Surg Am* 2014; **96**: e166 [PMID: 25274794 DOI: 10.2106/JBJS.M.01451]
- 13 Barbaix E, Lapierre M, Van Roy P, Clarijs JP. The sternoclavicular joint: variants of the discus articularis. *Clin Biomech* (Bristol, Avon) 2000; **15** Suppl 1: S3-S7 [PMID: 11078897 DOI: 10.1016/

- S0268-0033(00)00051-6]
- 14 **Emura K**, Arakawa T, Terashima T, Miki A. Macroscopic and histological observations on the human sternoclavicular joint disc. *Anat Sci Int* 2009; **84**: 182-188 [PMID: 19221859 DOI: 10.1007/s12565-009-0014-5]
 - 15 **Tubbs RS**, Loukas M, Slaphey JB, McEvoy WC, Linganna S, Shoja MM, Oakes WJ. Surgical and clinical anatomy of the interclavicular ligament. *Surg Radiol Anat* 2007; **29**: 357-360 [PMID: 17563831 DOI: 10.1007/s00276-007-0219-z]
 - 16 **van Tongel A**, MacDonald P, Leiter J, Pouliart N, Peeler J. A cadaveric study of the structural anatomy of the sternoclavicular joint. *Clin Anat* 2012; **25**: 903-910 [PMID: 22991168 DOI: 10.1002/ca.22021]
 - 17 **Outerbridge RE**. The etiology of chondromalacia patellae. *J Bone Joint Surg Br* 1961; **43-B**: 752-757 [PMID: 14038135]
 - 18 **Shimada K**, Takeshige N, Moriyama H, Miyauchi Y, Shimada S, Fujimaki E. Immunohistochemical study of extracellular matrices and elastic fibers in a human sternoclavicular joint. *Okajimas Folia Anat Jpn* 1997; **74**: 171-179 [PMID: 9446929 DOI: 10.2535/ofaj1936.74.5_171]
 - 19 **Van Tongel A**, Valcke J, Piepers I, Verschueren T, De Wilde L. Relationship of the Medial Clavicular Head to the Manubrium in Normal and Symptomatic Degenerated Sternoclavicular Joints. *J Bone Joint Surg Am* 2014; **96**: e109 [PMID: 24990983 DOI: 10.2106/JBJS.M.00623]
 - 20 **Tavakkolizadeh A**, Hales PF, Janes GC. Arthroscopic excision of sternoclavicular joint. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 405-408 [PMID: 19089407 DOI: 10.1007/s00167-008-0692-x]

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Retrospective Study

Epidemiology of open fractures in sport: One centre's 15-year retrospective study

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Abstract

AIM

To describe the epidemiology of sport-related open fractures from one centre's adult patient population over a 15-year period.

METHODS

A retrospective review of a prospectively-collected database was performed: The database contained information all sport-related open fractures, sustained from 1995 to 2009 in the Edinburgh, Mid and East Lothian Populations.

RESULTS

Over the 15-year period, there were 85 fractures recorded in 84 patients. The annual incidence of open sport-related fractures was 0.01 per 1000 population. The mean age at injury was 29.2 years (range 15-67). There were 70 (83%) males and 14 females (17%).

The 6 most common sports were soccer ($n = 19$, 22%), rugby ($n = 9$, 11%), cycling ($n = 8$, 9%), hockey ($n = 8$, 9%); horse riding ($n = 6$, 7%) and skiing ($n = 6$, 7%). The five most common anatomical locations were finger phalanges ($n = 30$, 35%); tibial diaphysis ($n = 19$, 23%); forearm ($n = 12$, 14%); ankle ($n = 7$, 8%) and metacarpals ($n = 5$, 6%). The mean injury severity score was 7.02. According to the Gustilo-Anderson classification system, 45 (53%) fractures were grade 1; 28 (33%) fractures were grade 2; 8 (9%) fractures were grade 3a; and 4 (5%) fractures were grade 3b. Out of the total number of fractures, 7 (8%) required plastic surgical intervention as part of management. The types of flaps used were split skin graft ($n = 4$), fasciocutaneous flaps ($n = 2$); and adipofascial flap ($n = 1$).

CONCLUSION

We analysed the epidemiology of open fractures secondary to sport in one centre over a 15-year period. Soccer and rugby were the most common causative sports while fractures of the finger phalanx and of the tibial diaphysis were the most common sites. Open fractures are uncommon in sport; however, when they are sustained they usually occur on muddy sport fields or forest tracks and therefore must be treated appropriately. It is important that clinicians and sports therapists have knowledge of these injuries, in order to ensure they are managed optimally.

Key words: Open; Fracture; Sport; Epidemiology; Injury; Trauma

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Core tip: We reviewed all open sport-related fractures presenting to our trauma centre over a 15-year period to provide comprehensive epidemiological data on this injury type. Open sport-related fractures occurred at an annual incidence of 0.01/1000 population. The mean age at injury was 29.2 years; the gender ratio was 7.4:1 (male:female). The most common causative sports were soccer and rugby. The most common fracture locations were finger phalanx and tibial diaphysis. Fourteen percent of the fractures were Gustilo-Grade 3; 8% required plastic surgical intervention. Open fractures in sport are a rare, but significant, injury; awareness and education is necessary among clinicians to optimize outcome.

Wood AM, Robertson GAJ, MacLeod K, Porter A, Court-Brown CM. Epidemiology of open fractures in sport: One centre's 15-year retrospective study. *World J Orthop* 2017; 8(7): 545-552 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v8/i7/545.htm> DOI: <http://dx.doi.org/10.5312/wjo.v8.i7.545>

INTRODUCTION

Open fractures are uncommon in the United Kingdom

sporting population, however they have a high morbidity, which makes the patient group significant. This institution has previously published work looking at the epidemiology of open fractures and found an incidence of 30.7 per 100000 per year^[1].

Sports and exercise is ever increasing in popularity, particularly team sports and multi-sport endurance^[2]. This is due to the impact of social and cultural influences, such as easier access to sporting facilities and social media. The epidemiology of acute sporting fractures has been described by Court-Brown *et al*^[3] 2008. The authors describe sports-related fractures as having a Type C distribution with unimodal peaks in both young males and females^[3]. They also noted a clear preponderance towards upper limb fractures in sports, the majority of which involve the finger phalanges, metacarpus or distal radius^[3]. Lastly they recorded an open fracture rate of 1.7% among sport-related fractures, with an annual incidence for open sport-related fractures of 0.02 per 1000 population. Court-Brown *et al*^[1] 2012 also described the epidemiology of open fractures, they conclude that 3.6% of all open fractures are a result of sport.

In order to obtain accurate epidemiological data, when the incidence of open fractures is this low, it is necessary to perform a long-term study of these fractures within a large population group^[3]. Thus, while there has been an increasing cohort of literature of the epidemiology of sport-related fractures, the literature describing the epidemiology of open fractures in sport remains minimal^[1,3].

We aim to provide the first long-term study describing the epidemiology of sport-related open fractures from one centre's adult patient population. This information will be useful for medical professionals treating patients participating in sport and sport governing bodies.

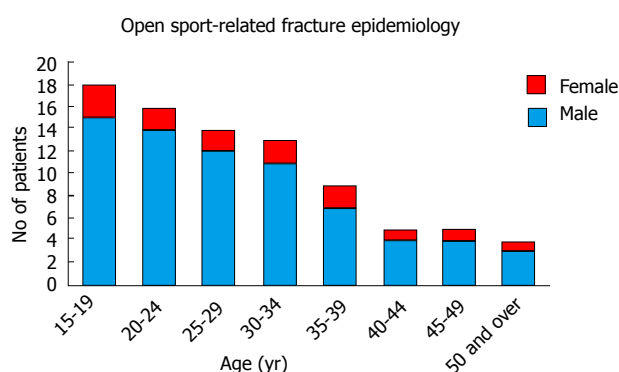
MATERIALS AND METHODS

All acute fractures presenting to the Royal Infirmary of Edinburgh, Orthopaedic Trauma Unit from the residents of Edinburgh, Mid and East Lothian, over the period of 1995 to 2009, were prospectively recorded on a database. This included all patients from the region, who were injured elsewhere, but were followed up under the Edinburgh Orthopaedic Trauma Unit: This was to provide accurate epidemiological data. Conversely, all non-resident patients who were injured within the region were excluded from the database. The mean population count for the region over the study period was 539858 (Population Count in 2000, $n = 534715$ ^[3]; Population Count in 2007, $n = 545000$ ^[4]).

The database was retrospectively reviewed in 2016, and all open fractures, sustained over the 15-year period (1995 to 2009), were identified. Subsequently, a subgroup, in which the injury was secondary to a sporting activity, was identified. Sporting activity was defined as participation in an athletic game or activity

Table 1 Total number of sport-related open fractures, divided by causative sport and the 5 most common fracture locations

Sport	Number	Percentage of the whole cohort (%)	Finger phalanx	Tibial diaphysis	Forearm	Ankle	Metacarpal
Soccer	19	22	3	9	1	1	0
Rugby	9	11	2	1	0	3	1
Cycling	8	9	3	1	2	0	0
Hockey	8	9	8	0	0	0	0
Horse riding	6	7	1	1	2	1	0
Skiing	6	7	3	1	2	0	0
Mountain bike	4	5	0	0	2	0	0
Quad bike	4	5	0	2	1	1	0
Basketball	3	4	2	0	1	0	0
Shinty	3	4	3	0	0	0	0
Sledging	3	4	0	2	0	1	0
Motorcross	2	2	0	0	0	0	2
Badminton	1	1	1	0	0	0	0
Bowling	1	1	1	0	0	0	0
Cricket	1	1	1	0	0	0	0
Golf	1	1	0	0	0	0	1
Snowboarding	1	1	0	1	0	0	0
Squash	1	1	1	0	0	0	0
Surfboard	1	1	1	0	0	0	0
Trampolining	1	1	0	0	1	0	0
White water rafting	1	1	0	1	0	0	0
Unknown	1	1	0	0	0	0	1
Totals	85	100	30	19	12	7	5

**Figure 1** Open sport-related fracture epidemiology.

at time of injury. The Gustilo-Anderson classification^[5] was used to describe the extent of soft tissue injury associated with the fracture: For all the fractures, the grading of this classification was based on the intra-operative findings after surgical debridement.

The database contained information on patient age and gender, site of the fracture, mode of injury, sport participated at time of injury, Gustilo grading for each fracture, and required treatment, including both Orthopaedic and Plastic Surgical procedures. Review of each presenting radiograph, as well as confirmation of the designated Gustilo grading^[4], was performed by the senior author, a Professor of Orthopaedic Trauma Surgery.

For analysis purposes, niche sporting activities, of a very similar nature, were grouped to allow for more meaningful interpretation of the data: Grouping however was only performed if the sports were considered to be suitably similar. For instance road cycling and track cycling were combined as cycling;

however, mountain biking, was considered a separate sport.

RESULTS

Epidemiology

There were 85 fractures sustained by 84 people over the 15-year period. The annual incidence of open sport-related fractures was 0.01 per 1000 population. Of the 84 patients, 70 (83%) were male and 14 (17%) were female (Figure 1). The mean age of the total cohort was 29.2 (range 15-67; SD 11.75; 95%CI: 2.5). The mean age of the female population was 31.93 years and the mean age of the male population was 28.62 years. Forty fractures occurred during competitive sport, nine during training for competitive sport and thirty-six during recreational sport. Two fractures were sustained by professional athletes and eighty-three fractures were sustained by recreational athletes.

Causative sports

The 6 most common sports were soccer ($n = 19$, 22%), rugby ($n = 9$, 11%), cycling ($n = 8$, 9%), hockey ($n = 8$, 9%); horse riding ($n = 6$, 7%) and skiing ($n = 6$, 7%) (Figure 2). Other common sports were mountain biking ($n = 4$, 5%), quad biking ($n = 4$, 5%), basketball ($n = 3$, 4%), shinty ($n = 3$, 4%) and sledging ($n = 3$, 4%). Table 1 shows the total number of fractures, divided by sport, and by fracture location.

Fracture location

The top 5 fracture locations were finger phalanges, 35% ($n = 30$); tibial diaphysis 22% ($n = 19$); forearm 14% ($n = 12$); ankle 8% ($n = 7$) and metacarpals 6%

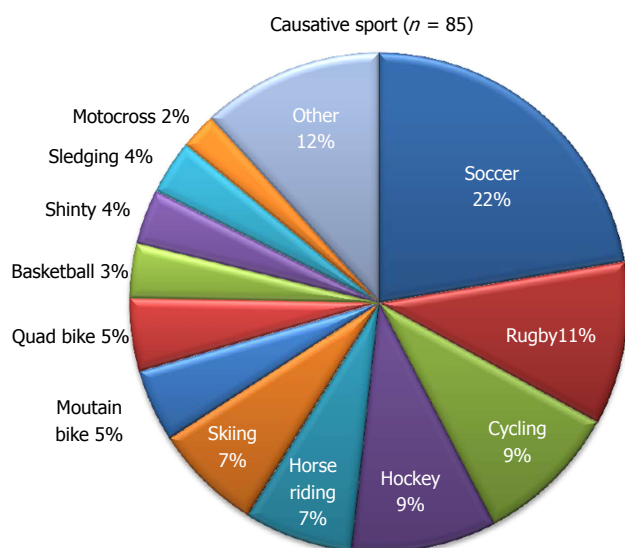


Figure 2 Causative sports for open sport-related fractures.

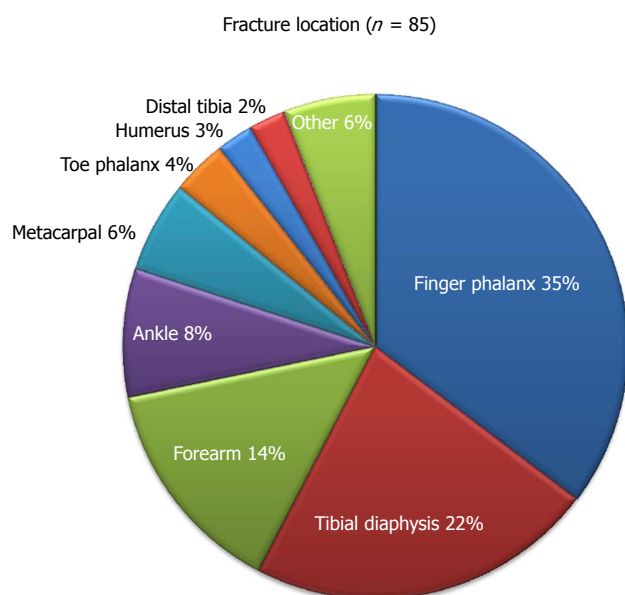


Figure 3 Fracture location for open sport-related fractures.

($n = 5$) (Figure 3). Of the forearm fractures, four were of the distal radius, four were of the proximal ulna, three were of the combined radial and ulna diaphysis and one was of the ulnar diaphysis. Other fracture sites included toe phalanges ($n = 3$); humerus ($n = 2$); distal tibia ($n = 2$); pelvis ($n = 1$); clavicle ($n = 1$); femur ($n = 1$); patella ($n = 1$) and talus ($n = 1$). The fractures involving finger phalanges, included 5 of the little finger; 6 of the ring finger; 3 of the middle finger; 4 of the index finger; 10 of the thumb and in 2 cases the finger involved was unknown. Of all the fractures, 59% (50/85) were of the upper limb. Table 2 shows the fracture locations for the top 6 sports.

Injury severity

According to the Gustilo-Anderson classification

Table 2 The six most common causative sports and their anatomical distribution

Anatomical location	Soccer	Rugby	Cycling	Hockey	Horse riding	Skiing
Ankle	1	3	0	0	1	0
Clavicle	0	0	1	0	0	0
Distal radius	0	0	0	0	2	0
Distal humerus	1	0	0	0	0	0
Femur	0	0	1	0	0	0
Finger phalanx	3	2	3	8	1	3
Metacarpal	0	1	0	0	0	0
Patella	0	1	0	0	0	0
Distal tibia	1	1	0	0	0	0
Proximal ulna	0	0	2	0	0	1
Radius and ulna	1	0	0	0	0	1
Talus	0	0	0	0	1	0
Tibial diaphysis	9	1	1	0	1	1
Toe phalanx	3	0	0	0	0	0
Ulna	0	0	0	0	0	0
Total	19	9	8	8	6	6

system^[5], 45 (53%) fractures were Grade 1; 28 (33%) fractures were Grade 2; 8 (9%) fractures were Grade 3a; and 4 (5%) fractures were Grade 3b (Figure 4).

The mean Injury Severity Score was 7.02 (SD 4.33; 95%CI: 0.92). There were 2 deaths during the 15-year period; 1 road-cyclist who had an open proximal ulna fracture; and 1 soccer player, who sustained a grade 3a open tibia fracture.

Primary orthopaedic management

Regarding the primary index procedures: Twenty-two fractures were treated with wound management and cast/splint application; twenty-six fractures with wound management and open reduction internal fixation; eighteen fractures with wound management and intra-medullary nailing; eleven fractures with wound management and kirschner-wire fixation; five fractures with wound management and external fixator application; and three fractures with wound management and tension band wire fixation (Table 3).

Plastic surgical intervention

There were 7 fractures (8%) that required plastic surgical intervention as part of their management. The types of flaps used were split skin graft ($n = 4$), fasciocutaneous flaps ($n = 2$); and adipofascial flap ($n = 1$) (Table 4).

DISCUSSION

The aim of this study was to describe the epidemiology of sport-related open fractures. The main findings were that sport-related open fractures demonstrated a uni-modal incidence of injury, with an annual incidence of 0.01 per 1000 population, a mean age at injury of 29.2 years and a male to female ratio of 7.4:1. Ninety-eight percent of these injuries were sustained by non-professional athletes. Over half of all fractures were

Table 3 Orthopaedic management of the open fractures

Fracture location	Wound management + splint/cast	Wound management + ORIF	Wound management + intra-medullary nail	Wound management + K-wire fixation	Wound management + external fixator	Wound management + tension band wire
Finger phalanx	20	3	-	6	1	-
Tibial diaphysis	-	2	17	-	-	-
Ankle	-	7	-	-	-	-
Metacarpal	-	2	-	3	-	-
Distal radius	-	2	-	-	2	-
Proximal ulna	-	1	-	-	-	3
Radius and ulna	-	3	-	-	-	-
Toe phalanx	1	-	-	2	-	-
Distal humerus	-	2	-	-	-	-
Distal tibia	-	1	-	-	1	-
Ulna diaphysis	-	1	-	-	-	-
Clavicle	1	-	-	-	-	-
Pelvis	-	1	-	-	-	-
Patella	-	1	-	-	-	-
Femur	-	-	1	-	-	-
Talus	-	-	-	-	1	-
Total	22	26	18	11	5	3

ORIF: Open reduction internal fixation; K-wire: Kirschner wire.

Table 4 Sport-related open fractures requiring plastic surgical intervention

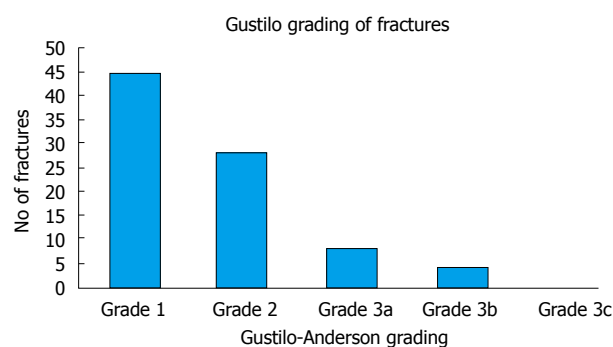
Sport	Gustilo grade	Procedure	Injury
Soccer	2	SSG	Tibial diaphysis
Soccer	3a	Adipofascial flap	Tibial diaphysis
Soccer	3a	SSG	Tibial diaphysis
Soccer	3b	Fasciocutaneous flap	Distal tibia
Quad bike	3b	SSG	Ankle
Quad bike	2	Fasciocutaneous flap	Tibial diaphysis
Sledging	3b	SSG	Ankle

SSG: Split skin graft.

located in the upper limb, with finger phalanx fractures the most common fracture location. Soccer was the most common causative sport, accounting for over one fifth of all injuries. Regarding injury severity, 14% were Gustilo-Anderson Grade 3 classification, with only 8% of all fractures requiring plastic surgical intervention.

This is in keeping with existing literature on sport-related fractures^[3,6]. Court-Brown *et al.*^[3,6] previously reported that 12.8% of all fractures are sustained during sporting activities. These injuries were noted to present in a uni-modal distribution, with a mean age at injury of 25.6 years and a gender ratio of 7.5:1^[3]. Upper limb sport-related fractures were also noted to be more common than lower limb sport-related fractures, with 77% of all sport-related fractures occurring within the upper limb fractures^[3,6]. One point seven percent (1.7%) of these sport-related fractures were open, providing an annual incidence of open sport-related fractures of 0.02 per 1000 population^[3,6]. Robertson *et al.*^[7,8] also noted that between 96% to 98% of all sport-related fractures occur in non-professional athletes.

In comparison of both studies, regarding the in-

**Figure 4** Gustilo-Anderson grading for open sport-related fractures.

creased mean age observed with our cohort, which specifically relates to open fractures, we feel this reflects a greater proportion of elderly athletes who sustain an open fracture during sport^[1]. Age has previously been identified as a risk factor for sustaining an open fracture: This is felt to be secondary both to the weakening effects of aging on the skin, as well as to the decreased levels of proprioception seen in the elderly, which predispose to more severe injury^[1,9]. Regarding the increased proportion of lower limb fractures in our cohort, we feel this is secondary to an increased proportion of tibial diaphyseal and ankle fractures, among the open fracture cohort. Both fractures have been noted to be at high risk of open injury with tibial diaphysis the second most common recorded open fracture and ankle fracture the fifth most common recorded open fracture^[1]. This provides a higher proportion of lower limb fractures among sport-related open fractures^[1].

Regarding the severity of injury within our study, the proportion of Gustilo-Anderson grade 3 fractures was slightly lower than that within previous studies^[9].

Court-Brown *et al.*^[1] reported a series of 2386 open fractures, within the general population, and 27% were Grade 3 grading. The difference between proportions is likely explained by the younger mean age of our “athletic” cohort at 29.2 years, with the mean age from Court-Brown *et al.*^[1] being 45.5 years. Age has been noted to be a risk factor to sustain a more serious grade of open fracture, due to the deleterious effects it has on the surrounding soft tissues and skin^[1,9]. This will also account for our marginally decreased requirement for plastic surgical intervention at 8%, compared to 13% from their data^[1,10].

In our study, soccer was the most common sport (22%) and within this category, the most common fracture was tibia diaphysis (47%). Soccer accounted for 4 of the 7 cases requiring plastic surgery intervention: 3 out of the 9 soccer-related tibial fractures were Gustilo-Anderson Grade 3. This represents the severity of these injuries. Robertson *et al.*^[7] have previously reported on soccer-related fractures. Similar to Court-Brown *et al.*^[1], they found that the majority of soccer-related fractures were of the upper limb (68%). In contrast, we found 74% of our soccer-related fractures were of the lower limb. Within our cohort, this reflects a high proportion of tibial diaphyseal, ankle and toe phalanx fractures, which have previously been documented as being high risk for open fractures^[1]. This contrast is likely explained by the higher energy “mechanism of injury” required to sustain an open fracture compared to a closed fracture^[1]: Within soccer, such higher energy “mechanisms of injury” most often involve high-speed collisions between players; with soccer being predominantly a lower limb sport, this then increases the likelihood of soccer-related open fractures being sustained in the lower limb^[1,3,7].

Rugby accounted for 11% of the open fractures secondary to sport. This is similar to the figures reported by Robertson *et al.*^[8] in their paper describing the epidemiology of rugby-related fractures, with rugby accounting for 17% of all sport-related fractures. To note in the present study, six of the nine rugby-related fractures were of the lower limb, with fractures of the ankle comprising half of the lower limb injuries. In contrast, both Robertson *et al.*^[8] and Garraway *et al.*^[11] reported that the upper limb was most at risk of fracture (83% and 42% of injuries respectively); however, as detailed above, there is an increased proportion of lower limb fractures in open fracture cohorts, due to higher proportions of tibial diaphyseal and ankle fractures^[1]. Indeed, Garraway and MacLeod^[11] did record that the lower limb was at greatest risk of dislocations and soft tissue injuries.

Cycling (including road cycling and track cycling) accounted for 9% of all fractures seen in the 15-year period. Mountain Biking accounted for only 5% and this may be a reflection of the protective equipment used in this sport, as road cyclists appear at a higher risk of open fracture compared to their mountain biking counterparts. Both sports showed a preponderance for upper limb injuries, with cycling recording 3 finger

phalanx fractures and 3 forearm fractures (out of a total of 6 fractures) and mountain biking recording 2 forearm fractures. This pattern of injury reflects the findings of Aitken *et al.*^[12], who reported that upper limb fractures occurred 10 times more commonly than lower limb fractures during mountain biking. To note, mountain biking is increasing in popularity, and with our trauma centre being located close to Scotland’s largest mountain biking centre (Glentress), one may expect to detect a significant incidence of injuries from this sport. However, Aitken *et al.*^[12], in their comprehensive study on recreational mountain biking injuries 2011, noted a trend away from serious injury in this sport, as a result of the use of personal protective equipment. This likely accounts for the low incidence observed in our study period.

Similarly, hockey accounted for 9% of all open sport-related fractures. This sport also demonstrated a preponderance for upper limb injuries, with all such fractures occurring within the finger phalanx. Court-Brown *et al.*^[13] have already shown that fractures of the finger phalanx is common in hockey, comprising half of all such fractures in the sport^[3]. Furthermore, Aitken *et al.*^[13] found that while field hockey only accounted for 7% of all sport-related finger phalanx fractures, it was the cause of 50% of all of the open sport-related finger phalanx fractures. Comparatively, this study found that hockey accounted for 40% of all open fractures of the finger. Aitken *et al.*^[13] went on to reason that such injuries are likely due to accidental contact between the hand and either a hockey stick or a hockey ball travelling at speed, and this may be further explained by the pattern of grip around the stick. Players often hold the stick low to the ground during tackles thus increasing the chance of contact with the ball or entrapment with another player’s stick^[13-15]. This continues to be an area where increased protection may benefit participants and decrease the incidence of these injuries^[13-15].

Horse riding accounted for 7% of the open fractures sustained. The mechanism by which injuries are sustained during horse riding are usually high energy - a fall from height at high speed - therefore, there is a clear potential for an open fracture to be sustained as a result of this mechanism^[16,17]. It is important to note that these fractures are often farmyard injuries and have a high risk of contamination^[16,17]. Therefore these fractures should be managed appropriately in line with BOAST guidelines^[18]. Previous studies on horse riding injuries, have shown that sprains are the most prevalent injury type (42%), followed by lacerations and bruises (40%), and then fractures and dislocations (33%)^[16]. There was a near equal proportion of upper and lower limb fractures in the current series (3 upper limb and 2 lower limb open fractures), and while our paper was specifically looking at open fractures, this finding is reflected in other studies. A retrospective study from the United States looking at horse riding injuries, showed that the lower extremity was injured

22.2% of the time and the upper extremity 21.5%, with the remaining injuries being to the head, chest and abdomen^[17].

Skiing accounted for 7% of all sporting-related open fractures. The majority of these were upper limb fractures (5 of 6), with 1 recorded ankle fracture. The low prevalence of open fractures secondary to skiing may reflect our institution's urban geographical location. However, it should be noted that there is an artificial ski slope on the outskirts of the city.

Within skiing, 50% of fractures were in the hand: This may be linked to the composition of the dry-ski slope material, with a high propensity to entrap fingers.

Anatomically, the most common location of fracture was the finger phalanx comprising 35% of all fractures. This again is in keeping with the findings from Court-Brown *et al.*^[3], who found the most common location for sport-related fractures was the finger phalanx, followed by distal radius, metacarpals, clavicle and ankle^[3]. Similar findings have been reported by Aitken *et al.*^[4] in another comprehensive series of sport-related fractures. In contrast, the current study found the next most common fracture locations for sport-related open fractures to be tibial diaphysis, forearm, ankle and metacarpal. This is in keeping with the incidence of open fractures within the general population, with the five most common fracture locations being finger phalanx, tibial diaphyseal, distal radius, toe phalanx and ankle^[1]. It would appear there is a difference between the common presenting locations for sport-related open fractures and sport-related closed fractures^[1,3,4,6]. The exact reasons behind this are difficult to fully define, though it appears that certain fracture locations (tibial diaphysis and ankle) are at an increased risk of open fractures: This is likely due to a combination of the common fracture patterns observed at these sites as well as the volume of surrounding soft tissue cover in these regions^[1]. As such, these fracture locations are more likely to be present within observational open fracture cohorts^[1]. Nevertheless, the number of fractures described in this series are low, and, while this reflects a low incidence of this injury type, we would recommend further large-scale studies on this topic, to better define the epidemiology of open fractures in sport^[1,3,4,6]. Similarly, as with previous papers from our institution, our study reflects the experience of our region: It is likely that the incidence of such fractures will vary in other centres, according to the types of sports that predominate in the studied area^[1,3,4,6].

Regarding further limitations of our study, patient outcomes were not obtained, and this certainly could be an area for future work. Obtained information on the time taken to return to sport or work after injury would be of significant relevance for sporting regulators: A high incidence of injuries requiring long periods of rehabilitation may lead to a review of rules and personal protective equipment: This can serve

to reduce the economic impact of such injuries in professional and recreational sport^[1,3,4,6,15].

In conclusion, the epidemiology of sport-related open fractures from one orthopaedic trauma centre over a 15-year period was reviewed. Soccer and rugby were the most common causative sports, while the finger phalanx and tibial diaphysis were the most common fracture locations. Only 14% of fractures were Gustilo Grade 3 and only 8% required plastic surgical intervention. While open fractures in sport are uncommon, they frequently occur on muddy sport fields or forest tracks and must be treated appropriately. A robust set of guidelines is in place from the British Orthopaedic Association and British Association of Plastic Reconstructive and Aesthetic Surgeons to enable this to be achieved, and these should followed accordingly. Furthermore, a good understanding of the range and variety of sport-related open fractures is beneficial for clinicians and sports therapists, as this allows planning for treatment protocols, rehabilitation and injury prevention.

COMMENTS

Background

Open fractures are uncommon in the United Kingdom sporting population, accounting for less than 2% of all sport-related fractures. However they have a high morbidity, which makes the patient group significant. Currently there is limited evidence in the literature describing the epidemiology of open fractures in sport.

Research frontiers

Despite comprising less than 2% of all sport-related fractures, open fractures in sport represent a very significant injury for the athlete, often resulting from a high energy mechanism and being sustained in an environment with high risk of wound contamination. However, due to the limited incidence of this fracture type, minimal research has been previously performed regarding its epidemiology. Given the potential significant morbidity associated with such injuries, an accurate understanding of the range and variety of sport-related open fractures will allow clinicians and sports therapists to better plan treatment protocols, rehabilitation and injury prevention methods for these fractures.

Innovations and breakthroughs

In the study, the authors analysed the epidemiology of open fractures in sport within our population over a 15-year period. Open sport-related fractures occurred at an annual incidence of 0.01/1000 population. The mean age at injury was 29.2 years; the gender ratio was 7.4:1 (male:female). Soccer and rugby were the most common causative sports while fractures of the finger phalanx and of the tibial diaphysis were the most common sites. 14% of the fractures were Gustilo-grade 3; 8% required plastic surgical intervention. This is the first study to provide a comprehensive description of the epidemiology of this injury type.

Applications

A comprehensive understanding of the predicted patterns of injury and most common causative sports, with this fracture type, can allow sports teams and medical personnel to appropriately plan for such injuries, producing treatment protocols and instigating injury prevention measures. This allows both optimization of the management and outcome of these injuries, as well as potential reduction in their future incidence.

Terminology

An open fracture is a fracture with an associated skin wound which allows the

external environment to communicate with the fracture. The Gustilo-Anderson Classification is a classification system which grades the severity of open fractures into three grades, based on the wound size, the underlying damage to the peri-osteal and neuro-vascular structures, and the ability to achieve direct wound closure. Please refer to the provided reference for the formal classification. A Split Skin Graft is a skin graft which comprises the epidermis and a portion of the dermis: the full thickness of the dermis is not excised in this graft type. An Adipofascial Flap is a portion of adipose and fascial tissue that is based on a perforating artery. This is dissected and elevated from its native location, maintaining the perforator blood supply, and transferred locally to the damage area requiring soft tissue coverage. A Fasciocutaneous Flap is a portion of skin, subcutaneous tissue and fascial tissue that is based on a perforating artery. This is dissected and elevated from its native location, maintaining the perforator blood supply, and transferred locally to the damage area requiring soft tissue coverage.

Peer-review

It is very interesting finding.

REFERENCES

- 1 **Court-Brown CM**, Bugler KE, Clement ND, Duckworth AD, McQueen MM. The epidemiology of open fractures in adults. A 15-year review. *Injury* 2012; **43**: 891-897 [PMID: 22204774 DOI: 10.1016/j.injury.2011.12.007]
- 2 **Fordham S**, Garbutt G, Lopes P. Epidemiology of injuries in adventure racing athletes. *Br J Sports Med* 2004; **38**: 300-303 [PMID: 15155432]
- 3 **Court-Brown CM**, Wood AM, Aitken S. The epidemiology of acute sports-related fractures in adults. *Injury* 2008; **39**: 1365-1372 [PMID: 18514656 DOI: 10.1016/j.injury.2008.02.004]
- 4 **Aitken SA**, Watson BS, Wood AM, Court-Brown CM. Sports-related fractures in South East Scotland: an analysis of 990 fractures. *J Orthop Surg (Hong Kong)* 2014; **22**: 313-317 [PMID: 25550009]
- 5 **Gustilo RB**, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. *J Bone Joint Surg Am* 1976; **58**: 453-458 [PMID: 773941]
- 6 **Court-Brown CM**, Caesar B. Epidemiology of adult fractures: A review. *Injury* 2006; **37**: 691-697 [PMID: 16814787 DOI: 10.1016/j.injury.2006.04.130]
- 7 **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]
- 8 **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]
- 9 **Court-Brown CM**, Biant LC, Clement ND, Bugler KE, Duckworth AD, McQueen MM. Open fractures in the elderly. The importance of skin ageing. *Injury* 2015; **46**: 189-194 [PMID: 25192864 DOI: 10.1016/j.injury.2014.07.021]
- 10 **Court-Brown CM**, Honeyman CS, Clement ND, Hamilton SA, McQueen MM. The role of primary plastic surgery in the management of open fractures. *Injury* 2015; **46**: 2443-2447 [PMID: 26456270 DOI: 10.1016/j.injury.2015.09.037]
- 11 **Garraway M**, Macleod D. Epidemiology of rugby football injuries. *Lancet* 1995; **345**: 1485-1487 [PMID: 7769905]
- 12 **Aitken SA**, Biant LC, Court-Brown CM. Recreational mountain biking injuries. *Emerg Med J* 2011; **28**: 274-279 [PMID: 20659880 DOI: 10.1136/emj.2009.086991]
- 13 **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]
- 14 **Bowers AL**, Baldwin KD, Sennett BJ. Athletic hand injuries in intercollegiate field hockey players. *Med Sci Sports Exerc* 2008; **40**: 2022-2026 [PMID: 18981949 DOI: 10.1249/MSS.0b013e318182afe3]
- 15 **Murtaugh K**. Field hockey injuries. *Curr Sports Med Rep* 2009; **8**: 267-272 [PMID: 19741355 DOI: 10.1249/JSR.0b013e3181b7f1f4]
- 16 **Christey GL**, Nelson DE, Rivara FP, Smith SM, Condie C. Horseback riding injuries among children and young adults. *J Fam Pract* 1994; **39**: 148-152 [PMID: 8057065]
- 17 **Thomas KE**, Annett JL, Gilchrist J, Bixby-Hammett DM. Non-fatal horse related injuries treated in emergency departments in the United States, 2001-2003. *Br J Sports Med* 2006; **40**: 619-626 [PMID: 16611723 DOI: 10.1136/bjsm.2006.025858]
- 18 British Orthopaedic Association and British Association of Plastic, Reconstructive and Aesthetic Surgeons. BOAST 4: The Management of Severe Open Lower Limb Fractures, 2014

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Retrospective Study

Acetabular revisions using porous tantalum components: A retrospective study with 5-10 years follow-up

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Institutional review board statement: The Research Ethics Board has not considered it necessary to formulate authorization for this retrospective study because the data was analyzed anonymously and the results were reported in an aggregate manner.

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: The authors declare that they have no conflict of interest or financial relationships in the realization of this work.

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Abstract

AIM

To evaluate the clinical and X-ray results of acetabular components and tantalum augments in prosthetic hip revisions.

METHODS

Fifty-eight hip prostheses with primary failure of the acetabular component were reviewed with tantalum implants. The clinical records and X-rays of these cases were retrospectively reviewed. Bone defect evaluations were based on preoperative CT scans and classified according to Paprosky criteria of Radiolucent lines and periprosthetic gaps; implant mobilization and osteolysis were evaluated by X-ray. An *ad hoc* database was created and statistical analyses were performed with SPSS software (IBM SPSS Statistics for Windows, version 23.0). Statistical analyses were carried out using the Student's *t* test for independent and paired samples. A *P* value of < 0.05 was considered statistically significant and cumulative survival was calculated by the Kaplan-Meier method.

RESULTS

The mean follow-up was 87.6 ± 25.6 mo (range 3-120 mo). 25 cases (43.1%) were classified as minor defects, and 33 cases (56.9%) as major defects. The preoperative HHS rating improved significantly from a mean of 40.7 ± 6.1 (range: 29-53) before revision, to a mean of 85.8 ± 6.1 (range: 70-94) at the end of the follow-up (Student's *t* test for paired samples: $P < 0.001$). Considering HHS only at the end of follow-up, no statistically significant difference was observed between patients with a major or minor defect (Student's *t* test for independent samples: $P > 0.05$). Radiolucent lines were found in 4 implants (6.9%). Postoperative acetabular gaps were observed in 5 hips (8.6%). No signs of implant mobilization or areas of periprosthetic osteolysis were found in the x-rays at the final follow-up. Only 3 implants failed: 1 case of infection and 2 cases of instability. Defined as the end-point, cumulative survival at 10 years was 95% (for all reasons) and 100% for aseptic loosening of the acetabular component.

CONCLUSION

The medium-term use of prosthetic tantalum components in prosthetic hip revisions is safe and effective in a wide variety of acetabular bone defects.

Key words: Porous tantalum; Bone defect; Acetabular revision; Osseointegration; Biological fixation; Augment; Retrospective study

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Core tip: Revisions of acetabular implant components are frequently associated with bone defects. Porous tantalum acetabular cups and augments were introduced to improve biological fixing and restore the normal centre of rotation. The greatest advantage is for major bone defects, where the tantalum cup and augments provide stable primary fixing with the biological potential for bone ingrowth. Nowadays, porous tantalum represents the ideal bone substitute in prosthetic revisions.

Evola FR, Costarella L, Evola G, Barchitta M, Agodi A, Sessa G. Acetabular revisions using porous tantalum components: A retrospective study with 5-10 years follow-up. *World J Orthop* 2017; 8(7): 553-560 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v8/i7/553.htm> DOI: <http://dx.doi.org/10.5312/wjo.v8.i7.553>

INTRODUCTION

The revision of the acetabular component of a prosthetic implant is frequently associated with a bone defect. Different types of treatment and its complications are described in the literature: The use of structural allograft from cadaver or synthetic bone substitutes with anti-protrusion rings or reconstruction

cages do not fix biologically and are at high risk of medium-term failure (15%-45% within 10 years)^[1-7]. The use of morcellised bone grafts (impaction grafting) with cemented acetabular inserts can cause fractures, resorption with implant migration, and transmission of infectious diseases^[8,9]. Implanting bilobed oblong cups or extra-large uncemented hemispherical so-called "jumbo cups" can destroy the rear column because the upper and lower bone defects are larger than the front and back ones^[10,11]. High hip centres alter joint bio-mechanics and are associated with greater risks of dislocation and mobilization^[12,13]. Cementless fixing in primary and revision implants has demonstrated greater survival in the medium and long-term compared to cemented fixing^[13-15].

Biological bone integration of the implant requires intimate contact between the components and bone and immediate mechanical stability during the operation; often the surgeon is forced to implant the acetabular component high up in the revisions leading to altered abductor muscle function and heterometry of the limbs^[16]. In the last decade porous tantalum-made acetabular cups and augments have been introduced to improve biological fixing in bone defects and allow the normal centre of rotation to be restored^[13,17].

Tantalum is a ductile metal, inert and bio-compatible *in vivo*. Porous tantalum, produced through a process of chemical deposition of the metal in a reticulated skeleton in glassy carbon, is 80% porous, has an average pore size of 550 microns, an elastic modulus of 3.1 Gigapascals (Gpa) and a friction coefficient of 0.88 to form a structure very similar to cancellous bone^[17]. Due to its three-dimensional structure and bioactivity, porous tantalum has shown complete bone integration in animal models in 4-6 wk from implantation^[18]. Furthermore, compared to titanium implants, it can fill up periprosthetic gaps of up to 5 mm^[17,18]. Therefore the use of tantalum components represents a viable alternative to traditional surgical techniques, especially in the presence of large bone defects, because the implant can achieve immediate stability. There are only a few studies in the literature with small samples of tantalum components in hip revisions, the majority of these studies being short term.

The aim of this study is to evaluate the clinical and radiographic results of acetabular components and tantalum augments in prosthetic hip revisions, and assess whether bone defect types can compromise outcomes or the medium term survival of the implants.

MATERIALS AND METHODS

From December 2006 to December 2011, 58 hip prostheses with primary failure of the acetabular component were reviewed with implants in tantalum. A retrospective review of the clinical records and X-rays of these cases was performed. Patients underwent clinical and radiographic evaluation before and after the review procedure at regular intervals. Clinical

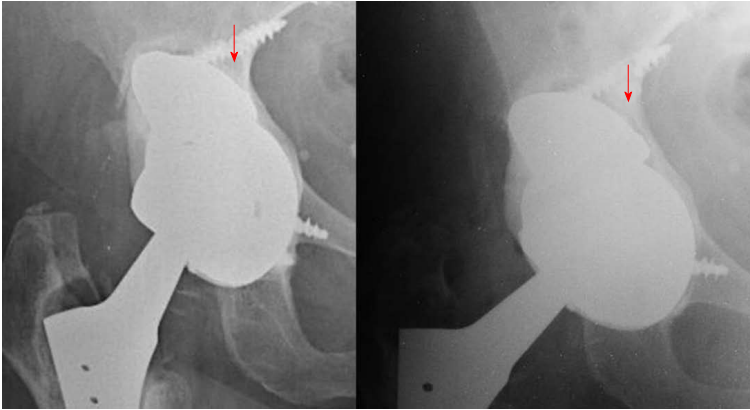


Figure 1 Radio-lucent line in the prosthesis.

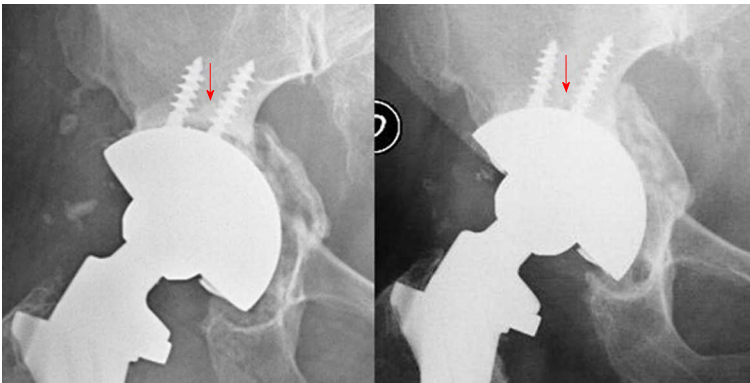


Figure 2 Gaps in the prosthesis.

evaluation was performed pre-operatively and at the end of the follow-up, using the Harris Hip Score (HHS): A score of 91 to 100 was considered as “excellent”, 81 to 90 as “good”, 71 to 80 as “fair”, and below 70 as “poor”.

Radiographic evaluation was performed with axial and front-rear views of the pelvis; X-rays were evaluated by two independent orthopedists (GL and SB) who did not take part in this project. Radio-lucent lines, periprosthetic gaps, implant mobilization and osteolysis were evaluated radiographically. Radio-lucent lines of the acetabular components and augments were described according to the DeLee *et al.*^[19] criteria and measured through a transparent ruler; radio-lucent lines are considered significant if > 2 mm or progressive (Figure 1). Acetabular gaps were defined as areas in which the prosthesis surface did not achieve direct initial contact with the bone in early postoperative X-rays. The gaps differentiate from radio-lucent lines appearing on subsequent X-rays and are measured through a transparent ruler; acetabular gaps were considered positive when > 1 mm on the initial postoperative X-ray (Figure 2). Implant mobilization is defined by angle inclinations over 8° compared to post-operative X-ray checks or the presence of radiolucent lines in all three DeLee and Charnley zones^[20,21]. X-ray evidence of stable implant fixing was shown by prosthesis contact with the bone and no radiolucent lines in 2 of the 3 zones. Osteolysis is the presence of a > 4 mm lucent area (by X-ray) near the prosthesis^[22].

The evaluation of bone defects was based on

preoperative CT scans and classified by Paprosky criteria^[23]. Type 1: Limited bone defect, with unaltered rhyme, wall and columns; type 2 (A, B, C): Unaltered columns, but with deformed rhyme and walls; type 3 (A and B): Destroyed posterior column.

According to Watson-Jones, an anterolateral approach has been used in all procedures, regardless of the type of surgery previously performed. Twenty-eight (48.3%) uncemented press-fit Trabecular Metal Monoblock Acetabular Cups (Zimmer®) and thirty (51.7%) Trabecular Metal Revision Shells (Zimmer®) were implanted. The decision to use adjunctive screw fixes in uncemented Monoblock cups was taken intra-operatively. For complex acetabular revisions, Revision Shells offer the most versatile option, because the polyethylene liner is cemented inside the cup with adjustable inclination and anteversion; furthermore, the non-modular component offers advantages over the modular component having a lower modulus of elasticity and better screw fixing and positioning directly through the tantalum shell.

The tantalum augments, of different shapes and sizes, with rim screw holes, are used to restore the center of rotation and the normal bio-mechanics of the hip, fill large bone defects ($> 50\%$) and restore the acetabular support margins, to allow greater prosthesis-bone contact and better mechanical stability^[16,18,22].

The decision to use augments was based on bone defect and intraoperative prosthetic stability. Augments are screw-fixed into the acetabulum and separated from the prosthesis with a thin layer of polymethyl-

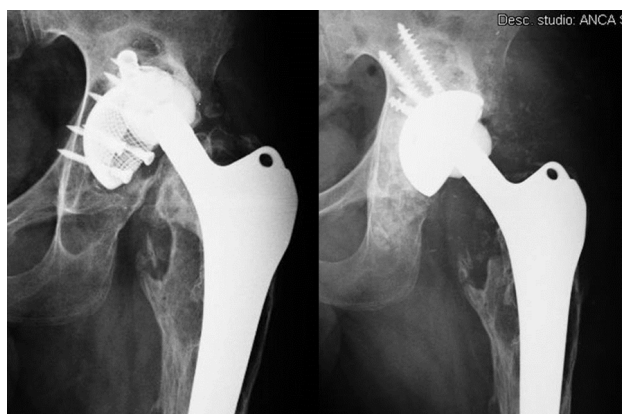


Figure 3 Acetabular revisions with minor bone defects.

methacrylate; they also reduce the use of morcellised bone or structural cadaver bone and are resistant to fractures, mobilization, and resorption, which, however, can affect massive grafts as a result of vascular integration and periprosthetic bone remodelling^[24]. Augments were used in 16 cases: 3 type 2C, 8 type 3A, 5 in type 3B. Autologous morcellised bone from acetabular reamers, or homologous from the frozen head of the femur, was inserted between the implant and the remaining bone defect and has been used in 38 revision procedures of (29 major and 3 minor). Structural bone grafts, synthetic bones nor demineralized bone matrices were not used.

Experienced prosthetic hip surgeons performed the revisions. After surgery, an abduction brace was applied for two days after surgery and partial load with crutches for at least thirty days was recommended. A specific rehabilitation program was used to prevent mobilization or early dislocation of the implant. Data were analyzed anonymously and results were reported in an aggregate manner.

Statistical analysis

All the data was made into an *ad hoc* database and statistical analyses were performed using the SPSS software (IBM SPSS Statistics for Windows, version 23.0). Descriptive statistics were used to characterize the population using frequencies and means \pm SD. Statistical analyses of HHS were carried out using the Student's *t* test for independent and paired samples. A *P* value of < 0.05 was considered statistically significant. A standard life table was constructed, and cumulative survival was calculated by means of the Kaplan-Meier method, using all causes and infections of the acetabular component as end-points.

Statistical analyses were performed by two Authors (Antonella Agodi and Martina Barchitta) using the SPSS software (IBM SPSS Statistics for Windows, version 23.0).

RESULTS

During the study period, a total of 58 acetabular

Table 1 Main characteristics of patients and procedures *n* (%)

Characteristic	
Age, mean \pm SD, yr	71.9 \pm 5.5
Gender	
Male	27 (46.6)
Female	31 (53.4)
Revision motive	
Aseptic loosening	49 (84.5)
Polyethylene wear	7 (12.1)
Infection	2 (3.4)
Paprosky's classification	
Type 2A	11 (19.0)
Type 2B	14 (24.1)
Type 2C	13 (22.4)
Type 3A	15 (25.9)
Type 3B	5 (8.6)
Augment usage among 2C, 3A and 3B	16 (48.5)
Average follow-up, mo, (\pm SD; range)	87.6 (\pm 25.6; range 3-120)

revisions were performed and reviewed. The main patient and procedure characteristics are reported in Table 1. There were 31 women (53.4%) and 27 men (46.6%) with a mean age of 71.9 years (range: 42-82 years) at the time of revision. The most frequent indicator for revision was aseptic loosening of the implant (84.5%).

According to Paprosky's classification, 11 hips (19.0%) were type 2A, 14 (24.1%) were type 2B, 13 (22.4%) were type 2C, 15 (25.9%) were type 3A and 5 (8.6%) were type 3B. Thus, a total of 25 cases (43.1%) were classified as minor defects (types 2A and 2B) (Figure 3) and 33 cases (56.9%) as major defects (types 2C, 3A and 3B) (Figure 4).

The mean follow-up was 87.6 ± 25.6 mo (range 3-120 mo). The preoperative HHS rating improved significantly from a mean of 40.7 ± 6.1 (range: 29-53) before revision, to a mean of 85.8 ± 6.1 (range: 70-94) at the end of the follow-up (Student's *t*-test for paired samples: $P < 0.001$), with 75.6% of patients in the "excellent" or "good" categories.

Considering only the HHS at the end of the follow-up, no statistically significant difference was observed between patients with a major defect (types 2C, 3A and 3B, mean HHS 86.3 ± 4.9) and patients with a minor defect (types 2A and 2B, mean HHS 85.3 ± 7.5) (Student's *t* test for independent samples: $P > 0.05$). HHS ratings of patients with implant failure were not included in these analyses.

Radiolucent lines were found in 4 implants (6.9%): In 3 implants the lines were not more than 2 mm or progressive and involved only one of the three DeLee and Charnley areas, while in 1 implant, which was revised because of infection, they were progressive. Therefore all implants, except the one revised for an infection, were X-ray defined as stable. The excellent osteoconductive properties of tantalum enabled rapid strong biological fixing, even where there was limited vital bone, especially in major defects.

Postoperative acetabular gaps were observed in 5 hips (8.6%) all of which disappeared during the initial

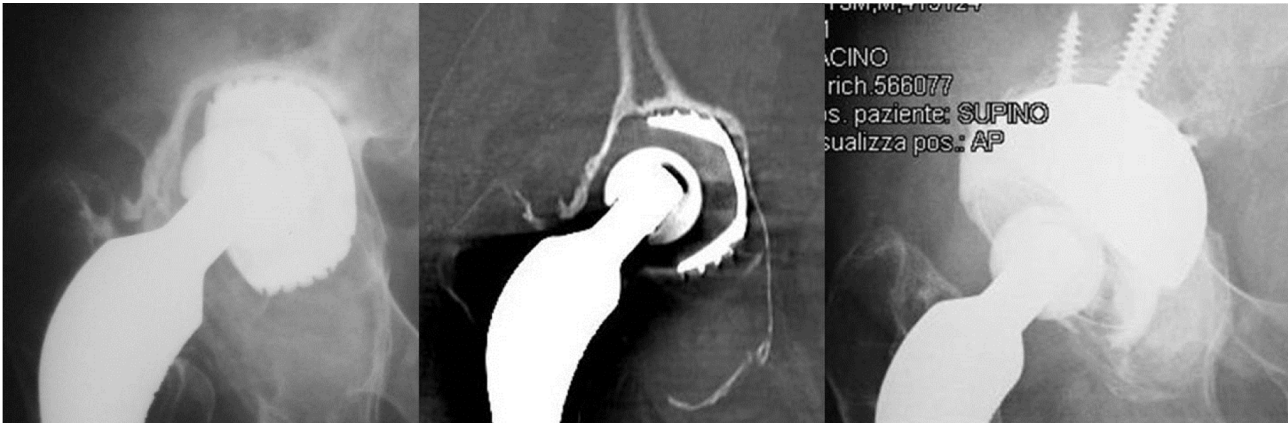


Figure 4 Acetabular revisions with major bone defects.

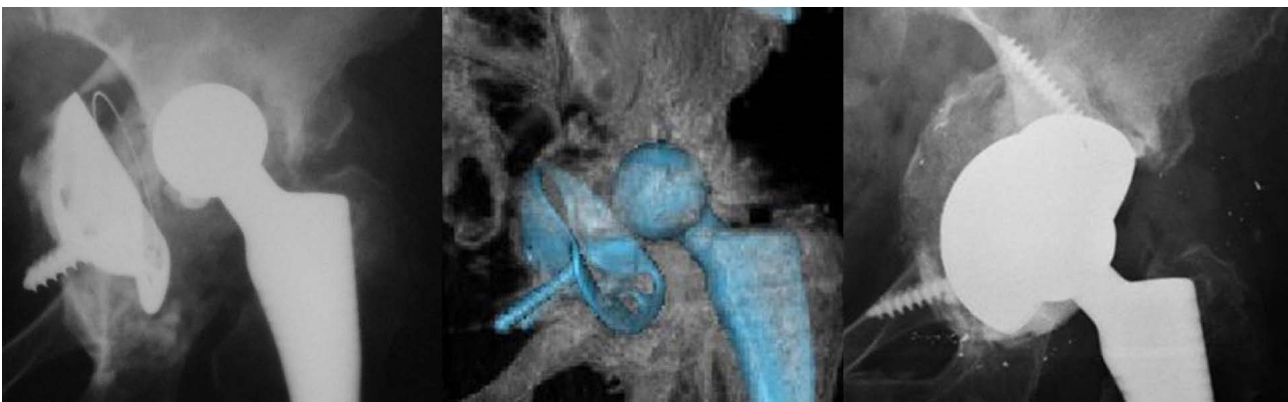


Figure 5 Failure of acetabular revision.

12 mo after surgery and thus were not found at the final follow-up.

No signs of implant mobilization or areas of periprosthetic osteolysis were found in the X-rays at the final follow-up. Morcellised bone grafts with augments to fill bone defects showed no signs of resorption in regular X-ray controls. Only 3 implants failed: 1 case of infection (6 mo after surgery) (Figure 5) and 2 cases of instability (3 and to 4 mo after surgery). The first patient with instability was treated with dislocation reduction and a tutor for 30 d; the second patient with instability required revision surgery implant a constrained liner for chronic instability. In the patient with infection, because of poor general condition and limited functional requirements, the implant was removed and treated with Girdlestone resection arthroplasty. Minor complications were: 2 cases of deep vein thrombosis treated with heparin, 1 case of superficial infection treated with surgical revision of the wound, 1 case of neuro apraxia of the sciatic nerve resolved spontaneously after 2 mo from surgery. None of the patients underwent revision for aseptic loosening until the final follow-up.

Defined as the end-point, cumulative survival at 10 years was 95% (for all reasons) and 100% for aseptic

loosening of the acetabular component (Figure 6).

DISCUSSION

Treatment of a failed acetabular component in total hip prosthesis is technically demanding because immediate and long term stability of the implant is required, as well as maintaining or increasing bone stock, restoring the centre of rotation, and preventing limb discrepancy.

Traditional hemispherical cups (titanium alloy and cobalt chromium alloy) are an effective solution in revisions where adequate bone stock (> 50%) is available to support the acetabular component and allow for bone ingrowth^[16,17,22,25,26]. In cases where the biological potential and mechanical stability of the prosthetic implant are compromised by bone deficit (< 50% acetabular bone available to support the acetabular component), alternative treatments should be used^[7,27].

Porous tantalum implants have been used since 1997 and provide excellent initial stability and bone ingrowth. The higher porosity (80%) promotes better growth of vascularized bone inside the prosthesis (microfixing) in comparison to common porous sur-

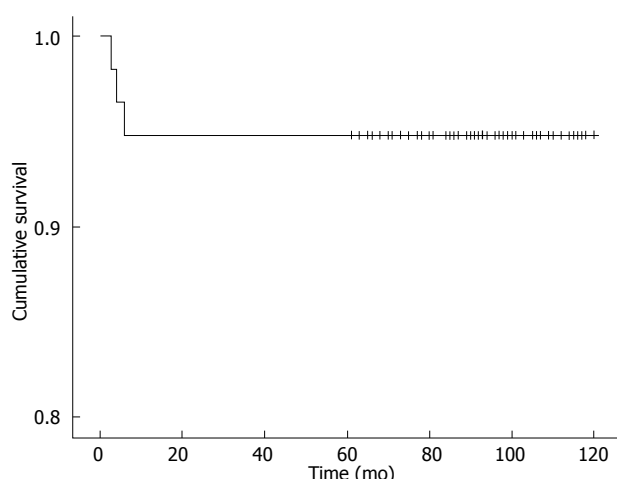


Figure 6 Survival analysis of the study's 58 patients.

faces; the high coefficient of friction to the cancellous (0.88) and cortical (0.74) bone ensures greater primary stability (macrofixing); the low modulus of elasticity (3.1 GPa) brings the material closer to the trabecular bone (1.5 GPa) compared to titanium (110 GPa) and cobalt-chromium (220 GPa), allowing greater load-induced bone remodelling and minimized stress shielding near the cup^[17]. The three-dimensional structure and excellent osteoconductive properties of porous tantalum provide faster and stronger biological fixing when there is limited vital bone availability, and facilitate the restoration of the bone stock^[28].

The ingrowth properties of porous tantalum are superior to bone graft in revision surgery; allograft reabsorption can lead to component instability, while porous tantalum maintains its structure and stability^[26]. A stable bone-implant interface and favourable osteoconductive properties of the material are important for bone ingrowth of prostheses. Furthermore, the availability of augments in tantalum has reduced the need for structural bone grafts in revisions and safer recovery of the hip rotation centre.

Clinical evaluation at the final follow-up showed a statistically significant increase in preoperative HHS from 40.7 to 85.8. In this study we did not find a statistically significant association between bone defect size and increased clinical results at final follow-up, demonstrating that the clinical results of acetabular revisions with tantalum components do not seem to be influenced by the degree of preoperative bone defect. However, other authors have shown that clinical outcomes are influenced by bone defects when using traditional techniques, such as structural bone grafting and reconstruction cages^[18,29].

X-rays revealed no prosthetic implant migration. Some non-progressive radiolucent lines in three implants were probably due to some fibrous fixing in part of the implant, and requires X-ray monitoring in the future.

Several authors report instability as the main

cause of failure of tantalum implants^[1,16]. In this study the survival of the implants for 10 years was 95%, considering the revision for any reason as end-point. Of the three reported failures, two were for implant dislocation. Only one failure showed incorrect positioning of the socket.

High numbers of dislocations in the literature suggest that special attention should be addressed to correcting the centre of rotation and implant positioning, and to using constrained implants in cases of deficient abductor mechanisms.

Limitations

This study has several limitations: (1) it is a retrospective study with a limited sample size, heterogeneous patient ages and a variety of bone defects; (2) restoring the normal rotation centre of the implant was not monitored by X-ray (calculating the vertical and horizontal distance from the inter-teardrop line); (3) the study did not consider the size of the acetabular component and femoral head diameter according to preoperative bone defect; and (4) this study has not control group for comparison. A future multi-centre study including homogeneous samples by age and bone defect would be useful in assessing the medium and long-term clinical and X-ray results of tantalum implants in prosthetic hip revisions.

In conclusion, the medium-term use of prosthetic tantalum components in prosthetic hip revisions is safe and effective in a wide variety of acetabular bone defects. The greatest advantage is found in major bone defects, where the tantalum cup and augments provide stable primary fixation with the biological potential for bone ingrowth. Despite these advantages, the metallic debris effects of this material are still unknown. Long-term studies are needed to evaluate the longevity of these implants and demonstrate their advantages over conventional methods such as massive grafting and reconstruction cages. Nowadays, porous tantalum represents the ideal bone substitute in prosthetic revisions.

COMMENTS

Background

This study evaluates the results of acetabular components and tantalum augments in prosthetic hip revisions, assessing whether the type of bone defect can compromise the outcome or the medium-term survival of the implants. In this study the authors did not find a statistically significant association between the size of the bone defect and increased clinical results. Defined as the end-point, cumulative survival at 10 years was 95% (for all reasons) and 100% for aseptic loosening of the acetabular component.

Research frontiers

Treating the failure of the acetabular component in total hip prosthesis is technically demanding because of significant bone defect. Nowadays, studies are being directed towards searching for a material which possesses bone-like biomechanical characteristics. Porous tantalum implants provide excellent initial stability, bone ingrowth and allow for greater load-induced bone remodelling near the cup.

Innovations and breakthroughs

There are few studies on hip revisions with tantalum components in the literature where the samples are small, have non-homogeneous bone defect severity and short term follow-ups. This study evaluates the medium-term clinical and X-ray results of tantalum components in acetabular revisions with major bone defects.

Applications

The use of prosthetic tantalum components in prosthetic hip revisions is safe and effective for large acetabular bone defects. Nowadays, porous tantalum represents the ideal bone substitute in prosthetic revisions and provides excellent mechanical stability of the implants.

Terminology

Tantalum is a ductile metal, inert and bio-compatible *in vivo*. Due to its three-dimensional structure and bioactivity, porous tantalum has a structure very similar to cancellous bone.

Peer-review

This is an interesting manuscript dealing with a popular field of revision hip arthroplasty.

REFERENCES

- 1 **Issack PS.** Use of porous tantalum for acetabular reconstruction in revision hip arthroplasty. *J Bone Joint Surg Am* 2013; **95**: 1981-1987 [PMID: 24196469 DOI: 10.2106/JBJS.L.01313]
- 2 **Bostrom MP, Lehman AP, Buly RL, Lyman S, Nestor BJ.** Acetabular revision with the Contour antiprotusio cage: 2- to 5-year followup. *Clin Orthop Relat Res* 2006; **453**: 188-194 [PMID: 17016217 DOI: 10.1097/01.blo.0000246533.37006.b0]
- 3 **Beckmann NA, Weiss S, Klotz MC, Gondan M, Jaeger S, Bitsch RG.** Loosening after acetabular revision: comparison of trabecular metal and reinforcement rings. A systematic review. *J Arthroplasty* 2014; **29**: 229-235 [PMID: 23719095 DOI: 10.1016/j.arth.2013.04.035]
- 4 **Brüggemann A, Fredlund E, Mallmin H, Hailer NP.** Are porous tantalum cups superior to conventional reinforcement rings? *Acta Orthop* 2017; **88**: 35-40 [PMID: 27892748 DOI: 10.1080/17453674.2016.1248315]
- 5 **Sessa G, Costarella L, Pavone V, Graceffa A, Evola G, Evola FR.** Equine bone tissue in acetabular revision: our experience. *Minerva Ortopedica e Traumatologica* 2010; **61**: 469-476
- 6 **Flecher X, Paprosky W, Grillo JC, Aubaniac JM, Argenson JN.** Do tantalum components provide adequate primary fixation in all acetabular revisions? *Orthop Traumatol Surg Res* 2010; **96**: 235-241 [PMID: 20488141 DOI: 10.1016/j.otsr.2009.11.014]
- 7 **Van Kleunen JP, Lee GC, Lementowski PW, Nelson CL, Garino JP.** Acetabular revisions using trabecular metal cups and augments. *J Arthroplasty* 2009; **24**: 64-68 [PMID: 19339154 DOI: 10.1016/j.arth.2009.02.001]
- 8 **Busch VJ, Gardeniers JW, Verdonschot N, Slooff TJ, Schreurs BW.** Acetabular reconstruction with impaction bone-grafting and a cemented cup in patients younger than fifty years old: a concise follow-up, at twenty to twenty-eight years, of a previous report. *J Bone Joint Surg Am* 2011; **93**: 367-371 [PMID: 21325588 DOI: 10.2106/JBJS.I.01532]
- 9 **van Egmond N, De Kam DC, Gardeniers JW, Schreurs BW.** Revisions of extensive acetabular defects with impaction grafting and a cement cup. *Clin Orthop Relat Res* 2011; **469**: 562-573 [PMID: 20931308 DOI: 10.1007/s11999-010-1618-8]
- 10 **Hendricks KJ, Harris WH.** Revision of failed acetabular components with use of so-called jumbo noncemented components. A concise follow-up of a previous report. *J Bone Joint Surg Am* 2006; **88**: 559-563 [PMID: 16510823 DOI: 10.2106/JBJS.E.00389]
- 11 **Dearborn JT, Harris WH.** Acetabular revision arthroplasty using so-called jumbo cementless components: an average 7-year follow-up study. *J Arthroplasty* 2000; **15**: 8-15 [PMID: 10654456]
- 12 **Dearborn JT, Harris WH.** High placement of an acetabular component inserted without cement in a revision total hip arthroplasty. Results after a mean of ten years. *J Bone Joint Surg Am* 1999; **81**: 469-480 [PMID: 10225792]
- 13 **Flecher X, Appy B, Parratte S, Ollivier M, Argenson JN.** Use of porous tantalum components in Paprosky two and three acetabular revision. A minimum five-year follow-up of fifty one hips. *Int Orthop* 2017; **41**: 911-916 [PMID: 27766385 DOI: 10.1007/s00264-016-3312-2]
- 14 **Whitehouse MR, Masri BA, Duncan CP, Garbuz DS.** Continued good results with modular trabecular metal augments for acetabular defects in hip arthroplasty at 7 to 11 years. *Clin Orthop Relat Res* 2015; **473**: 521-527 [PMID: 25123241 DOI: 10.1007/s11999-014-3861-x]
- 15 **Evola FR, Evola G, Graceffa A, Sessa A, Pavone V, Costarella L, Sessa G, Avondo S.** Performance of the CLS Spotorno uncemented stem in the third decade after implantation. *Bone Joint J* 2014; **96-B**: 455-461 [PMID: 24692610 DOI: 10.1302/0301-620X.96B4.32607]
- 16 **Banerjee S, Issa K, Kapadia BH, Pivec R, Khanuja HS, Mont MA.** Systematic review on outcomes of acetabular revisions with highly-porous metals. *Int Orthop* 2014; **38**: 689-702 [PMID: 24178061 DOI: 10.1007/s00264-013-2145-5]
- 17 **Batuyong ED, Brock HS, Thiruvengadam N, Maloney WJ, Goodman SB, Huddleston JI.** Outcome of porous tantalum acetabular components for Paprosky type 3 and 4 acetabular defects. *J Arthroplasty* 2014; **29**: 1318-1322 [PMID: 24405625 DOI: 10.1016/j.arth.2013.12.002]
- 18 **Fernández-Fairen M, Murcia A, Blanco A, Meroño A, Murcia A, Ballester J.** Revision of failed total hip arthroplasty acetabular cups to porous tantalum components: a 5-year follow-up study. *J Arthroplasty* 2010; **25**: 865-872 [PMID: 19748208 DOI: 10.1016/j.arth.2009.07.027]
- 19 **DeLee JG, Charnley J.** Radiological demarcation of cemented sockets in total hip replacement. *Clin Orthop Relat Res* 1976; **(121)**: 20-32 [PMID: 991504]
- 20 **Massin P, Schmidt L, Engh CA.** Evaluation of cementless acetabular component migration. An experimental study. *J Arthroplasty* 1989; **4**: 245-251 [PMID: 2795031]
- 21 **Zicat B, Engh CA, Gokcen E.** Patterns of osteolysis around total hip components inserted with and without cement. *J Bone Joint Surg Am* 1995; **77**: 432-439 [PMID: 7890792]
- 22 **Weeden SH, Schmidt RH.** The use of tantalum porous metal implants for Paprosky 3A and 3B defects. *J Arthroplasty* 2007; **22**: 151-155 [PMID: 17823035 DOI: 10.1016/j.arth.2007.04.024]
- 23 **Paprosky WG, Perona PG, Lawrence JM.** Acetabular defect classification and surgical reconstruction in revision arthroplasty. A 6-year follow-up evaluation. *J Arthroplasty* 1994; **9**: 33-44 [PMID: 8163974]
- 24 **Macheras GA, Papagelopoulos PJ, Kateros K, Kostakos AT, Baltas D, Karachalios TS.** Radiological evaluation of the metal-bone interface of a porous tantalum monoblock acetabular component. *J Bone Joint Surg Br* 2006; **88**: 304-309 [PMID: 16498001 DOI: 10.1302/0301-620X.88B3.16940]
- 25 **Del Gaizo DJ, Kancherla V, Sporer SM, Paprosky WG.** Tantalum augments for Paprosky IIIA defects remain stable at midterm followup. *Clin Orthop Relat Res* 2012; **470**: 395-401 [PMID: 22090355 DOI: 10.1007/s11999-011-2170-x]
- 26 **Moličnik A, Hanc M, Rečnik G, Krajnc Z, Ruprecht M, Fokter SK.** Porous tantalum shells and augments for acetabular cup revisions. *Eur J Orthop Surg Traumatol* 2014; **24**: 911-917 [PMID: 24241214 DOI: 10.1007/s00590-013-1354-3]
- 27 **Davies JH, Laflamme GY, Delisle J, Fernandes J.** Trabecular metal used for major bone loss in acetabular hip revision. *J Arthroplasty* 2011; **26**: 1245-1250 [PMID: 21481564 DOI: 10.1016/j.arth.2011.02.022]
- 28 **Lachiewicz PF, Soileau ES.** Tantalum components in difficult acetabular revisions. *Clin Orthop Relat Res* 2010; **468**: 454-458 [PMID: 19582528 DOI: 10.1007/s11999-009-0940-5]

- 29 Skyttä ET, Eskelinen A, Paavolainen PO, Remes VM. Early results of 827 trabecular metal revision shells in acetabular revision. *J*

Arthroplasty 2011; **26**: 342-345 [PMID: 20932708 DOI: 10.1016/j.arth.2010.01.106]

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Retrospective Study

Non-ossifying fibromas: Case series, including in uncommon upper extremity sites

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Author contributions: Sakamoto A drafted the manuscript; Arai R and Okamoto T participated in the design of the study; Matsuda S conceived of the study, participated in its design and coordination, and helped draft the manuscript; all authors read and approved the final manuscript.

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Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient had been notified at the home page of National Hospital Organization, Kokura Medical Center that the data could be used for a clinical study.

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Abstract

AIM

To investigate non-ossifying fibromas (NOFs) common fibrous bone lesions in children that occur in bones of the lower extremities.

METHODS

We analyzed 44 cases of NOF including 47 lesions, which were referred with a working diagnosis of neoplastic lesions. Lesions were located in the upper extremities (1 proximal humerus, 1 distal radius) and the lower extremities (25 distal femurs, 12 proximal and 4 distal tibias, and 4 proximal fibulas).

RESULTS

Three cases had NOFs in multiple anatomical locations (femur and fibula in 1 case, femur and tibia in 2 cases). Overall, larger lesions > 4 cm and lesion expansion at the cortex were seen in 21% and 32% of cases, respectively. Multiple lesions with bilateral symmetry in the lower extremities suggest that these NOFs were developmental bone defects. Two patients suffered from fracture and were treated without surgery, one in the radius and one in the femur. Lesions in the upper extremities (*i.e.*, humerus of a 4-year-old female and radius of a 9-year-old male) expanded at the cortex and lesion size increased with slow ossification.

CONCLUSION

NOFs in the lower extremity had fewer clinical problems, regardless of their size and expansiveness. In these two upper extremity cases, the NOFs had aggressive biological features. It seems that there is a site specific difference, especially between the upper extremity and the lower extremity. Furthermore, NOFs in the radius are predisposed to fracture because of the slender structure of the radius and the susceptibility to stress.

Key words: Non-ossifying fibroma; Humerus; Radius; Fibula; Upper extremity

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Core tip: Non-ossifying fibromas (NOFs) are common lesions in the lower extremities of children. We analyzed 44 cases of NOF including 47 lesions comprising 2 upper extremity cases and 45 lower extremity cases. Larger lesions > 4 cm and lesion expansion at the cortex were seen in 21% and 32% of cases, respectively. Lesions in the upper extremities in the humerus and the radius expanded at the cortical bone, and lesion size increased with slow ossification, suggestive of aggressive biological features. Furthermore, NOFs in the radius are predisposed to fracture because of the slender structure of the radius and the susceptibility to stress.

Sakamoto A, Arai R, Okamoto T, Matsuda S. Non-ossifying fibromas: Case series, including in uncommon upper extremity sites. *World J Orthop* 2017; 8(7): 561-566 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v8/i7/561.htm> DOI: <http://dx.doi.org/10.5312/wjo.v8.i7.561>

INTRODUCTION

Non-ossifying fibromas (NOFs) are a common type of benign fibrous lesion that tend to occur in the metaphysis of the long bones in the lower extremities^[1,2]. NOF can be diagnosed based on its presentation on plain radiographs^[3,4] where it typically appears as a small, cortical osteolytic lesion. Approximately 30% of young patients in their first or second decade of life can have a NOF^[2]. Typically, NOFs are asymptomatic and lesions are found incidentally. A lesion is usually self-limiting and disappears by the age of 20 to 25 years in most cases^[3]. Therefore, lesions are considered to be a developmental bone defect rather than a true neoplasm^[1,2]. Histologically, NOFs are composed of spindle-shaped fibroblasts, multinucleated giant cells, and foamy histiocytes, which are identical to a benign fibrous histiocytoma (BFH), which is a neoplastic lesion^[2]. BFHs occur predominantly in adults, and a BFH is considered to have more aggressive biological features compared with a NOF. Interestingly, the current case series includes some patients with NOFs in less common sites such as the humerus, radius, and

fibula. Herein we discuss upper and lower extremity NOFs and emphasize the anatomical differences between them.

MATERIALS AND METHODS

A clinical summary of the 44 cases of NOF is shown in Table 1. A total of 47 lesions were referred to our institution with a working diagnosis of neoplastic lesions. A diagnosis of NOF was made based on plain radiographic findings. NOF appears as a cortically based osteolytic lesion with an osteosclerotic rim. In cases with atypically large lesions, a magnetic resonance image (MRI) examination was added in order to exclude aggressive bone tumors, such as osteosarcomas. The NOF cases we analyzed were in 26 males and 18 females. The average age at the first visit was 10.5 (range, 4 to 16) years. The NOFs were located in a humerus ($n = 1$), radius ($n = 1$), femurs ($n = 25$), tibias ($n = 16$), and fibulas ($n = 4$). Among these cases, lesions occurred in multiple locations in 3 cases with femur involvement, in 2 cases with tibia involvement and in 1 case with femur and fibula involvement. Bilateral lesions, in which the size and the location were almost symmetrical such that we counted them as a single lesion, were seen in 3 cases with femur involvement. The location of each lesion was also classified as anterior, medial, lateral, posterior, or inter-medullary. Findings of expansion at the cortices adjacent to lesions were assessed. A lesion > 4 cm in size was defined as large.

RESULTS

Among the NOF cases, a lesion size > 4 cm was seen in 10 out of 47 (21%) cases. Cortical expansions were seen in 15 out of 47 (32%) cases. The cases of upper extremity NOFs involved 1 humerus and 1 radius. A 4-year-old female had a NOF on the proximal side of her humerus. Plain radiographs revealed a multinodular osteolytic lesion in the cortex on the anterior aspect of the humerus. Thinning and expansion of the adjacent cortex was observed. During a 7-mo follow-up, it was noted that the size of the lesion had increased. Ossification was seen, but the earlier osteolytic finding was still prominent on a follow-up radiograph taken 31 mo later (Figure 1). A 9-year-old male had a NOF on the distal diaphysis of his radius. The lesion was discovered when he sustained a pathological fracture at the site of the lesion. Upon initial assessment, the plain radiographs revealed an irregularity of the adjacent cortex, suggesting a fracture. An osteolytic lesion with marginal sclerosis was seen. The size of the lesion was observed to increase at a 2 years and 5 mo follow-up because the patient had refractured his radius at the lesion site. Although ossification was evident on the proximal aspect of the lesion, an osteolytic lesion was also prominent at the 3-year follow-up (Figure 2).

The cases of lower extremity NOFs involved femurs,

Table 1 Clinical summary of 44 cases with non-ossifying fibromas

Bone site	NOFs, <i>n</i>	M:F	Mean age, yr	R/L/B extremities, <i>n</i>	Lesion > 4 cm, <i>n</i> (%)	Ant/med/lat/post/intramed location, <i>n</i>	Expansion, <i>n</i> (%)	Fracture, <i>n</i> (%)
Humerus	1							
Proximal	1	0:1	4.0	1/0/0	1 (100)	1/0/0/0/0	1 (100)	0
Radius	1							
Distal	1	1:0	7.0	0/1/0	0	0/0/0/0/1	1 (100)	1 (100)
Femur	25							
Distal	25	15:10	9.2	9/9/7	5 (20)	0/5/0/20/0	5 (20)	1 (4)
Tibia	16							
Proximal	12	8:4	14.5	6/6/0	2 (17)	0/4/1/7/0	3 (25)	0
Distal	4	2:2	13.5	3/1/0	2 (50)	0/0/4/0/0	2 (50)	0
Fibula	4							
Proximal	4	2:2	12.5	2/2/0	0	0/0/1/3/0	3 (75)	0
Total lesions ¹	47	26:18	10.5	21/19/7	10 (21)	1/9/6/30/1	15 (32)	2 (4)

¹Total cases *n* = 44. Ant: Anterior; B: Bilateral; F: Female; intramed: Intramedullary; L: Left; lat: Lateral; M: Male; med: Medial; NOFs: Non-ossifying fibromas; post: Posterior; R: Right.

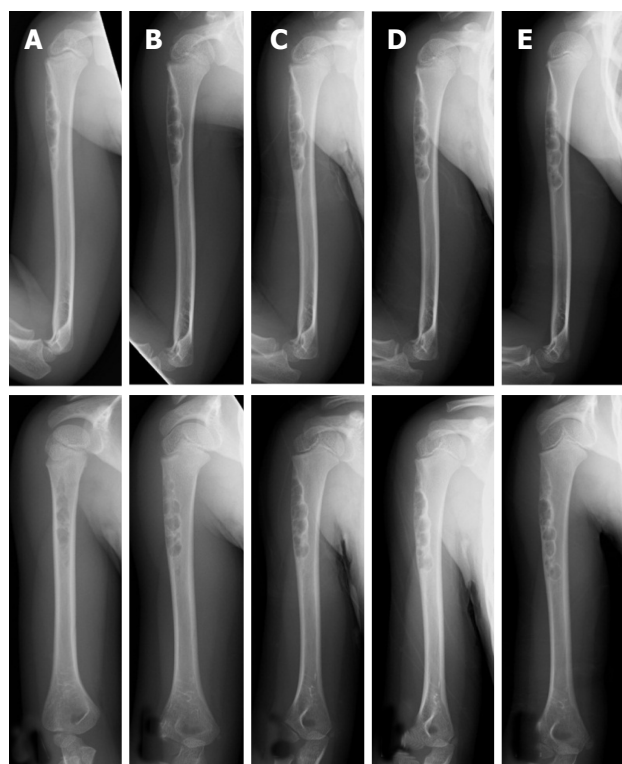


Figure 1 Plain radiographs of a non-ossifying fibroma in the humerus of a 4-year-old female. An osteolytic lesion is shown at the cortex in the proximal humerus (A). Radiographs taken after 7 mo (B), 1 year (C), 1 year and 7 mo (D), and 2 years and 7 mo (E) together reveal the location of the lesion became more distal with growth of the child. The size of the lesion increased as it slowly ossified (plain radiographs: Anteroposterior view, top; lateral view, bottom).

tibias, and fibulas. All femoral lesions were at distal locations. Both large-sized lesions with expansion at the cortex were seen in 20% of cases with femoral involvement. One case of NOF in the femur was diagnosed with a concurrent fracture based on an MRI finding of a high signal intensity at the cortex adjacent to the lesion (Figure 3). Of the 16 cases with tibia involvement, 12 lesions were in a proximal location and 4 were distal. Large-sized lesions occurred in 2

out of 12 (17%) cases in the proximal tibia and in 2 out of 4 (50%) cases in the distal tibia. Extension at the cortex was seen in 3 out of 12 (25%) cases in the proximal tibia and in 2 out of 4 (50%) cases in the distal tibia. These femoral and tibial lesions were in either the medial, lateral, or posterior locations, in contrast to the anterior location in the case of humerus involvement. All 4 cases of NOFs in fibulas presented with lesions in proximal locations. NOF cases with cortical expansion were seen in 3 out of 4 (75%) cases with fibula involvement. One fibular case had multiple lesions that included the femur (Figure 4).

DISCUSSION

NOF predominantly occurs in the lower extremities, especially around the knee^[1,2]. In the current series, the frequency of a distal location in the femur was rather low, because all the referred cases were considered as potential neoplastic lesions, and when small more typical NOFs in the distal femur were identified, the patients were not referred. NOFs are not considered to be true neoplasms, but rather a developmental bone defect^[1-3]. Cases with multiple affected locations, such as the femur and fibula or the femur and tibia, support the notion of a natural developmental defect.

Findings of lesion size increases with expansion at the cortex suggest NOFs can be more aggressive in nature. Cytological abnormalities of translocation (1;4)(p31;q34) and del(4)(p14) supplied evidence for some NOFs with neoplastic characteristics^[5,6]. It is possible that NOFs could have a neoplastic nature because histologically they are indistinguishable from the neoplastic lesions of BFH, which are more aggressive in nature than those of NOFs^[7]. Using image analysis techniques to differentiate between BFHs and NOFs, BFHs appear more likely to have less distinct borders that are central rather than eccentric^[7,8]. BFHs tend to occur in adults, while the vast majority of cases of NOF occur in children. However, it has been

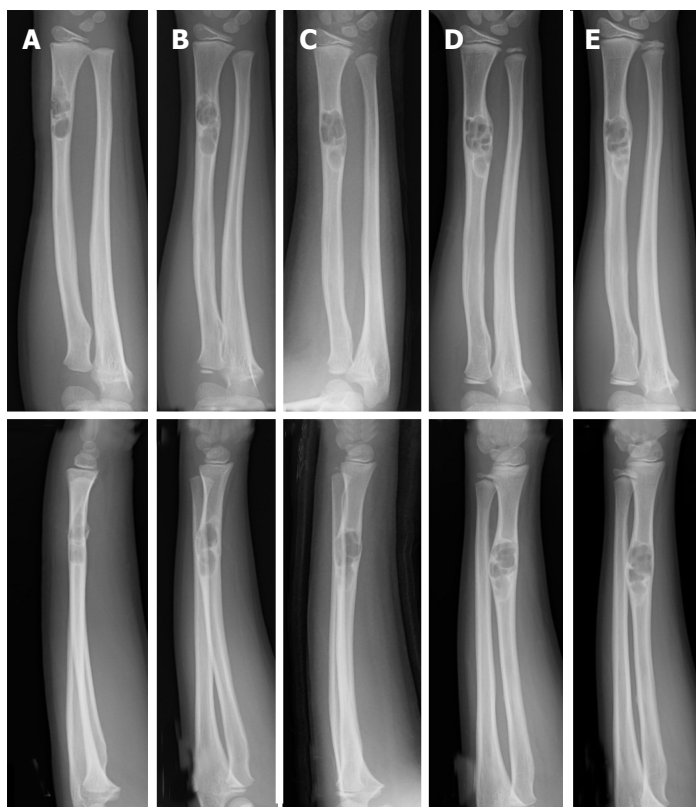


Figure 2 Plain radiographs of a non-ossifying fibroma in the radius of a 9-year-old male. At the initial assessment an osteolytic lesion in the distal radius is shown with an osteosclerotic rim. Fracture of the irregular adjacent cortex is revealed (A). Radiographs taken after 11 mo (B), 2 years and 1 mo (C), 2 years and 5 mo (D), and 3 years (E). The size of the lesion increased and ossification at the distal end was observed (plain radiographs: Anteroposterior view, top; lateral view, bottom).



Figure 3 Plain radiograph and MRI of a NOF in the femur of a 13-year-old male who sustained a fracture. The plain radiographs reveal a multinodular lesion located at the medial posterior part of the distal femur. The lesion is osteolytic at the distal end and ossified at the proximal end. The lesion has expanded at the medial cortex (A). T2-weighted fat-suppression MRIs show high signal intensity and suggest the presence of a fracture (B) (coronal, top; axial, bottom). Radiographs taken after 1 year (C), 1 year and 8 mo (D), and 2 years and 8 mo (E); these radiographs reveal the lesion had enlarged as well as ossified (plain radiographs: anteroposterior view, top; lateral view, bottom).

proposed that BFHs may be underestimated among patients less than 20 years of age, and the diagnosis

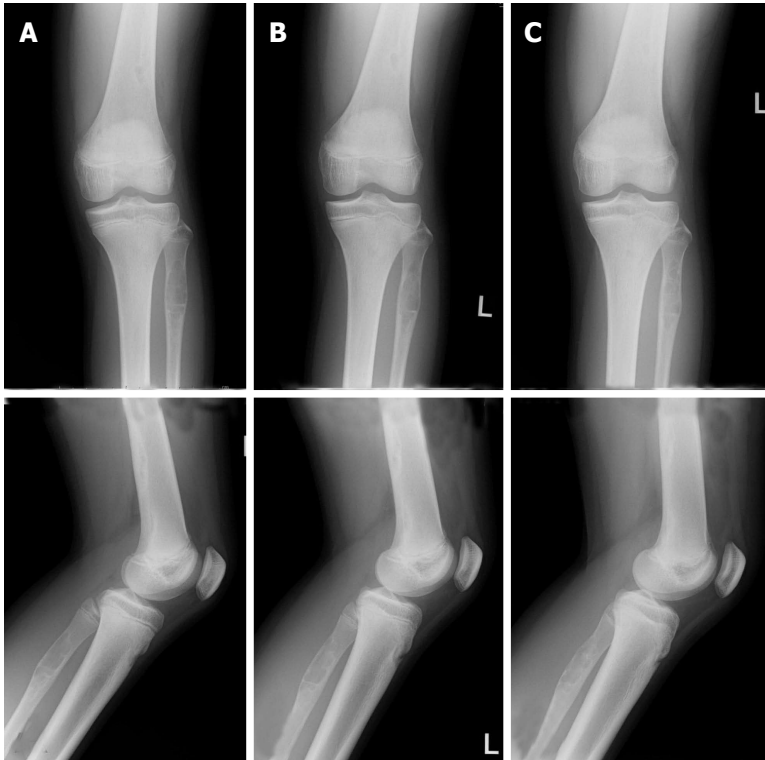


Figure 4 Plain radiographs of non-ossifying fibromas in the femur and the fibula of a 13-year-old female. The radiographs reveal an osteolytic lesion in the proximal fibula, as well as a NOF in the distal femur (A). Radiographs taken after 9 mo (B) and 1 year and 9 mo (C); the femoral and fibular lesions ossified (plain radiographs: Anteroposterior view, top; lateral view, bottom).

of BFH should be considered when NOF-like pathology is accompanied by pain or rapid lesion growth^[7]. In the current series, NOFs in the lower extremities ossified, even in cases with large lesions that increased in size, but none was diagnosed as BFH.

NOFs located in the humerus and radius were included in this study although the upper extremities are an uncommon site for these lesions. Both lesions had extended at the cortex and lesion size increased over time; however, ossification was observed despite osteolytic findings still being prominent at 3 years of follow up. Although the number of upper extremity NOF cases was small, they can have an aggressive nature with BFH-like features when compared with the NOFs in the lower extremities. The NOF located in the radius resulted in a complication when the patient sustained repeated fractures. NOF lesions that occupy more than 50% of the transverse diameter of the involved bone are more likely to lead to a fracture^[2,9]. The slender anatomical structure of the radius would also have contributed to the risk of a pathological fracture at the location of the NOF in this case.

In conclusion, NOFs in lower extremities have the non-neoplastic characteristics of a developmental bone defect. In contrast, NOFs in the humerus and the radius tended to have more aggressive biological characteristics similar in nature to those of BFHs with expansion at the cortex, an increase in size, and slow ossification. It seems that there is a site specific difference between the upper and lower extremities.

In addition, NOFs in the radius are potentially prone to fracture because of the slender structure of the affected bone.

COMMENTS

Background

Non-ossifying fibromas (NOFs) are a common type of benign fibrous lesion that tend to occur in the metaphysis of the long bones in the lower extremities. The upper extremity is less common for NOFs. NOFs are considered to be a developmental bone defect rather than a true neoplasm. However, the histology of NOFs is identical to that of benign fibrous histiocytoma, which is a neoplastic lesion.

Research frontiers

Small NOFs have no clinical significance. The neoplastic characterization of NOFs was difficult. Therefore, the authors collected NOF cases that were referred with a working diagnosis of neoplastic lesions. Consequently, large NOFs with possible aggressive characteristics, as well as NOFs in rare locations, were collected.

Innovations and breakthroughs

The authors analyzed 44 cases of NOFs including 47 lesions comprising two upper extremity cases and 45 lower extremity cases. Clinical information and plain radiographs were collected. The findings associated with possible aggressiveness were further analyzed, such as incidence of fracture and radiographic observations of size and expansiveness. It seems that there is a site specific difference between the upper and lower extremities. NOFs in the lower extremity are considered to be a developmental bone defect rather than a true neoplasm, even though NOFs can be large and have expansion at the cortex. Lesions in the humerus and the radius were expanded at the cortex and lesion size increased with slow ossification. Furthermore, NOFs in the radius are predisposed to fracture because of the slender structure of the radius and

its susceptibility to stress.

Applications

The results are useful for clinicians in the making a diagnosis of NOF and following up the patients.

Terminology

NOF: Non-ossifying fibroma; BFH: Benign fibrous histiocytoma; MRI: Magnetic resonance image.

Peer-review

This is a well-designed paper about a rarely seen clinical condition.

REFERENCES

- 1 **Hetts SW**, Hilchey SD, Wilson R, Franc B. Case 110: Nonossifying fibroma. *Radiology* 2007; **243**: 288-292 [PMID: 17392261 DOI: 10.1148/radiol.2431040427]
- 2 **Dorfman HD**, Czerniak B. Bone tumors. St Louis, MO, Mosby, 1998. *Hum Pathol* 1999; **30**: 1269
- 3 **Betsy M**, Kupersmith LM, Springfield DS. Metaphyseal fibrous defects. *J Am Acad Orthop Surg* 2004; **12**: 89-95 [PMID: 15089082 DOI: 10.5435/00124635-200403000-00004]
- 4 **Hod N**, Levi Y, Fire G, Cohen I, Ayash D, Somekh M, Horne T. Scintigraphic characteristics of non-ossifying fibroma in military recruits undergoing bone scintigraphy for suspected stress fractures and lower limb pains. *Nucl Med Commun* 2007; **28**: 25-33 [PMID: 17159546 DOI: 10.1097/MNM.0b013e328012e3de]
- 5 **Nelson M**, Perry D, Ginsburg G, Sanger WG, Neff JR, Bridge JA. Translocation (1; 4)(p31; q34) in nonossifying fibroma. *Cancer Genet Cytogenet* 2003; **142**: 142-144 [PMID: 12699892 DOI: 10.1016/S0165-4608(02)00805-1]
- 6 **Tarkkanen M**, Kaipainen A, Karaharju E, Böhling T, Szymanska J, Heliö H, Kivioja A, Elomaa I, Knuutila S. Cytogenetic study of 249 consecutive patients examined for a bone tumor. *Cancer Genet Cytogenet* 1993; **68**: 1-21 [PMID: 8330278 DOI: 10.1016/0165-4608(93)90068-W]
- 7 **Ceroni D**, Dayer R, De Coulon G, Kaelin A. Benign fibrous histiocytoma of bone in a paediatric population: a report of 6 cases. *Musculoskelet Surg* 2011; **95**: 107-114 [PMID: 21409501 DOI: 10.1007/s12306-011-0115-x]
- 8 **Al-Jamali J**, Gerlach UV, Zajonc H. Benign fibrous histiocytoma of the distal radius: a report of a case and a review of the literature. *Hand Surg* 2010; **15**: 127-129 [PMID: 20672403 DOI: 10.1142/S0218810410004722]
- 9 **Easley ME**, Kneisl JS. Pathologic fractures through nonossifying fibromas: is prophylactic treatment warranted? *J Pediatr Orthop* 1997; **17**: 808-813 [PMID: 9591988 DOI: 10.1097/01241398-199711000-00021]

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Observational Study

Distal radius volar rim plate: Technical and radiographic considerations

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Abstract

AIM

To determine technical considerations and radiographic outcomes of the Synthes volar rim distal radius plate to treat complex intra-articular fractures.

METHODS

This review highlights technical considerations learnt using this implant since it was introduced in a major trauma unit in November 2011, including anatomical reduction and whether this was maintained radiographically.

RESULTS

Twenty-six of the 382 internally fixed distal radial fractures at our unit (6.8%) were deemed to require this plate in order to achieve optimal fracture fixation between November 2011 and May 2014. A further dorsal and/or radial plate was necessary in 35% and variable angle screws were used in 54% of cases. Post-operatively, mean radial height, inclination, volar tilt and ulnar variance restored were 11.7 mm, 21°, 4.3° and -1.2 mm respectively. There were no cases of non-union or flexor/extensor tendon rupture; one case of loss of fracture reduction. Overall incidence of plate removal was 15% with one plate removed for flexor and one for extensor tendon irritation

CONCLUSION

The use of a rim plate enables control of challenging far

distal fracture patterns. However, additional plates were required to improve and maintain reduction. Variable angle screws were necessary in half the cases to avoid intra-articular screw penetration. If used judiciously, this implant can achieve stable fixation despite the complexity of the fracture pattern.

Key words: Distal radius fractures; Volar rim plate; Volar plating distal radius

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Core tip: Far distal intra-articular fractures of the distal radius are not easily treated with standard volar plates. The rim plate is designed to sit distal to the watershed line, allowing purchase of bone fragments and subchondral support of the articular surface, enabling early mobilization. In view of the implant's design, variable angle screws are necessary to avoid intra-articular screw penetration. Intra-operatively, reduction and stable fixation should be assessed fluoroscopically during wrist movement, and if necessary, an additional dorsal plate applied to allow mobilization. Judicious use of this implant can restore anatomical reduction and stable fixation in this complex subset of fractures.

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INTRODUCTION

The application of locking plate technology to distal radius fracture fixation enables dorsally unstable fracture configurations to be reliably reduced and internally fixed using a volar approach and volar implant placement. The volar approach has gained widespread popularity due to the perceived benefits of greater soft tissue cover over the implant and less tendon irritation than with the dorsal approach. This technique may be used for the majority of distal radius fractures, however an understanding of fracture anatomy and biomechanics as well as correct implant choice and placement are critical to a successful outcome. Indeed one implant cannot provide a stable fixation for all configurations through the volar approach^[1]. The non-specialist trauma surgeon will be familiar with the volar approach but should recognize those fracture configurations that may need dorsal or combined volar and dorsal approaches. In these complex intra-articular cases the use of pre-operative computerised tomography (CT) aids planning the surgical approach and choice of implant.

The AO-23B3 fracture with a small distal and volar fragment and the AO-23C3 fracture with articular

comminution are two fracture subtypes where a standard volar plate positioned proximal to the watershed line^[2] will not provide a sufficient buttress for the distal fragments and there is a risk of secondary volar displacement of the fragment along with the carpus distal to the plate. An early plate design for these fracture subtypes was the Synthes juxta-articular plate but due to the distal plate positioning and angular design tendon irritation was problematic, often necessitating implant removal after fracture union. The distal screws were originally inserted in a fixed angle configuration that is proximally directed to avoid screw penetration of the radio-carpal joint, which was a significant risk if the distal fragment was small or the volar tilt incompletely corrected. In addition, there was no second row angled buttress for dorsal joint surface support.

The Synthes variable angle two column plate design was developed from the extra-articular and juxta-articular designs and offers an anatomically contoured plate, which is positioned close to the watershed line and can be used for fixation of the majority of distal radius fractures. However, reliable fixation of the far distal fracture subtype remains problematic. The variable angle distal radius rim plate was introduced in our unit in autumn 2011 and is designed for these complex fractures. It is inserted *via* a volar approach and is placed over the watershed line as it is pre-contoured to fit the volar rim of the distal radius. The edges of the plate are designed to provide a smooth surface against which the flexor digitorum profundus and flexor pollicis longus tendons may glide with minimal irritation. Due to the distal placement of the plate, there is a theoretical risk of intra-articular screw placement. To reduce this risk, the screw options include fixed or variable angle subtypes to allow proximal direction of screws away from the joint. These also allow purchase of small fracture fragments where a fixed angle screw would enter a fracture line. There are a number of important technical considerations for plate positioning, anatomical fracture reduction, avoiding screw penetration to the joint and minimising the risk of secondary displacement. This is especially pertinent with the AO-23C3 fracture configuration when successful volar buttress of small distal fragments may unmask distal and dorsal instability necessitating supplementary dorsal plating.

MATERIALS AND METHODS

This paper reports on a series of twenty-six consecutive cases of Synthes variable angle 2.4 distal radius rim plates used for distal radius fracture fixation at a major trauma and tertiary referral hand centre between November 2011 and May 2014. All patients treated with this implant were identified from a database of distal radius fracture fixations compiled from theatre logbooks and cross-referenced with implant logbooks. The pre-operative radiographs and CT scans were used to assess

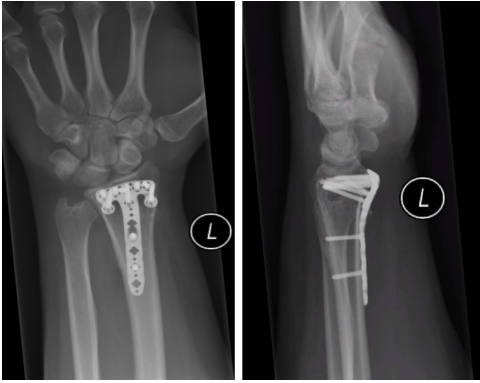


Figure 1 Posteroanterior and lateral radiographs of fracture fixation using a Synthes variable angle 2.4 distal radius rim plate to highlight the distal placement of the implant.

fracture configuration. All post-operative radiographs were reviewed to measure volar tilt, inclination and radial height in order to assess restoration of anatomy. All radiographs were reviewed taken in the same radiology unit using the same machine calibration. Operative records and imaging, medical and therapy records were used to monitor progression of the fracture to union and retention of post-operative fracture reduction.

The primary outcome measures were initial and final radiographic alignment parameters to assess maintenance of fracture reduction, and implant removal. Secondary outcome measures were the use of variable angle screws, the need for accessory plate support and tendon irritation/rupture.

RESULTS

During the study period, 382 distal radius fractures were treated operatively with internal fixation, the majority using a volar approach (83.5%). Twenty-six distal radius fixations utilised rim plates accounting for 6.8% of all operations. The rim plate was used in isolation in seventeen cases (Figure 1), however an additional dorsal or dorso-radial approach to reduce and maintain reduction of fracture fragments was required in 35% of cases. This equates to half the total number of distal radial fractures requiring combination plating, highlighting the complexity of the fractures for which rim plates were used.

The use of variable angle screws was higher in this subset of patients, with 54% of cases requiring a median of four such screws. Variable angle screws were required to reduce the risk of joint penetration and to optimise screw configurations in comminuted fractures when a fixed angle screw would sit within a fracture line and not provide sufficient subchondral support.

All fractures were classified as either AO-23B3 or AO-23C3 with a significant degree of articular and metaphyseal comminution. To evaluate the degree of fracture comminution, the size of the dorso-ulnar and radial styloid fracture fragments were assessed on pre-

operative CT scans.

Analysis of the CT coronal and axial sections demonstrated no significant difference in the size of the dorsal fragments between the groups treated with a single volar rim plate and those treated with a combined approach using a second dorso-ulnar buttress plate.

In all twenty-six cases there was a significant level of comminution, which also involved the distal radio-ulnar joint in twenty-two cases (five of these cases having a simple coronal split through this joint and the others having multi-fragmentary fracture configurations) (Figure 2). The main sites of articular comminution were in the dorso-ulnar and volar-ulnar regions of the distal radius rather than the radial styloid, where most of the fragmentation was metaphyseal.

In six cases (23%) there was a volar instability pattern at presentation with volar translation of the carpus together with the distal volar ulnar fragments. Involvement of the lunate fossa had a die punch fracture configuration in all cases (Figure 3). The dorso-ulnar fragments sustained a higher degree of comminution when compared to their volar counterpart in sixteen of the twenty six cases (Figure 4).

Standard volar variable angle plates are sited too proximal to secure and buttress these volar lip marginal fragments (Figure 4), therefore allowing carpal translation to occur despite apparent adequate fixation intra-operatively. By stabilizing these volar marginal lip fragments, the rim plate avoids this potential for secondary displacement^[1,2].

Fracture reduction was assessed by measuring volar tilt, radial inclination, radial height and ulnar variance on the post-operative radiographs. Alignment was restored to 4.3 ± 5.5 degrees volar tilt, mean radial inclination of 21.2 degrees (range: 15-30 degrees), 11.7 mm (range: 7-16 mm) radial height and -1.2 mm (range: -4.5-2.5) ulnar variance.

Six patients did not complete follow-up in our unit. Two patients were not from our region and attended follow-up at their local units, and four patients declined the offer of follow-up beyond six weeks. The patients who discontinued follow up have not been referred back to our unit with complications of tendon irritation or rupture.

The 20 patients completing follow-up all demonstrated radiographic fracture union by 12 wk from surgery. There are no cases of either flexor or extensor tendon rupture and two cases of tendon irritation. Post-operative loss of reduction occurred in one polytrauma case, with loss of volar tilt and height. No intervention was required and the patient was asymptomatic at eighteen months after surgery.

Four patients required removal of metalwork. One patient clinically had first extensor compartment tendon irritation due to a prominent screw following an isolated volar operative approach; one patient had pain on grip strength testing, which may have represented flexor tendon irritation. This resolved after removal of the volar plate and a dorsal lunate fossa fragment buttress

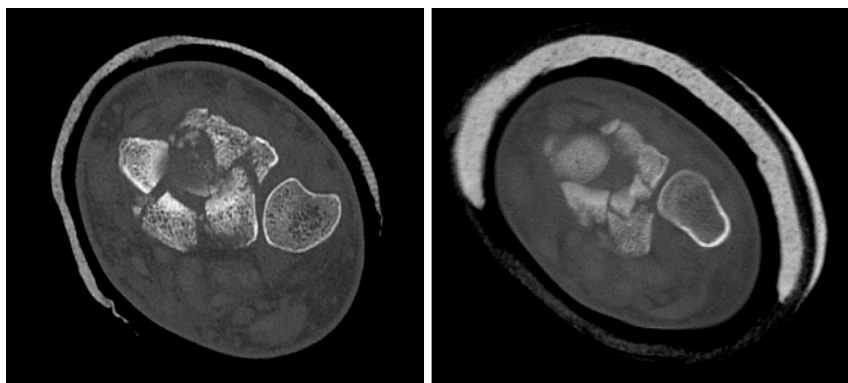


Figure 2 Axial computerised tomograms showing far distal involvement and comminution of the distal radio-ulnar joint.

plate. One case had radiographic signs of avascular necrosis of the lunate fossa fragment. This was asymptomatic until a second fall after which the patient developed new onset dorso-radial pain symptoms. A diagnostic arthroscopy identified screw penetrance into the joint; one case had the volar plate removed at the same time as a triangular fibrocartilagenous complex repair for symptoms of distal radio-ulnar joint instability.

DISCUSSION

The indications for a variable angle volar rim plate are for the infrequent AO-23B3 and AO-23C3 distal radius fractures where the distal and volar fragments cannot be adequately buttressed with standard extra-articular and variable angle two column volar plates.

Prior to the launch of the volar rim plate these distal fractures were managed in our unit with a volar juxta-articular plate or with an extra-articular plate and supplementary distal lag screws. However, this plate has a higher profile and angular design and therefore is more likely to cause flexor tendon irritation necessitating implant removal.

Alternatively they were treated by a dorsal only approach if the primary instability was thought to be dorsal, however an unmasked volar instability could result in volar displacement of the carpus with the volar distal fracture fragment at the lunate facet buttress.

Rarely they were treated with a external fixator or a temporary 3.3 mm 16 hole distraction bridge plate spanning the fracture site and carpus^[3]. Both of these techniques offer reliable fracture union, but unlike the volar rim plate, it is not possible to restore most aspects of distal radius anatomy as well as radio-carpal and distal radio-ulnar congruity. They also have other specific complications, including stiffness, pin tract infection and metacarpal fracture at the site of distal pin or screw insertion^[4].

Due to the complexity of these fractures, a pre-operative CT scan is required for in depth assessment of the fracture configuration. Unfortunately, there were no predictors on the scans which can be used to identify

fractures that are more likely to need additional plating *via* a dorsal or dorso-radial approach. We attempted to correlate the size of the fracture fragments with the need for additional plates, but no correlation was evident. This decision was made intra-operatively on assessment of fracture stability after volar plating.

In this series of rim plate fixations of distal radius fractures a combined dorsal and volar plating approach was required in 35% of procedures (Figure 5). If the distal fracture configuration with potential for volar and dorsal instability is identified from the pre-operative CT scan it is important that the treating surgeon is familiar with the dorsal approach in case an adjuvant dorsal plate is required. The alternative is to refer the case on to a specialist wrist surgeon who is familiar with both approaches. Whilst the rim plate increases the numbers of fractures and configurations that may be managed with internal fixation through the volar approach it does not obviate the need for the dorsal approach.

The rim plate has a low profile to allow its placement distal to the watershed line without increasing the risk of flexor tendon irritation. Despite its distal placement, in this series, there were no cases of flexor tendon rupture and only two of the four cases of implant removal were for flexor or extensor tendon irritation. This is consistent with the literature which suggests that attrition flexor tendon rupture is infrequent yet may occur with prominent higher profile plates placed at the watershed line, but is unlikely in cases where plates are designed to be placed more distal to this line, probably due to their contoured design and low profile^[5].

Signs of tendon irritation were noted at clinic review between three and six months post-operatively when range of motion had been restored and the patients had regained grip strength and pre-injury activity levels. None of the other cases were symptomatic or had signs of tendon irritation up to one year after surgery. Hence we suggest a minimum follow up until six months post-operatively and removal of implants if there are clinical signs of tendon irritation, rather than awaiting patients to be symptomatic thus decreasing



Figure 3 Axial computerised tomograms showing far distal involvement and comminution of the distal radio-ulnar joint.



Figure 4 Sagittal computerized tomogram showing the pattern of significant intra-articular comminution of the far distal dorso-ulnar and volar-ulnar regions of the distal radius and the volar lip marginal fragment.

the risk of attrition tendon ruptures. The published recommendations for removal of previous volar plate designs include only symptomatic patients who had plate prominence more than 2 mm volarly at the watershed line or plate position within 3 mm of the volar rim^[6].

The volar rim of the lunate fossa is anatomically designed to resist volar carpal translation and the short radiolunate ligament, which attaches to the volar lip fragment, stabilizes the carpus on the distal radius. The carpus can therefore translate volarly with the distal volar and ulnar fracture fragment of the distal radius. This fragment must be anatomically reduced and buttressed to prevent this volar instability. Standard volar variable angle plates are sited too proximal to secure and buttress these volar lip marginal fragments, therefore allowing carpal translation to occur despite apparent adequate fixation intra-operatively. The rim plate contour is designed to overhang and engage the distal volar lip fragments avoiding this potential for secondary displacement. Due to the variable angle screw option, this plate also allows purchase on these small fragments without joint penetration.

Even though the radial styloid had more metaphyseal than distal comminution in this series, variable angle screws were required, as fixed angle screws



Figure 5 PA and lateral radiograph showing combined dorsal and volar plating using a volar rim plate.

did not adequately engage the bone fragments due to their fixed trajectory, and in most cases the angle of these screws was changed as necessary to ensure stable fixation.

Unfortunately, this was not always enough to achieve adequate fracture stabilization. After volar plate fixation, all fractures were assessed for stability to ensure that the fracture and carpus are stable through a full range of motion. In 35% of cases this was not the case. Therefore an additional plate was placed either along the radial styloid to bridge and secure this styloid fracture; or over the lunate fossa fragment *via* a dorsal approach. In the latter cases, which all had a higher degree of dorso-ulnar than volar-ulnar comminution, rim plates were used to engage the distal volar lip fragments and act as a subchondral raft supporting the radio-carpal joint, aiding adequate restoration of radial height, tilt and angulation. The additional dorsal plates were then applied to buttress the dorso-ulnar fragments, preventing their displacement and translation whilst enhancing radio-carpal and distal radio-ulnar joint stability.

The distal radio-ulnar joint was involved in 85% of cases, with varying degrees of central comminution; a simple split in the coronal plane occurred in only 5 cases. Congruity was restored through the volar approach by using the variable angle screw option and changing the angle of screw insertion to capture the dorso-ulnar fragments. However this was not possible in all cases and an additional buttress plate was applied to the dorso-ulnar fragments in cases of significant comminution.

Besides allowing bone purchase of the distal radial fragments, which is important for fracture stability^[7], variable angle screws decrease the risk of intra-articular screw penetration into the radio-carpal and distal radio-ulnar joints by allowing multidirectional angulation of screws, if necessary. This risk is heightened due to the degree of intra-articular comminution in these fractures and small size of the fragments that are often only large enough to allow fixation with a single screw, sometimes only by using this variable angle option. Some studies have highlighted increased incidence of

removal of metalwork^[8] due to intra-articular placement of fixed angle screws probably as a result of incomplete restoration of volar tilt, distal plate positioning or angulation of the plate.

In this series there was only one case of radio-carpal screw penetration which was noted arthroscopically in a patient who was asymptomatic until sustaining a fall six months following fracture fixation and subsequently developed dorso-radial wrist pain. The implant was removed at the same sitting. In this case, it is hard to determine whether the screw was placed in an intra-articular position at surgery, whether this occurred after the second fall, or whether it was due to avascular necrosis of the lunate fossa fragments secondary to the original injury and plate fixation.

This low incidence of intra-articular screw penetration was perhaps due to careful pre- and intra-operative planning of screw positioning, the liberal use of variable angle screws and the use of additional dorsal plates to aid stability if volar screw placement to capture the dorsal fragments was deemed to be at risk of breaching the articular surface.

Post-operative radiographs showed correction of radial height, inclination and ulnar variance similar to that quoted in the literature for standard volar locking plates used for AO-23A2, A3, C1-3^[9], with only one case of loss of volar tilt correction after fracture fixation using a solitary volar approach. This required no further surgical intervention as the patient remained asymptomatic.

The main difference with this implant is the inability to restore volar tilt to the same extent as with standard volar plates, where a mean correction of 6 degrees (0-18 degrees) is described in the literature^[10-13] and 4.3 degrees in our series. Our results using the rim plate are therefore within the lower limits of this range for standard volar locking plates. This is partly due to the complexity of the fracture pattern and metaphyseal comminution, but also due to the far distal plate position requiring wrist hyperextension for adequate plate and distal screw placement, hence placing limitations on the degree of correction of volar tilt that can be achieved. The joint comminution precludes distal first fixation and then reduction to the shaft of radius.

Limitations

Ideally, the study should include a larger cohort of patients, and a longer duration of follow up in clinic can be considered. Unfortunately, as these fractures are not common this is not possible unless a multicentre approach is used.

In conclusion, this case series of variable angle distal radius rim plates highlights the fact that these implants are indicated for the far distal and complex intra-articular fractures of the distal radius, but cannot achieve enough stability in isolation for all fractures. Some fractures require additional plating techniques, therefore we recommend that all AO-23C3 fractures

should be assessed with a pre-operative CT scan. If trauma surgeons are not confident with dorsal plating techniques, it would be appropriate to consider referral to a specialised wrist surgeon who can base decisions on a combination of factors including pre-operative imaging, intra-operative findings and their experience with the various techniques and implants available. When used appropriately, good results can be achieved using this plate with correction and maintenance of distal radial anatomy. There were few cases of tendon irritation and no cases of flexor or extensor tendon rupture but we recommend prompt removal of implants if there are signs of tendon irritation.

Key considerations

Pre-operative CT scan provides information of fracture configuration and consideration of referral to specialist wrist surgeon if necessary; Radial styloid fixation often requires variable angle screws as the fixed angle trajectory does not always provide adequate hold; Variable angle screws in the lunate facet buttress may prevent penetration of the radio-carpal or DRUJ but may not adequately capture dorsal fragments; Volar tilt restoration is less reliable than the other alignment parameters due to the technique of plate insertion; Intra-operative assessment of stability of fracture fixation necessary after volar plating for assessment of dorsal fracture stability; additional dorsal and/or radial plates are necessary to stabilize these fractures in 35% of cases; plate positioning distal to the watershed line can lead to tendon irritation and risk of attrition rupture requiring removal of implant.

COMMENTS

Background

Far distal intra-articular fractures of the distal radius involving the volar rim are a specific subset of fractures which are difficult to treat in view of the small size of the fracture fragments, location and instability. If stable fixation is not achieved, volar carpal subluxation can occur due to the attachment of the marginal bone fragments to the short radiolunate ligament. Standard volar plate placement proximal to the watershed line poses problems when treating these fractures.

Research frontiers

In recent years, various plates have been designed with various contours and lower profiles to facilitate fracture fixation and decrease the risk of tendon irritation yet still achieve anatomical reduction, stable fixation and allow early mobilization.

Innovations and breakthroughs

The rim plate is a pre-contoured low profile implant, having standard locking and variable angle locking screw options, to allow plate placement distal to the watershed line whilst decreasing the risk of screw penetration into the joint. The aim of this design is to allow fixation of the intra-articular fractures of the distal radius which involve the marginal volar rim. Besides the risk of screw penetration into the radio-carpal and distal radio-ulnar joints when using such a distally sited plate, the other main risk is tendon irritation and rupture. Recent literature has shown that low profile plates can be safely applied at and beyond the watershed line if used appropriately.

Applications

This study shows that this implant allows subchondral support of the articular

surface achieving anatomical reduction. Judicious use of a combination of distal standard locking and variable angle locking screws allows purchase of bone fragments, especially of the dorso-ulnar fragment and avoids intra-articular screw penetration. The manuscript also provides information about the need for additional fixation in certain cases and the risk of tendon irritation.

Peer-review

The manuscript aimed to retrospectively report the clinical outcomes of fixation of far distal intra-articular distal radial fractures using variable angle distal radius rim plate. This topic is interesting and the language is excellent.

REFERENCES

- 1 **Tan KG**, Chew WY. Beware! The volar ulnar fragment in a comminuted Bartons fracture. *Hand Surg* 2013; **18**: 331-336 [PMID: 24156574 DOI: 10.1142/S0218810413500354]
- 2 **Orbay JL**, Touhami A. Current concepts in volar fixed-angle fixation of unstable distal radius fractures. *Clin Orthop Relat Res* 2006; **445**: 58-67 [PMID: 16505728 DOI: 10.1097/01.bio.0000205891.96575.0f]
- 3 **Power D**, Mishra A, Vetharajan N. Response to: Beware the volar ulnar fragment in a comminuted Bartons fracture. *Hand Surg* 2014; **19**: 325 [PMID: 24875527 DOI: 10.1142/S0218810414200020]
- 4 **Hanel DP**, Lu TS, Weil WM. Bridge plating of distal radius fractures: the Harborview method. *Clin Orthop Relat Res* 2006; **445**: 91-99 [PMID: 16505725 DOI: 10.1097/01.bio0000205885.58458.f9]
- 5 **Hanel DP**, Ruhlman SD, Katolik LI, Allan CH. Complications associated with distraction plate fixation of wrist fractures. *Hand Clin* 2010; **26**: 237-243 [PMID: 20494750 DOI: 10.1016/j.hcl.2010.01.001]
- 6 **Soong M**, Earp BE, Bishop G, Leung A, Blazar P. Volar locking plate implant prominence and flexor tendon rupture. *J Bone Joint Surg Am* 2011; **93**: 328-335 [PMID: 21239658 DOI: 10.2106/JBJS.J.00193]
- 7 **Kitay A**, Swanstrom M, Schreiber JJ, Carlson MG, Nguyen JT, Weiland AJ, Daluiski A. Volar plate position and flexor tendon rupture following distal radius fracture fixation. *J Hand Surg Am* 2013; **38**: 1091-1096 [PMID: 23647641 DOI: 10.1016/j.jhssa.2013.03.011]
- 8 **Mehling I**, Müller LP, Delinsky K, Mehler D, Burkhart KJ, Rommens PM. Number and locations of screw fixation for volar fixed-angle plating of distal radius fractures: biomechanical study. *J Hand Surg Am* 2010; **35**: 885-891 [PMID: 20513572 DOI: 10.1016/j.jhssa.2010.03.027]
- 9 **Sahu A**, Charalambous CP, Mills SP, Batra S, Ravenscroft MJ. Reoperation for metalwork complications following the use of volar locking plates for distal radius fractures: a United Kingdom experience. *Hand Surg* 2011; **16**: 113-118 [PMID: 21548144 DOI: 10.1142/S0218810411005205]
- 10 **Arora R**, Lutz M, Hennerbichler A, Krappinger D, Espen D, Gabl M. Complications following internal fixation of unstable distal radius fracture with a palmar locking-plate. *J Orthop Trauma* 2007; **21**: 316-322 [PMID: 17485996 DOI: 10.1097/BOT.0b013e318059b993]
- 11 **Musgrave DS**, Idler RS. Volar fixation of dorsally displaced distal radius fractures using the 2.4-mm locking compression plates. *J Hand Surg Am* 2005; **30**: 743-749 [PMID: 16039367 DOI: 10.1016/j.jhssa.2005.03.006]
- 12 **Ring D**, Jupiter JB, Brennwald J, Buehler U, Hastings H. Prospective multicenter trial of a plate for dorsal fixation of distal radius fractures. *J Hand Surg Am* 1997; **22**: 777-784 [PMID: 9330133 DOI: 10.1016/S0363-5023(97)80069-X]
- 13 **Dario P**, Matteo G, Carolina C, Marco G, Cristina D, Daniele F, Andrea F. Is it really necessary to restore radial anatomic parameters after distal radius fractures? *Injury* 2014; **45** Suppl 6: S21-S26 [PMID: 25457314 DOI: 10.1016/j.injury.2014.10.018]

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Return to sport following tibial plateau fractures: A systematic review

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Abstract

AIM

To systematically review all studies reporting return to sport following tibial plateau fracture, in order to provide information on return rates and times to sport, and to assess variations in sporting outcome for different treatment methods.

METHODS

A systematic search of CINAHAL, Cochrane, EMBASE, Google Scholar, MEDLINE, PEDro, Scopus, SPORTDiscus and Web of Science was performed in January 2017 using the keywords "tibial", "plateau", "fractures", "knee", "athletes", "sports", "non-operative", "conservative", "operative", "return to sport". All studies which recorded return rates and times to sport following tibial plateau fractures were included.

RESULTS

Twenty-seven studies were included: 1 was a randomised controlled trial, 7 were prospective cohort studies, 16 were retrospective cohort studies, 3 were case series. One study reported on the outcome of conservative management ($n = 3$); 27 reported on the outcome of surgical management ($n = 917$). Nine studies reported on Open Reduction Internal Fixation (ORIF) ($n = 193$), 11 on Arthroscopic-Assisted Reduction Internal Fixation (ARIF) ($n = 253$) and 7 on Frame-Assisted Fixation (FRAME) ($n = 262$). All studies recorded "return to sport"

rates. Only one study recorded a "return to sport" time. The return rate to sport for the total cohort was 70%. For the conservatively-managed fractures, the return rate was 100%. For the surgically-managed fractures, the return rate was 70%. For fractures managed with ORIF, the return rate was 60%. For fractures managed with ARIF, the return rate was 83%. For fractures managed with FRAME was 52%. The return rate for ARIF was found to be significantly greater than that for ORIF (OR 3.22, 95%CI: 2.09-4.97, $P < 0.001$) and for FRAME (OR 4.33, 95%CI: 2.89-6.50, $P < 0.001$). No difference was found between the return rates for ORIF and FRAME (OR 1.35, 95%CI: 0.92-1.96, $P = 0.122$). The recorded return time was 6.9 mo (median), from a study reporting on ORIF.

CONCLUSION

Return rates to sport for tibial plateau fractures remain limited compared to other fractures. ARIF provides the best return rates. There is limited data regarding return times to sport. Further research is required to determine return times to sport, and to improve return rates to sport, through treatment and rehabilitation optimisation.

Key words: Tibial; Plateau; Fracture; Knee; Return; Sport; Rate; Time

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Core tip: We performed a systematic review assessing all studies which reported return rates and times to sport following tibial plateau fractures. Twenty-seven studies were included: All recorded return rates; only one study recorded return times. One study reported on conservative treatment; all 27 studies reported on surgical treatment. The surgical techniques comprised Open Reduction Internal Fixation (ORIF), Arthroscopic-Assisted Reduction Internal Fixation (ARIF) and Frame-Assisted Fixation (FRAME). The return rates were: Total Cohort-70%; conservatively-managed cohort-100%; surgically-managed cohort-70%; ORIF-60%, ARIF-83%, FRAME-52%. ARIF provided the best return rates to sport. Data however is limited, particularly for return times to sport. Further research in this area is required.

Robertson GAJ, Wong SJ, Wood AM. Return to sport following tibial plateau fractures: A systematic review. *World J Orthop* 2017; 8(7): 574-587 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v8/i7/574.htm> DOI: <http://dx.doi.org/10.5312/wjo.v8.i7.574>

INTRODUCTION

Tibial plateau fractures comprise 1% of all fractures^[1,2]; despite their limited frequency, due to their intra-articular nature, they commonly result in significant functional morbidity^[2-5]. These fractures involve either

the lateral tibial plateau, the medial tibial plateau, or both; injury patterns are commonly classified by the Schatzker or the AO/OTA classification^[2-5]. Such injuries normally arise from high energy trauma: The common reported mechanisms include road traffic accidents, falls from a height, pedestrian struck by motor vehicle or high-impact sporting collision^[1-5]. Despite sport being a well-documented cause for this injury, there is limited evidence on the predicted return rates and return times to sport following tibial plateau fractures^[2,4,5]. This arises for the fact that most outcome studies on this injury type provide validated functional outcomes scores, failing to differentiate specific details on recovery of sporting function^[2,4,5].

The treatment of tibial plateau fracture is based on the location and displacement of the fracture^[2-5]. All undisplaced fractures are routinely managed non-operatively, with a period of knee immobilisation for 4 to 8 wk in a cast or a brace: This is combined with sequential range of motion exercises and a graduated weightbearing protocol^[3]. For displaced fractures, the standard treatment is surgical reduction and fixation of the fracture^[2-5]. A number of surgical techniques have been reported in the literature, and the choice of technique is directed by the fracture pattern^[2-5]. Techniques can be classified into three categories: Those which involve open reduction and internal fixation of the fracture (ORIF), those which involve arthroscopic-assisted reduction and fixation of the fracture (ARIF), and those which involve frame (external fixation) assisted fixation of the fracture (FRAME)^[2-5]. The choice of internal fixation can vary from cannulated screws to multiple locking plates, depending on the nature of the fracture^[2-5]. Associated intra-articular injuries, when present, are also commonly treated in conjunction with fracture fixation^[2-5]. While there is growing evidence on the clinical and radiological outcomes of such techniques, there remains limited evidence on return to sport following such injuries^[2-5].

The aim of this systematic review was to assess all studies reporting return rates and times to sport following treatment for tibial plateau fractures, in order to provide clarification on the optimal treatment methods for this injury, as well as to provide prognostic information on return to sport following these fractures.

MATERIALS AND METHODS

Literature search

A systematic literature search was carried out in January 2017 from the following databases: MEDLINE (PubMed), Cochrane Collaboration Database, EMBASE, SPORTDiscus, CINAHAL, Google Scholar, Physiotherapy Evidence Database (PEDro), Scopus and Web of Science. This was to locate all articles, published in English language, in peer-reviewed journals, reporting on return rates and return times to sports following treatment for tibial plateau fractures. No distinction

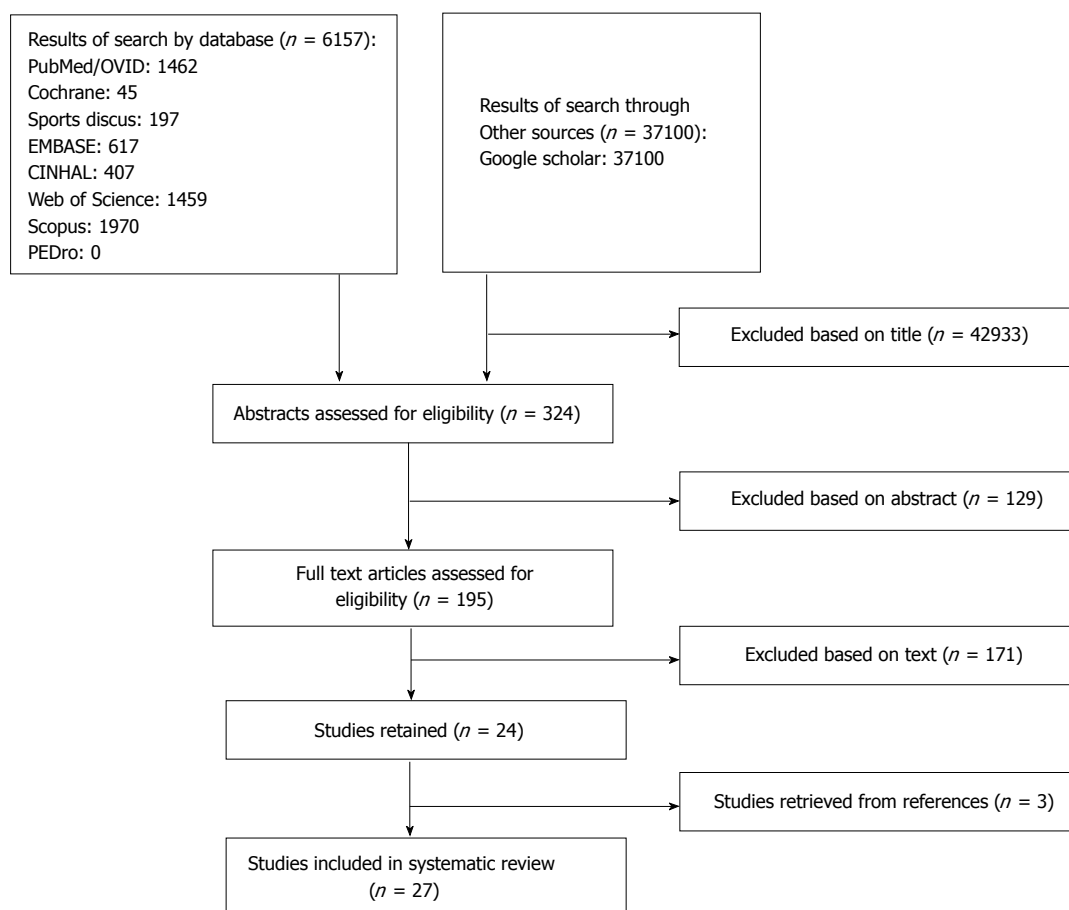


Figure 1 Selection of articles for inclusion in the review in accordance with the PRISMA protocol^[6].

was made regarding the location or nature of fracture, nor level and type of sports activity performed. The keywords used for the search were "tibial", "plateau", "fractures", "knee", "athletes", "sports", "non-operative", "conservative", "operative", "return to sport". There was no limit regarding the year of publication.

The authors followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines to design the review^[6]. The abstract of each publication was independently reviewed by all three authors (Greg AJ Robertson, Seng J Wong and Alexander M Wood) to establish its suitability for inclusion within the review. As per the PRISMA guidelines, the inclusion and exclusion criteria for review are listed in Table 1^[6]. The quality of reporting of meta-analyses flow diagram in Figure 1 presents the search results and selection process for the review^[6]. Article categories excluded from the review included case reports, expert opinions, literature reviews, instructional courses, biomechanical reports, and technical notes. If exclusion could not be confirmed from the abstract alone, the full-text version of the study was accessed to confirm eligibility. Review of the reference lists of relevant articles were also performed to identify additional studies that could be suitable for inclusion. Discrepancies between the reviewers' choice of articles for inclusion were resolved

by consensus discussion.

The review database contained data on patient demographics, mode of injury, pre-operative radiological investigations, fracture location, fracture classification, operative and non-operative management techniques, rehabilitation protocols, return rates to sport, return times to sports, rate of fracture union, time to fracture union, complications, required re-interventions and predictive factors for return to sports.

The primary outcome measures were return rates to sport and return times to sport. The secondary outcome measures were return rates to pre-injury level of sport, rate of fracture union, time to fracture union and associated complications. Return to sport was defined as resumption of sporting activities following completion of treatment; return to pre-injury level of sport was defined as the return to specified pre-injury level of sporting activities following completion of treatment. Return time to sport was defined as: The time period from commencement of non-operative modalities to sporting return for conservatively-managed patients; and the time period from primary surgical treatment to sporting return for surgically-managed patients. Where return to sport or fracture union was not possible from the primary treatment method alone, with requirement for conversion to a secondary treatment, this was

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Acute tibial plateau fractures	Extra-articular proximal tibial fractures
Elite or recreational athletes	Stress fractures of the proximal tibial
Return rate to sporting activity reported	No sporting outcome data reported
Return time to sporting activity reported	Paediatric fractures (age under 15)
Two or more fractures reported	Reviews, case reports, abstracts or anecdotal articles
Peer-reviewed journals	Animal, cadaver or <i>in vitro</i> studies
English language	

recorded as a failure for the primary treatment method.

Quality assessment

The modified Coleman Methodology Score (CMS) was used to assess the quality of the included papers^[7]. This is a 10-point-criteria validated scoring system, which has been previously used in multiple similar systematic reviews^[7-10]. The scoring methodology utilised is that presented by Del Buono *et al.*^[7]. This provides a final score ranging from 0 to 100, indicating the quality of study included^[7]. Two of the authors (Greg AJ Robertson and Alexander M Wood) performed scoring of each of the included studies. Using the intra-class correlation co-efficient statistic, the inter-observer reliability of the scores was noted as 0.91 (95%CI: 0.89-0.93).

Statistical analysis

Meta-analysis comparisons were performed for return rates to sport between cohorts of the synthesis data of sufficient size. There was insufficient data to perform meta-analysis comparisons on return times to sport. The meta-analysis was performed on RevMan Version 5.3 (The Cochrane Group). Odds ratios (ORs), with a random effects model, were used to assess comparisons between the dichotomous data. The heterogeneity of included studies was analysed with the I^2 statistic and was judged to be significant if I^2 was > 50%. The significance level was $P < 0.05$.

RESULTS

Search

The details of the selection process for the included articles are listed in Figure 1. In total, 324 unique abstracts and 195 unique articles were assessed.

Patient demographics

We identified 27 relevant publications^[11-37], published from 1988^[18] to 2016^[14], focusing on clinical and functional outcomes of patients who returned to sports activity after tibial plateau fractures (Tables 2-6). One was a randomised controlled trial (RCT)^[11], 7 were prospective cohort studies^[14,16,25,26,28,30,32], 16 were retrospective cohort studies^[12,13,15,17,18,20-24,27,29,34-37] and

3 were case series^[19,31,33].

Of the 1134 fractures, 613 (54%) occurred in male patients, 428 (38%) in female patients, and 93 (8%) failed to specify gender. Ninety-nine of the fractures were open injuries^[11,12,17,20-23]. Two patients had bilateral tibial plateau fractures^[22]. Of the 1134 fractures recorded, sport-related follow-up data was available for 920 (81.1%). The mean age at the time of injury ranged from 34.8 years^[31] to 52.2 years^[37]. The commonly reported modes of injury were road traffic accidents, falls from height, pedestrian struck by motor vehicle and collisions during sports: The most commonly reported sport was skiing (Tables 2-6).

Fracture classification and location

Twenty-six of the twenty-seven studies used formal fracture classifications to describe the fracture types^[11-17,19-37]. Six studies used the Schatzker Classification alone to define fracture pattern^[17,20,27-29,32]. Five studies used the AO/OTA classification alone^[13,22,30,35,37]. Three studies used the Hohl and Moore Classification alone^[14,19,24]. Twelve used both the AO/OTA and the Schatzker Classification^[11,12,15,16,21,23,25,26,31,33,34,36]. One study reported on postero-lateral tibial plateau fractures with no classification used^[18].

The reported fracture configurations from each study are recorded in Tables 2-6. Four studies in the ARIF cohort, restricted patient inclusion to low-energy fracture patterns (Schatzker I-III, AO/OTA A-B)^[27,30,31,33]. There were no restriction of fracture types in the ORIF^[11-19] and FRAME^[11,12,20-24] cohorts. One study reported on undisplaced fractures^[18]; all 27 studies reported on displaced fractures^[11-37]. Seven studies included open fractures: All used the Gustillo-Anderson Classification to classify the soft tissue damage^[11,12,17,20-23].

Twenty-one studies recorded associated injuries^[11-14,16-22,24-30,32,34-36]. For twelve studies, the reported injuries comprised solely of intra-articular knee injuries^[12,14,16,18,19,28-30,32,34-36]. For six studies, the reported injuries comprised both intra-articular knee injuries and non-knee-related trauma injuries^[11,17,21,22,24,25]. For three studies, the reported injuries comprised solely of non-knee-related trauma injuries^[13,20,27]. The commonest intra-articular knee injuries were meniscal tears, tibial spine avulsions fractures, anterior cruciate ligament (ACL) ruptures, posterior cruciate ligament ruptures and medial collateral ligament ruptures^[11,12,14,16-19,21,22,24,25,28-30,32,34-36]. The non-knee-related trauma injuries comprised head, chest and abdominal traumatic injuries, as well as associated spinal, upper limb and lower limb fractures^[11,13,17,20-22,24,25,27].

Of the 920 tibial plateau fractures with follow-up data, 917 were surgically managed^[11-37] and 3 were conservatively managed^[18]. Of the surgically managed fractures, 193 were treated with ORIF^[11-19], 253 were treated ARIF^[24-34] and 262 were treated with FRAME^[11,12,20-24]. For 209 fractures, the outcome data

Table 2 Conservatively managed fractures - only patients with follow-up data included

Ref.	N	Study design	Mean follow-up	Treatment	Mode of injury	Fracture types	Report of IA injuries	IA injury repair	Coleman score	Return rate	Return rate by treatment modality	Return rate to same level of sport	Return time (range)	Rate of union	Time to union (range)
Waldrop <i>et al</i> ^[18] (1988)	3	RCS	59 mo	Knee immobilisation	Falls RTA skiing	Postero-lateral (undisplaced)	Yes	Yes	69	3/3 (100%)	Cons: 3/3 (100%)	3/3 (100%)	N/A	N/A	N/A

Mean values unless otherwise stated. RCS: Retrospective cohort study; RTA: Road traffic accident; Cons: Conservative; N/A: No data available; IA: Intra-articular.

Table 3 Fractures treated by Open Reduction Internal Fixation - only patients with follow-up data included

Ref.	n	Study design	Mean follow-up	Treatment	Mode of injury	Fracture types	Report of IA injuries	IA injury repair	Coleman score	Return rate	Return rate by treatment modality	Return rate to same level of sport	Return time (range)	Rate of union	Time to union (range)
Ahearn <i>et al</i> ^[12] (2014)	21	RCS	40.5 mo	PF (21)	Falls RTA pedestrian	Schatzker VI Bicondylar	No	Not reported	62	14/21 (67%)	PF: 14/21 (67%)	4/21 (19%)	N/A	21/21 (100%)	N/A
Brunner <i>et al</i> ^[19] (2009)	5	CS	39 mo	PF (5)	Skiing (4) Falls (1)	Moore type II	Yes	Yes	61	5/5 (100%)	PF: 5/5 (100%)	N/A	N/A	N/A	N/A
Canadian Orthopaedic Trauma Society ^[11] (2006)	33	RCT	24 mo	PF (33)	Falls RTA Pedestrian Sports Work Cycling	Schatzker V and VI	Yes	Yes	74	4/33 (12%)	PF: 4/33 (12%)	4/33 (12%)	N/A	N/A	N/A
Chang <i>et al</i> ^[16] (2014)	16	PCS	28.7 mo	PF (16)	N/A	Schatzker VI AO/OTA C2-3	Yes	Yes	66	14/16 (88%)	PF: 14/16 (88%)	14/16 (88%)	N/A	16/16 (100%)	20.2 wk
Keogh <i>et al</i> ^[13] (1992)	13	RCS	17 mo	PSF (13)	RTA (5) Falls (5) Work (2) Sport (1)	Schatzker I-VI	No	Not reported	45	11/13 (85%)	PSF: 11/13 (85%)	N/A	N/A	N/A	N/A
Morin <i>et al</i> ^[14] (2016)	15	PCS	18.2 mo	SF (15)	Skiing (15)	Postero-Medial Moore Type I	Yes	Yes	73	13/15 (87%)	SF: 13/15 (87%)	0/15 (0%)	N/A	N/A	N/A
Stevens <i>et al</i> ^[17] (2001)	46	RCS	100 mo	PF (46)	RTA (13) Pedestrian (13) Falls (9) Sports (6) Work (2)	Schatzker I-VI	Yes	Yes	70	21/46 (46%)	PF: 21/46 (46%)	6/46 (13%)	N/A	46/46 (100%)	N/A
van Dreumel <i>et al</i> ^[15] (2015)	26	RCS	74 mo	SF PF	Falls (57%) RTA (25%) Other (14%)	Schatzker I-VI AO/OTA B1-C3	No	Not reported	79	15/26 (58%)	SF: N/A PF: N/A	15/26 (58%)	6.9 (2-18) mo (median)	N/A	N/A
Waldrop <i>et al</i> ^[18] (1988)	3	RCS	59 mo	PF (6) ORBG (12)	Falls RTA Skiing	Postero-Lateral (displaced)	Yes	Yes	69	18/18 (100%)	PF: 6/6 (100%) ORBG: 12/12 (100%)	17/18 (100%)	N/A	N/A	N/A

Mean values unless otherwise stated. RCS: Retrospective cohort study; PCS: Prospective cohort study; RCT: Randomised controlled trial; CS: Case series; ORIF: Open reduction internal fixation; PF: Plate fixation; SF: Screw fixation; PSF: Percutaneous screw fixation; ORBG: Open reduction and bone grafting; RTA: Road traffic accident; Pedestrian - Pedestrian struck by Motor Vehicle; AO/OTA: Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association; N/A: No data available; IA: Intra-articular.

was reported within combined surgical cohorts, with no differentiation for treatment method used^[35-37].

Choice of radiological imaging

All of the studies used plain radiographs as initial

Table 4 Fractures treated by Arthroscopic-Assisted Reduction and Internal Fixation - Only patients with follow-up data included

Ref.	n	Study design	Mean follow-up	Treatment	Mode of injury	Fracture types	Report of IA injuries	IA injury repair	Coleman score	Return rate	Return rate by treatment modality	Return rate to same level of sport	Return time (range)	Rate of union	Time to union (range)
Chan <i>et al</i> ^[26] (2003)	18	PCS	48 mo	APF (18)	RTA (17) Falls (1)	Schatzker V and VI	Yes	Yes	68	13/18 (72%)	APF: 13/18 (72%)	13/18 (72%)	N/A	N/A	N/A
Chan <i>et al</i> ^[25] (2008)	54	PCS	87 mo	APF (54)	RTA (50) Falls (4)	Schatzker I-VI	Yes	Yes	80	48/54 (89%)	APF: 48/54 (89%)	48/54 (89%)	N/A	54/54 (100%)	N/A
Chiu <i>et al</i> ^[34] (2013)	25	RCS	86 mo	APF (25)	N/A	Schatzker IV-VI	Yes	Yes	73	22/25 (88%)	APF: 22/25 (88%)	22/25 (88%)	N/A	25/25 (100%)	N/A
Duan <i>et al</i> ^[29] (2008)	39	RCS	34 mo	APSF (37)	RTA (19) Falls (11) Sports (9)	Schatzker I-V	Yes	Yes	57	30/39 (77%)	APSF: 30/39 (77%)	30/39 (77%)	N/A	39/39 (100%)	12 (11-14) wk
Gill <i>et al</i> ^[28] (2001)	25	PCS	24 mo	APSF (25)	Skiing (25)	Schatzker I-IV	Yes	Yes	79	21/25 (84%)	APSF: 21/25 (84%)	21/25 (84%)	N/A	N/A	N/A
Guanche <i>et al</i> ^[31] (1993)	5	CS	N/A	APSF (5)	N/A	Schatzker I-III	No	Not reported	55	5/5 (100%)	APSF: 5/5 (100%)	5/5 (100%)	N/A	5/5 (100%)	N/A
Holzach <i>et al</i> ^[30] (1994)	15	PCS	35.3 mo	APSF (10)	Skiing (15)	AO/OTA B2.2 and B3.1	Yes	Yes	76	13/15 (87%)	APSF: 13/15 (87%)	13/15 (87%)	N/A	N/A	N/A
Hung <i>et al</i> ^[32] (2003)	31	PCS	36 mo	APF (31)	RTA (30) Falls (1)	Schatzker I-VI	Yes	Yes	76	26/31 (84%)	APF: 26/31 (84%)	26/31 (84%)	N/A	31/31 (100%)	12 (11-14) wk
Itokazu <i>et al</i> ^[24] (1996)	16	RCS	30 mo	APSF (5) ACF (7) APF (4)	N/A	Hohl II and III	Yes	Yes	49	16/16 (100%)	APSF: 5/5 (100%) ACF: 7/7 (100%) APF: 4/4 (100%)	16/16 (100%)	N/A	16/16 (100%)	N/A
Kampa <i>et al</i> ^[27] (2016)	20	RCS	30 mo	APSF (20)	Falls (52%) Sport (48%)	Schatzker I-III	Yes	Yes	71	10/20 (50%)	APSF: 10/20 (50%)	10/20 (50%)	N/A	20/20 (100%)	N/A
Pizanis <i>et al</i> ^[33] (2012)	5	CS	24 mo	APF (5)	N/A	AO/OTA B2 and B3	No	Not reported	61	5/5 (100%)	APF: 5/5 (100%)	5/5 (100%)	N/A	N/A	N/A

Mean values unless otherwise stated. RCS: Retrospective cohort study; PCS: Prospective Cohort Study; CS: Case series; APSF: Arthroscopic-assisted reduction and percutaneous screw fixation; ACF: Arthroscopic-assisted reduction and cement filling; APF: Arthroscopic-assisted plate fixation; RTA: Road traffic accident; AO/OTA: Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association; NA: No data available; IA: Intra-articular.

Table 5 Fractures treated by frame application - only patients with follow-up data included

Ref.	n	Study design	Mean follow-up	Treatment	Mode of injury	Fracture types	Report of IA injuries	IA injury repair	Coleman score	Return rate	Return rate by treatment modality	Return rate to same level of sport	Return time (range)	Rate of union	Time to union (range)
Ahearn <i>et al</i> ^[12] (2014)	15	RCS	41 mo	Frame and IF (15) Non-Bridging Frames (15)	Falls RTA Pedestrian	Schatzker VI (Bicondylar)	No	Not reported	62	11/15 (73%)	Frame and IF: 11/15 (73%)	3/15 (20%)	N/A	15/15 (100%)	N/A

Chin <i>et al</i> ^[20] (2005)	18	RCS	28 mo	Frame and IF (16) Arthro Frame (2) Bridging Frames (3) Non-Bridging Frames (15)	RTA Pedestrian Falls Skiing Cycling	Schatzker V and VI	No	Not reported	61	15/18 (83%)	Frame and IF: N/A Arthro Frame: N/A	7/18 (39%)	N/A	15/18 (83%)	14 (11-22) wk
Canadian Orthopaedic Trauma Society ^[11] (2006)	33	RCT	24 mo	Frame and IF (33) Bridging Frames (4) Non-Bridging Frames (29)	Falls RTA Pedestrian Sports Work Cycling	Schatzker V and VI	Yes	Yes	74	10/33 (30%)	Frame and IF: 10/33 (30%)	10/33 (30%)	N/A	N/A	N/A
Itokazu <i>et al</i> ^[24] (1996)	1	RCS	30 mo	Arthro Frame (1) Non-Bridging Frame (1)	N/A	Hohl II and III	Yes	Yes	49	1/1 (100%)	Arthro Frame: 1/1 (100%)	1/1 (100%)	N/A	1/1 (100%)	N/A
Katsenis <i>et al</i> ^[21] (2005)	46	RCS	38 mo	Frame and IF (46) Bridging Frames (30) Non-Bridging Frames (16)	RTA Falls	Schatzker V and VI AO/OTA C1-3	Yes	Not reported	72	25/46 (54%)	Frame and IF: 25/46 (54%)	N/A	N/A	45/46 (98%)	13.5 (11-18) wk
Katsenis <i>et al</i> ^[22] (2009)	127	RCS	60 mo (mini-mum)	Frame and IF (127) Bridging and Non-Bridging Frames (127)	RTA (96) Falls (29) Sports (2)	AO/OTA C1-3	Yes	Not reported	68	68/127 (54%)	Frame and IF: 68/127 (54%)	N/A	N/A	126/127 (99%)	13.7 (10-20) wk
Weigel <i>et al</i> ^[23] (2002)	22	RCS	98 mo	Frame and IF (22) Non-Bridging Frames (22)	RTA (16) Fall (3) Pedestrian (2) Assault (1) Sport (1) Crush (1)	Schatzker II, IV, V and VI AO/OTA C1-3	No	Not reported	54	7/22 (32%)	Frame and IF: 7/22 (32%)	N/A	N/A	N/A	N/A

Mean values unless otherwise stated. RCS: Retrospective cohort study; PF: Plate fixation, PSF: Percutaneous screw fixation; APSF: Arthroscopic Percutaneous screw fixation; Arthro Frame: Arthroscopic-assisted frame application; Arthro Frame and IF: Arthroscopic-assisted frame application with internal fixation; RTA: Road traffic accident; AO/OTA: Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association; N/A: Data not available; IA: Intra-articular.

assessment of the fractures^[11-37]. Eleven studies reported using a combination of plain radiographs and CT Scans

for fracture imaging^[14,16,19,20,22,24,25,29,30,32,34]. Four studies, reported using a combination of plain radiographs, CT

Table 6 Surgical cohorts with combined outcome data - only patients with follow-up data included

Ref.	n	Study design	Mean follow-up	Treatment	Mode of injury	Fracture types	Report of IA injuries	IA injury repair	Coleman score	Return rate	Return rate by treatment modality	Return rate to same level of sport	Return time (range)	Rate of union	Time to union (range)
Kraus <i>et al</i> ^[36] (2012)	79	RCS	53 mo	PF PSF APSF	Sports (54%) RTA (20%) Falls (18%)	Schatzker I-VI AO/OTA A2-C3	Yes	Yes	47	65/79 (82%)	ORIF: N/A PSF: N/A APSF: N/A	N/A	N/A	N/A	N/A
Loibl <i>et al</i> ^[37] (2013)	92	RCS	94 mo	PF PSF ARSF	Skiing (92%)	AO/OTA B1-C3	No	Not reported	55	81/92 (88%)	ORIF: N/A PSF: N/A APSF: N/A	57/92 (62%)	N/A	N/A	N/A
Scheerlinck <i>et al</i> ^[35] (1998)	38	RCS	62 mo	APSF (30) Arthro Frame (2) Arthro Frame and IF (6)	N/A	AO/OTA B1-C3	Yes	Yes	68	32/38 (84%)	APSF: N/A Arthro Frame: N/A Arthro Frame and IF: N/A	24/38 (63%)	N/A	N/A	N/A

Mean values unless otherwise stated. RCS: Retrospective cohort study; PF: Plate fixation; PSF: Percutaneous screw fixation; APSF: Arthroscopic percutaneous screw fixation; Arthro frame: Arthroscopic-assisted frame application; Arthro frame and IF: Arthroscopic-assisted frame application with internal fixation; RTA: Road traffic accident; AO/OTA: Arbeitsgemeinschaft für osteosynthesefragen/orthopaedic trauma association; N/A: Data not available; IA: Intra-articular.

and MRI Scans for fracture imaging^[21,26-28].

Study design

The mean CMS for all the studies was 65.5 (range 45-80) (Tables 2-6)^[11-37]. For the study reporting on conservative management, the CMS was 69 (Table 2)^[18]. For the studies reporting on surgical management, the mean CMS was 65.5 (range 45-80) (Tables 3-6)^[11-37]. For the ORIF cohort, the mean CMS was 66.6 (range 45-79) (Table 3)^[11-19]. For the ARIF cohort, the mean CMS was 67.7 (range 49-80) (Table 4)^[24-34]. For the FRAME cohort, the mean CMS was 62.9 (range 49-74) (Table 5)^[11,12,20-24].

Management

Conservative management: This comprised of knee immobilisation for 4 to 8 wk, during which the patient performed quadriceps strengthening exercises^[18]. Following this, the patients commenced range of motion exercises, with progressive weightbearing and physiotherapy^[18].

Surgical management: The surgical technique could be categorised into three main categories: ORIF, ARIF, FRAME.

For the ORIF cohort, surgical techniques comprised open reduction of the fracture followed by internal fixation^[11-19]. Depending on the severity of the fracture, the internal fixation ranged from cannulated screws to locked plate fixation (Table 3). Concomitant management of intra-articular injuries was performed in six studies^[11,14,16-19]. Bone graft was used in three studies to augment fixation^[11,12,19]; synthetic bone

graft substitute was used in one study to augment fixation^[16].

For the ARIF cohort, surgical techniques comprised reduction of the fracture under arthroscopic guidance followed by internal fixation^[24-34]. Depending on the severity of the fracture, the internal fixation ranged from cannulated screws to locked plate fixation (Table 4). Concomitant management of intra-articular injuries was performed in nine studies^[24-30,32,34]. Bone graft was used in six studies to augment fixation^[25-27,29,30,32]; synthetic bone graft substitute was used in four studies to augment fixation^[27,28,33,34].

For the FRAME cohort, surgical techniques comprised fracture reduction by traction and open intervention, followed by Frame Application^[11,12,20-24]. In six studies, limited internal fixation was performed as part of the procedure^[11,12,20-23]. In two studies, reduction of the fracture was assisted by arthroscopic visualisation of the fracture^[20,24]. Four studies used either bridging or non-bridging frames, with bridging frames reserved for cases with significant knee joint instability^[11, 20-22]; three studies used non-bridging frame exclusively^[12,23,24] (Table 5). Concomitant management of intra-articular injuries was performed in two studies^[11,24]. Bone graft was used in three studies to augment fixation^[11,12,20]; synthetic bone graft substitute was used in two studies to augment fixation^[21,22].

Post-operative rehabilitation regimes were reported by all but one study^[11-22,24-37]. These comprised limited weightbearing for 6 to 12 wk^[11-22, 24-37]. There was a variety of range of motion (ROM) protocols based on the severity of fracture, the surgical technique used and associated injuries: Some studies advocated full

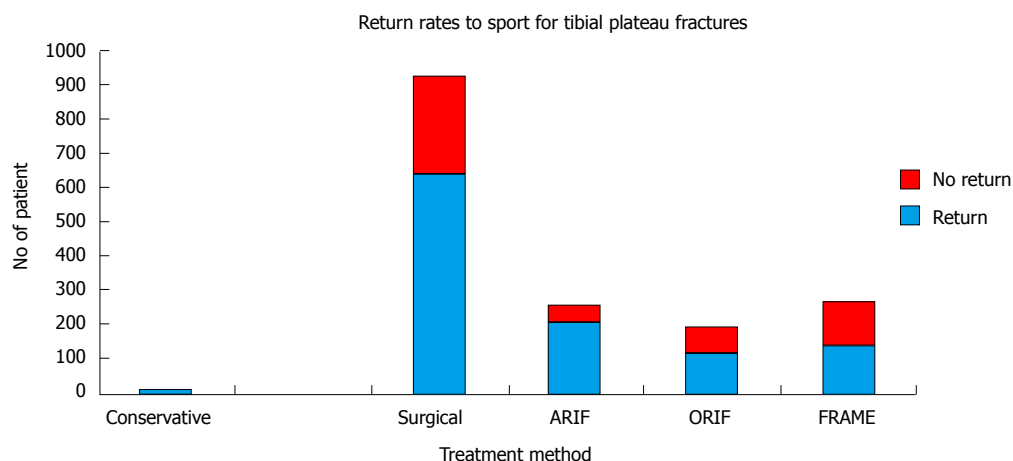


Figure 2 Return rates to sport for tibial plateau fractures. ARIF: Arthroscopic-Assisted Reduction Internal Fixation; ORIF: Open Reduction Internal Fixation; FRAME: Frame-Assisted Fixation.

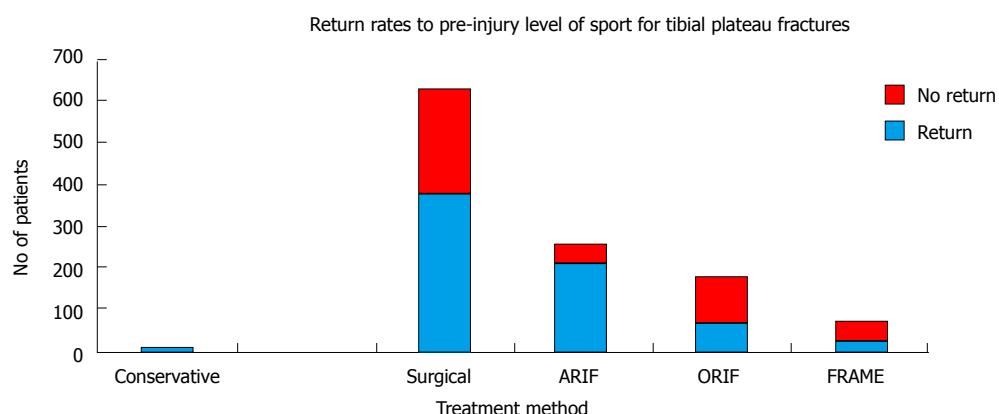


Figure 3 Return rates to pre-injury level of sport for tibial plateau fractures. ARIF: Arthroscopic-Assisted Reduction Internal Fixation; ORIF: Open Reduction Internal Fixation; FRAME: Frame-Assisted Fixation.

ROM exercises immediately post-operative, while other advised knee immobilisation for 4 to 6 wk post-operative^[11-22,24-37].

Associated surgical procedures

Seventeen of the studies reported concomitant management of intra-articular knee injuries at the time of surgical procedures^[11,14,16-19,24-30,32,34-36]. These included meniscal repair, partial and total (medial or lateral) meniscectomy, tibial spine avulsions fixation and ACL re-attachment/repair^[11,14,16-19,24-30,32,34-36].

Functional assessment

Twenty-six of the studies used validated scoring systems to assess post-intervention functional status^[11-30,32-37]. These included both the conservatively managed^[18] and surgically-managed patients^[11-30,32-37]. The only study not to use a validated scoring systems was in the ARIF cohort^[31]. The most commonly used scores were the Rasmussen Score (7 studies)^[13,25,26,28,29,33,34], the Lysholm Knee Score (6 studies)^[14,19,27,33,36], the Short-Form 36 (SF-36) health status questionnaire (6 studies)^[11,12,17,19,20,23] and the Hospital for Special

Surgery Knee Score (4 studies)^[11,16,32,35].

Return rates to sports

Conservative management: The return rates for the conservatively-managed tibial plateau fractures are provided in Table 7 and Figure 2.

The return rates to pre-injury level sport for the conservatively-managed tibial plateau fractures are provided in Table 7 and Figure 3.

Surgical management: The return rates for the various methods of surgical management are provided in Table 7 and Figure 2.

On meta-analysis of the synthesis data, the return rates for the ARIF cohort were found to be significant higher than both: The return rates for the ORIF cohort (OR = 3.22, 95%CI: 2.09-4.97, $P < 0.001$; $I^2 = \text{N/A}$); and the return rates for the FRAME cohort (OR 4.33, 95%CI: 2.89-6.50, $P < 0.001$; $I^2 = \text{N/A}$). There was no significant difference between the return rates of the ORIF cohort and the FRAME cohort (OR 1.35, 95%CI: 0.92-1.96, $P = 0.122$; $I^2 = 0\%$, $P = 0.40$). The return rates to pre-injury level sport for the various methods

Table 7 Summary of the return times to sport, return rates to sport, times to union and rates of union by treatment modality

Mode of treatment	<i>n</i> (total)	Return rates to sport	Return times to sport	Return rate to pre-injury level	Rates of union	Mean times to union
All ^[11-37]	920	642/920 (70%) ^[11-37]	6.9 mo (median) ^[15]	374/628 (60%) ^[11,12,14-18,20,24-35,37]	475/480 (99%) ^[12,16,17,20-22,24-27,29,31,34]	13.6 wk ^[16,20-22,29,32]
Non-surgical ^[18]	3	3/3 (100%) ^[18]	N/A	3/3 (100%) ^[18]	N/A	N/A
Surgical ^[11-37]	917	639/917 (70%) ^[11-37]	6.9 mo (median) ^[15]	371/625 (59%) ^[11,12,14-18,20,24-35,37]	475/480 (99%) ^[12,16,17,20-22,24-27,29,31,34]	13.6 wk ^[16,20-22,29,32]
Surgical						
ORIF ^[11-19]	193	115/193 (60%) ^[11-19]	6.9 mo (median) ^[15]	60/175 (34%) ^[11,12,14-18]	83/83 (100%) ^[12,16,17]	20.2 wk ^[16]
ARIF ^[24-34]	253	209/253 (83%) ^[24-34]	N/A	209/253 (83%) ^[24-34]	190/190 (100%) ^[24-27,29,31,34]	12.0 wk ^[29,32]
FRAME ^[11,12,20-24]	262	137/262 (52%) ^[11,12,20-24]	N/A	21/67 (31%) ^[11,12,20,24]	202/207 (98%) ^[12,20-22,24]	13.7 wk ^[20-22]
Non-specific surgical cohort ^[35-37]	209	178/209 (85%) ^[35-37]	N/A	81/130 (62%) ^[35,37]	N/A	N/A

ORIF: Open Reduction Internal Fixation; ARIF: Arthroscopic-Assisted Reduction Internal Fixation; FRAME: Frame-Assisted Fixation; NA: No data available.

of surgical management are provided in Table 7 and Figure 3.

On meta-analysis of the synthesis data, the return rates to pre-injury level sport for the ARIF cohort were found to be significant higher than both: The return rates to pre-injury level sport for the ORIF cohort (OR 9.10, 95%CI: 5.80-14.29, $P < 0.001$; $I^2 = \text{N/A}$); and the return rates to pre-injury level sport for the FRAME cohort (OR = 10.40, 95%CI: 5.65-19.15, $P < 0.001$; $I^2 = \text{N/A}$). There was no significant difference between the return rates to pre-injury sport of the ORIF cohort and the FRAME cohort (OR 1.14, 95%CI: 0.63-2.09, $P = 0.664$; $I^2 = 3\%$, $P = 0.31$).

Return times to sports

Conservative management: There were no reported return times for the conservatively-managed tibial plateau fractures (Table 7).

Surgical management: Only one study on the surgically managed fractures reported return times to sport. This was from the ORIF cohort. The reported return time was 6.9 mo (median) with a range of 2 to 18 mo^[15]. This represented a return time to full level sport^[15].

Fracture union

Conservative management: The study reporting on conservatively-managed fractures, did not record post-treatment fracture union^[18].

Surgical management: Fracture union was recorded in 13 studies^[12,16,17,20-22,24-27,29,31,34], with all 13 studies recording rates of union^[12,16,17,20-22,24-27,29,31,34] and only 6 studies recording times to union^[16,20-22,29,32] (Table 7). For those managed by ORIF, the union rate was 100%^[12,16,17] and the mean time to union was 20.2 wk^[16]. For those managed by ARIF, the union rate was 100%^[24-27,29,31,34] and the mean time to union was 12.0 wk^[29,32]. For those managed by FRAME, the union rate

was 98%^[12,20-22,24] and the mean time to union was 13.7 wk^[20-22].

Complications

Conservative management: For the conservatively-managed tibial plateau fractures, there were no complications reported^[18].

Surgical management: For the ORIF cohort, 8 of the studies reported complications^[11-13,15-19]: One study reported no complications^[14]. The reported complications included wound infection (0%-40%), prominent metalwork (0%-56%), post-operative knee stiffness requiring intervention (0%-8%), nerve-related symptoms (0%-6%), and loss of fixation requiring revision (0%-10%)^[11-19]. Removal of metalwork ranged from 0%-56% (mean 27%); re-intervention rate ranged 0%-93% (mean 39%)^[11-19].

For the ARIF cohort, nine of the studies reported complications^[24-30,32,34]; two studies reported no complications^[31,33]. The reported complications included wound infection (0%-7%), prominent metalwork (0%-20%), post-operative knee stiffness requiring intervention (0%-8%), DVT (0%-10%), nerve-related symptoms (0%-20%), loss of fixation requiring revision (0%-3%)^[24-34]. Removal of metalwork ranged from 0%-20% (mean 2%) and re-intervention rate ranged 0%-20% (mean 4%)^[24-34].

For the FRAME cohort, all studies reported complications^[11,12,20-24]. These included pin site infection (0%-57%), nerve-related symptoms (0%-10%), DVT (0%-13%) delayed union (0%-14%) post-treatment knee stiffness requiring intervention (0-5%), and post-treatment mal-alignment requiring intervention (0%-18%)^[11,12,20-24]. All cases required frame removal; beyond this, re-intervention rate ranged 0%-35% (mean 14%)^[11,12,20-24].

Predictive factors

A randomised controlled trial by the Canadian Orth-

opaedic Trauma Society^[11], comparing ORIF to FRAME for Schatzker VI fractures, found that there was a trend towards earlier return to pre-injury sporting activity levels at 6 mo ($P = 0.031$) and 12 mo ($P = 0.024$) post-injury for FRAME compared to ORIF. This difference, however, disappeared at 24 mo post-injury ($P = 0.128$)^[11].

These results are in keeping with those from Ahearn *et al.*^[12], who found there was no significant long-term difference between FRAME and ORIF, in terms of return to sporting activities, at a mean follow-up of 41 mo.

Loibl *et al.*^[37] noted poorer outcomes regarding return to sport for the more severe fracture types (AO/OTA B3 and C3). They also found that participation in downhill skiing post-injury decreased more for patients 61 years and older (56% decline) compared to patients younger than 60 years (45% decline): Post-injury frequency of sports ($r = 0.22$, $P < 0.05$) and duration of sports ($r = 0.25$, $P < 0.05$) was weakly correlated with the patient's age at injury^[37].

Kraus *et al.*^[36] found that, while patients with high-energy fracture patterns (AO/OTA Type C) could continue to participate in sports post-injury, at a frequency and duration similar to those of low-energy fracture patterns (AO/OTA Type A and B) ($P = 0.357$), the variety of sports they could return to was significantly reduced ($P < 0.004$). Conversely, however, they found that the presence of a concomitant ligamentous injuries was not associated with a poorer return to sporting activity ($P = 0.365$)^[36].

DISCUSSION

The main findings of this review are that seventy percent of patients with a tibial plateau fracture returned to sport following injury, with only sixty percent able to return to their pre-injury level of sport. Conservative management offered very acceptable results for undisplaced fractures, with a return to sport rate of 100%. Regarding surgical techniques for displaced fractures, ARIF offered the best return rates at 83%; however, such results were likely influenced by less severe fracture patterns being more amenable to this technique. There was no difference seen in return rates between ORIF and FRAME. There was a significant limitation in the reporting of data with only one study reporting return times to sport for this fracture type.

In comparison to previous similar systematic reviews, the methodological quality of the studies in this review was improved, with a mean modified CMS of 66^[7-10]. In keeping with this, there was one recorded RCT^[11]. However, all other included studies comprised Level 2 to 4 evidence^[11-37], demonstrating a need for further high quality research in this field to better define the optimal treatment modalities for these injuries.

From our data we found that conservative manage-

ment offered a good return rates to sport at 100%. Similarly, return rates to previous level of sport were very satisfactory at 100%. However, this was from a cohort of three fractures, on which there were no return times reported^[18]: This reflects a significant limitation of data in this area. Despite this, the rate of persisting symptoms and complications following this treatment was 0%^[18]. Thus, with the restricted evidence available, conservative management appears to be a very acceptable treatment for undisplaced fractures. Clinicians should, however, remain vigilant for fracture displacement during follow-up: If this is occurs, surgical management should be offered^[3].

From our data we found that surgical management offered limited return rates to sport at 70%. Again, the evidence in this area was restricted, with only one study in this cohort reporting return times to sport^[15]. Despite such limitations, with the reported median return time of 6.9 mo, it appears that sporting rehabilitation following such injuries is notably prolonged^[15]. Despite the restricted reporting on return times to sport, there was sufficient data on return rates to sport to allow comparison between the three main treatment methods: ORIF, ARIF and FRAME. ARIF offered the best return rates at 83%, with a similar value for return to pre-injury level of sport. In comparison, the return rates for ORIF and FRAME were 60% and 52% respectively, and the return rate to pre-injury level of sport were 34% and 31%. The positive findings for ARIF are in keeping with the current literature: A recent systematic review found ARIF to provide encouraging clinical and radiological outcomes from an assessment of 12 studies^[2]. It has been suggested that this technique provides the surgeon with a superior assessment of fracture reduction intra-operatively, as well as allowing direct intra-operative assessment and management of concomitant intra-articular knee injuries^[2]. Indeed, within our review, 9 of the 11 studies using ARIF, reported associated arthroscopic procedures at time of surgery^[24-30,32,34]. However, to note, six of the nine studies in the ORIF cohort also reported associated management of intra-articular injuries, with a number of these studies avoiding arthroscopic-assisted reduction due to the complexity of fractures encountered^[11,14,16-19]. It has been noted that the use of arthroscopic-assisted reduction techniques for Schatzker V and VI fractures can significantly prolong operating time, and increase the risk of post-operative infection and compartment syndrome^[38]. Certainly, on assessment of the fracture types recorded in the studies of the ARIF cohort, at least four studies restricted the technique to low-energy fracture patterns (Schatzker I-III, AO/OTA Type A and B)^[27,30,31,33]. In comparison, there were no such restrictions of fracture types in the ORIF^[11-19] and FRAME^[11,12,20-24] cohorts. Thus, it is likely that selection of fracture type had a confounding influence on the results from our review^[36,37]. Nevertheless, it appears that, particularly for the lower-energy fracture patterns,

ARIF offers athletes the best possibility to return to sport post-treatment.

Other notable findings were that FRAME offered a quicker return to pre-injury sporting levels than ORIF for Schatzker V and VI fractures^[11]. This may reflect a lesser insult to the surrounding soft tissue with FRAME compared to ORIF, so enabling a quicker return of function^[11]. However, return rates to sport for the two techniques, beyond 2 years follow-up, from two studies, showed no difference^[11,12]. Thus it remains debatable if FRAME is truly better than ORIF in allowing return to sport following high energy bicondylar tibial plateau fractures. Further notable findings were that two other studies found that return to sport following tibial plateau fractures was adversely affected by increasing severity of fracture pattern and by advancing age of the patient^[36,37]. It would appear that for increasing severity of fracture pattern, with the associated damage to cartilage and surrounding structures, recovery of sporting function in the knee becomes more challenging^[36,37]. Such effects are then confounded by increasing age of the patient, through the reduced physiological reserve and reduced healing potential that is often associated with this^[36,37].

In comparison to previous studies, there was an improvement in the reporting of both rehabilitation methods and functional outcome scores^[7-10]. All but one of the studies reported comprehensive rehabilitation protocols, with the majority providing detailed descriptions of weight-bearing status, immobilisation method and range of motion protocols^[11-22,24-37]. Similarly, twenty-six of the twenty-seven studies used formal validated scoring methods to allow assessment of post-treatment function^[11-30,32-37].

Assessment of the rehabilitation methods revealed there was notable variation between the techniques. These were largely centred on range of motion protocols and methods of post-operative immobilisation^[11-22,24-37]. With the numbers available, it was not possible to assess the effect of variation in rehabilitation methods on return to sport. Appreciably, such variations are guided by the severity of the injury and associated damage to the surrounding ligaments^[11-22,24-37]. However, with the considerable variations observed, it appears there is definite ability, within future studies, to assess, refine and optimise rehabilitation techniques.

The most notable finding, in comparison to previous similar reviews^[7-10], was the significant lack of reporting on return times to sport. This, in part, reflects the limited description of return to sport in the included studies, with this often being briefly reported as a secondary outcome measure^[11-37]. However, this also reflects the prolonged rehabilitation associated with such fractures, with return to sport often outdating the standard follow-up duration for these injuries^[3,15]. Nevertheless, the restricted reporting on return to sport for these fractures was a significant shortcoming, limiting both inter-study comparisons and collection

of certain relevant details such as return to pre-injury level of sport^[7-10]. Future studies should aim to provide more comprehensive descriptions of return rates and times to sport, detailing the level of sport to which the athlete returned, as well as the time taken to return to both training and full-level sport.

There are several limitations to this review

Firstly, due to the limited reporting in most studies, it was not possible to develop synthesis data for return times to sport for this injury. Given the usefulness of such information for athletes and clinicians alike, future studies should be encouraged to record such information as able.

Similar to this, due to the paucity of reporting in the included studies, it was not possible to analyse the synthesis data for the effect of certain factors such as fracture severity, concomitant injuries, and required re-intervention on sporting return. Given the importance of such data on treatment decisions and final outcome, the generalised data provided can be of limited value for the individual athlete. However, the authors have tried to illustrate such information, where possible, including details on fracture severity, the presence of associated intra-articular injuries and rates of complications and further surgery accordingly.

Thirdly, the reporting of return rates to sport throughout the studies was limited. Few provided comprehensive descriptions, with the majority only providing a brief summary of sporting outcomes. This limits our ability to compare sporting outcome both between studies as well as between treatment modalities. In order to limit this effect, sporting outcome was divided in two distinct categories (return to sport, return to same level of sport), enabling a clear outcome from each study.

Lastly, due to the limited size of certain sub-cohorts within the synthesis data, it was only possible to perform six meta-analysis comparisons: further comparisons between sub-sets of the surgical techniques would have been preferable but unfortunately this was not possible due to sub-cohort size.

In conclusion, thirty percent of all athletes who suffer a tibial plateau fracture may not be able to return to sport post-injury. Conservative management forms the first-line treatment for all undisplaced fractures, and provides good results regarding return to sport. Surgical fixation is reserved for displaced fractures. The choice of surgical technique is guided by the severity and pattern of the fracture. With low-energy fracture patterns, ARIF appears to offer the best possibility of return to previous level of sport. With high-energy fracture patterns, there appears no clear difference between ORIF and FRAME for return rates to sport. There was a significant limitation on reporting of return times to sport following these injuries. Thus, despite the available data, further well-designed research is required to better define return rates and

times to sport following tibial plateau fractures.

COMMENTS

Background

Tibial plateau fractures account for 1% of all fractures. The main causes for these injuries include road traffic accidents, falls from a height, pedestrian struck by motor vehicle and high-impact sporting collisions. Despite sport being a common cause for this injury, the literature on return rates and return times to sport for this fracture type remains limited. Such data is valuable to sporting medical personnel and sports teams alike, as this can allow optimisation of management and rehabilitation technique for this injury, ensuring optimisation of sporting outcome for the affected athletes.

Research frontiers

Despite comprising only 1% of all fractures, tibial plateau fractures represent an injury with significant morbidity, due to the intra-articular nature of the fracture. This is particularly the case for athletes sustaining this injury, as return to sport can be significantly affected. Despite sport being a well-documented cause for this injury, data on return to sport following this fracture remains limited, as most studies present outcome data through combined scoring systems, failing to differentiate sporting outcomes. Given the significant difficulties experienced by athletes planning to return to sport following this injury, accurate information on the return rates and return times to sport for this fracture type, stratified by fracture classification and treatment modality, can allow sporting medical personnel and sports team to appropriately select the optimal treatment modality for each patient and adequately schedule rehabilitation programmes following these injuries. By optimising the treatment and rehabilitation of these injuries, this can ensure that affected athletes achieves the optimal sporting outcome possible.

Innovations and breakthroughs

In this systematic review, the authors identified 27 studies which reported either return rates or return times to sport following tibial plateau fractures: All studies recorded return rates; only one study recorded return times. One study reported on the outcome of conservative-managed fractures; all 27 studies reported on the outcome of surgically-managed fractures. The surgical techniques comprised Open Reduction Internal Fixation (ORIF), Arthroscopic-Assisted Reduction Internal Fixation (ARIF) and Frame-Assisted Fixation (FRAME). The return rates were: Total cohort 70%; Conservatively-Managed cohort 100%; Surgically-Managed cohort 70%. For the different surgical techniques, the return rates were: ORIF cohort 60%, ARIF cohort 83% and FRAME cohort 52%. The recorded return time was 6.9 mo (median), from a study reporting on ORIF. ARIF was more commonly used for lower energy fracture patterns (Schatzker I-III; AO/OTA Type A and B), while ORIF and FRAME were used for all fracture patterns. ARIF provided the best return rates to sport, particularly for the lower energy fracture patterns. Data however is limited, particularly for return times to sport. Further research in this area is required.

Applications

A comprehensive understanding of the expected return rates and return times to sport following tibial plateau fractures, stratified by fracture pattern and treatment modality, ensures the treating clinician can appropriately select the optimal method of management, to allow the best possibility of return to sport post-injury. Such information can also allow sports team to realistically plan rehabilitation schedules, with a better understanding of the required treatment duration before athletes will be able return to sport. This allows optimization of both the management and outcome of these injuries.

Terminology

ARIF: Fixation of a Tibial Plateau Fracture with Internal Fixation and an Arthroscope to ensure accurate articular surface reduction; FRAME: Fixation of a Tibial Plateau Fracture with an External Fixation Device; Non-Bridging Frame: An External Fixation Device which does not bridge across the knee joint; Bridging Frame: An External Fixation Device which bridges across the knee joint; Arthroscopic-Assisted Frame Application: Fixation of a Tibial Plateau Fracture with an External Fixation Device and an Arthroscope to ensure accurate articular surface reduction; Frame Application with Internal Fixation: Fixation of a Tibial

Plateau Fracture with an External Fixation Device along with Internal Fixation; AO/OTA Classification: The Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association Tibial Plateau Fracture Classification. This comprises three main categories: Type A: Extra-Articular; Type B: Partial Articular; Type C: Articular; Schatzker Classification: The Schatzker Tibial Plateau Fracture Classification. This comprises six groups: I - Lateral Plateau Split Fracture; II - Lateral Plateau Split-Depression Fracture; III - Lateral Plateau Depression Fracture; IV Medial Plateau Fracture; V - Bicondylar Fracture; VI - Bicondylar Fracture with Metaphyseal-Diaphyseal Disassociation.

Peer-review

The manuscript is nice and well written.

REFERENCES

- 1 **Court-Brown CM**, Caesar B. Epidemiology of adult fractures: A review. *Injury* 2006; **37**: 691-697 [PMID: 16814787 DOI: 10.1016/j.injury.2006.04.130]
- 2 **Chen HW**, Liu GD, Wu LJ. Clinical and radiological outcomes following arthroscopic-assisted management of tibial plateau fractures: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3464-3472 [PMID: 25246171 DOI: 10.1007/s00167-014-3256-2]
- 3 **Court Brown C**, McQueen MM, Tornetta III P. Trauma. Philadelphia: Lippincott Williams & Wilkins, 2006
- 4 **McNamara IR**, Smith TO, Shepherd KL, Clark AB, Nielsen DM, Donell S, Hing CB. Surgical fixation methods for tibial plateau fractures. *Cochrane Database Syst Rev* 2015; **(9)**: CD009679 [PMID: 26370268 DOI: 10.1002/14651858.CD009679.pub2]
- 5 **Jiwanlal A**, Jeray KJ. Outcome of Posterior Tibial Plateau Fixation. *J Knee Surg* 2016; **29**: 34-39 [PMID: 26509660 DOI: 10.1055/s-0035-1564729]
- 6 **Moher D**, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; **339**: b2535 [PMID: 19622551 DOI: 10.1136/bmj.b2535]
- 7 **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/ldv039]
- 8 **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]
- 9 **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]
- 10 **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]
- 11 **Canadian Orthopaedic Trauma S**. Open reduction and internal fixation compared with circular fixator application for bicondylar tibial plateau fractures. Results of a multicenter, prospective, randomized clinical trial. *J Bone Joint Surg Am* 2006; **88**: 2613-2623 [PMID: 17142411 DOI: 10.2106/JBJS.E.01416]
- 12 **Ahearn N**, Oppy A, Halliday R, Rowett-Harris J, Morris SA, Chesser TJ, Livingstone JA. The outcome following fixation of bicondylar tibial plateau fractures. *Bone Joint J* 2014; **96-B**: 956-962 [PMID: 24986951 DOI: 10.1302/0301-620X.96B7.32837]
- 13 **Keogh P**, Kelly C, Cashman WF, McGuinness AJ, O'Rourke SK. Percutaneous screw fixation of tibial plateau fractures. *Injury* 1992; **23**: 387-389 [PMID: 1428164]
- 14 **Morin V**, Pailhé R, Sharma A, Rouchy RC, Cognault J, Rubens-Duval B, Saragaglia D, Moore I postero-medial articular tibial fracture in alpine skiers: Surgical management and return to sports activity. *Injury* 2016; **47**: 1282-1287 [PMID: 27037028 DOI: 10.1016/j.injury.2016.03.024]
- 15 **van Dreumel RL**, van Wunnik BP, Janssen L, Simons PC, Janzing HM. Mid- to long-term functional outcome after open reduction and internal fixation of tibial plateau fractures. *Injury* 2015; **46**:

- 1608-1612 [PMID: 26071324 DOI: 10.1016/j.injury.2015.05.035]
- 16 **Chang SM**, Hu SJ, Zhang YQ, Yao MW, Ma Z, Wang X, Dargel J, Eysel P. A surgical protocol for bicondylar four-quadrant tibial plateau fractures. *Int Orthop* 2014; **38**: 2559-2564 [PMID: 25172362 DOI: 10.1007/s00264-014-2487-7]
 - 17 **Stevens DG**, Beharry R, McKee MD, Waddell JP, Schemitsch EH. The long-term functional outcome of operatively treated tibial plateau fractures. *J Orthop Trauma* 2001; **15**: 312-320 [PMID: 11433134]
 - 18 **Waldrop JI**, Macey TI, Trettin JC, Bourgeois WR, Hughston JC. Fractures of the posterolateral tibial plateau. *Am J Sports Med* 1988; **16**: 492-498 [PMID: 3056051]
 - 19 **Brunner A**, Honigsmann P, Horisberger M, Babst R. Open reduction and fixation of medial Moore type II fractures of the tibial plateau by a direct dorsal approach. *Arch Orthop Trauma Surg* 2009; **129**: 1233-1238 [PMID: 19238408 DOI: 10.1007/s00402-009-0841-9]
 - 20 **Chin TY**, Bardana D, Bailey M, Williamson OD, Miller R, Edwards ER, Esser MP. Functional outcome of tibial plateau fractures treated with the fine-wire fixator. *Injury* 2005; **36**: 1467-1475 [PMID: 16243333 DOI: 10.1016/j.injury.2005.05.008]
 - 21 **Katsenis D**, Athanasiou V, Megas P, Tyllianakis M, Lambiris E. Minimal internal fixation augmented by small wire transfixion frames for high-energy tibial plateau fractures. *J Orthop Trauma* 2005; **19**: 241-248 [PMID: 15795572]
 - 22 **Katsenis D**, Dendrinis G, Kouris A, Savas N, Schoinochoritis N, Pogiatis K. Combination of fine wire fixation and limited internal fixation for high-energy tibial plateau fractures: functional results at minimum 5-year follow-up. *J Orthop Trauma* 2009; **23**: 493-501 [PMID: 19633458 DOI: 10.1097/BOT.0b013e3181a18198]
 - 23 **Weigel DP**, Marsh JL. High-energy fractures of the tibial plateau. Knee function after longer follow-up. *J Bone Joint Surg Am* 2002; **84-A**: 1541-1551 [PMID: 12208910]
 - 24 **Itokazu M**, Matsunaga T, Ishii M, Kusakabe H, Wyni Y. Use of arthroscopy and interporous hydroxyapatite as a bone graft substitute in tibial plateau fractures. *Arch Orthop Trauma Surg* 1996; **115**: 45-48 [PMID: 8775710]
 - 25 **Chan YS**, Chiu CH, Lo YP, Chen AC, Hsu KY, Wang CJ, Chen WJ. Arthroscopy-assisted surgery for tibial plateau fractures: 2- to 10-year follow-up results. *Arthroscopy* 2008; **24**: 760-768 [PMID: 18589264 DOI: 10.1016/j.arthro.2008.02.017]
 - 26 **Chan YS**, Yuan LJ, Hung SS, Wang CJ, Yu SW, Chen CY, Chao EK, Lee MS. Arthroscopic-assisted reduction with bilateral buttress plate fixation of complex tibial plateau fractures. *Arthroscopy* 2003; **19**: 974-984 [PMID: 14608317]
 - 27 **Kampa J**, Dunlay R, Sikka R, Swiontkowski M. Arthroscopic-Assisted Fixation of Tibial Plateau Fractures: Patient-Reported Postoperative Activity Levels. *Orthopedics* 2016; **39**: e486-e491 [PMID: 27135456 DOI: 10.3928/01477447-20160427-03]
 - 28 **Gill TJ**, Moezzi DM, Oates KM, Sterett WL. Arthroscopic reduction and internal fixation of tibial plateau fractures in skiing. *Clin Orthop Relat Res* 2001; **(383)**: 243-249 [PMID: 11210961]
 - 29 **Duan XJ**, Yang L, Guo L, Chen GX, Dai G. Arthroscopically assisted treatment for Schatzker type I-V tibial plateau fractures. *Chin J Traumatol* 2008; **11**: 288-292 [PMID: 18822192]
 - 30 **Holzach P**, Matter P, Minter J. Arthroscopically assisted treatment of lateral tibial plateau fractures in skiers: use of a cannulated reduction system. *J Orthop Trauma* 1994; **8**: 273-281 [PMID: 7965287]
 - 31 **Guanche CA**, Markman AW. Arthroscopic management of tibial plateau fractures. *Arthroscopy* 1993; **9**: 467-471 [PMID: 8216581]
 - 32 **Hung SS**, Chao EK, Chan YS, Yuan LJ, Chung PC, Chen CY, Lee MS, Wang CJ. Arthroscopically assisted osteosynthesis for tibial plateau fractures. *J Trauma* 2003; **54**: 356-363 [PMID: 12579065 DOI: 10.1097/01.TA.0000020397.74034.65]
 - 33 **Pizanis A**, Garcia P, Pohlmann T, Burkhardt M. Balloon tibioplasty: a useful tool for reduction of tibial plateau depression fractures. *J Orthop Trauma* 2012; **26**: e88-e93 [PMID: 22430523 DOI: 10.1097/BOT.0b013e31823a8dc8]
 - 34 **Chiu CH**, Cheng CY, Tsai MC, Chang SS, Chen AC, Chen YJ, Chan YS. Arthroscopy-assisted reduction of posteromedial tibial plateau fractures with buttress plate and cannulated screw construct. *Arthroscopy* 2013; **29**: 1346-1354 [PMID: 23820261 DOI: 10.1016/j.arthro.2013.05.003]
 - 35 **Scheerlinck T**, Ng CS, Handelberg F, Casteleyn PP. Medium-term results of percutaneous, arthroscopically-assisted osteosynthesis of fractures of the tibial plateau. *J Bone Joint Surg Br* 1998; **80**: 959-964 [PMID: 9853485]
 - 36 **Kraus TM**, Martetschlager F, Müller D, Braun KF, Ahrens P, Siebenlist S, Stöckle U, Sandmann GH. Return to sports activity after tibial plateau fractures: 89 cases with minimum 24-month follow-up. *Am J Sports Med* 2012; **40**: 2845-2852 [PMID: 23118120 DOI: 10.1177/0363546512462564]
 - 37 **Loibl M**, Bäumllein M, Massen F, Gueorguiev B, Glaab R, Perren T, Rillmann P, Ryf C, Naal FD. Sports activity after surgical treatment of intra-articular tibial plateau fractures in skiers. *Am J Sports Med* 2013; **41**: 1340-1347 [PMID: 23733831 DOI: 10.1177/0363546513489524]
 - 38 **Wang Z**, Tang Z, Liu C, Liu J, Xu Y. Comparison of outcome of ARIF and ORIF in the treatment of tibial plateau fractures. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 578-583 [PMID: 27553298 DOI: 10.1007/s00167-016-4285-9]

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Systematic review on the use of autologous matrix-induced chondrogenesis for the repair of articular cartilage defects in patients

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Abstract

AIM

To systematically review the results of studies looking at autologous matrix-induced chondrogenesis (AMIC) in humans.

METHODS

A literature search was performed, adhering to the PRISMA guidelines, to review any studies using such techniques in humans. Our initial search retrieved 297 articles listed on MEDLINE, Google Scholar, CINAHL and EMBASE. From these studies, 15 studies meeting the eligibility criteria were selected and formed the basis of our systematic review.

RESULTS

The study designs, surgical techniques and outcome measures varied between the studies. Although all studies reported improvements in patient outcome measures, this was not necessarily correlated with magnetic resonance imaging findings. Although there were many additional procedures performed, when AMIC was performed in isolation, the results tended to peak at 24 mo before declining.

CONCLUSION

Although short-term studies suggest improved patient reported outcomes with a variety of scaffolds, surgical techniques and rehabilitation regimes, the literature remains equivocal on whether the defect size and location, and patient factors affect the outcome. Patient

benefit appears to be maintained in the short-to-medium term but more high level studies with extensive and robust validated outcome measures should be conducted to evaluate the medium- and long-term effect of the AMIC procedure.

Key words: Autologous matrix-induced chondrogenesis; Cartilage defects; Humans, PRISMA

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Core tip: Studies looking at autologous matrix-induced chondrogenesis (AMIC) in humans suggest improved patient reported outcomes in the short-to-medium term but there is significant variation in the scaffolds, surgical techniques and rehabilitation regimes used. The literature remains equivocal on whether the defect size and location, and patient factors affect the outcome. More high level studies with extensive and robust validated outcome measures should be conducted to evaluate the medium- and long-term effect of the AMIC procedure.

Shaikh N, Seah MKT, Khan WS. Systematic review on the use of autologous matrix-induced chondrogenesis for the repair of articular cartilage defects in patients. *World J Orthop* 2017; 8(7): 588-601 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v8/i7/588.htm> DOI: <http://dx.doi.org/10.5312/wjo.v8.i7.588>

INTRODUCTION

Cartilage defects have a limited capacity for repair^[1,2]. Untreated focal defects have the potential to progress to more generalised lesions and can cause significant morbidity. The frequent outcome for arthritis in large joints such as the knee is surgical intervention for joint replacement. This procedure is generally successful in older sedentary patients, but the limited lifetimes of prostheses make it much less desirable for younger and develop new strategies for the treatment of focal cartilage defects to prevent secondary osteoarthritis.

Various surgical procedures have been implemented to reduce pain, and postpone or prevent the need for joint replacement, while simultaneously withstanding the daily activities of the patient^[3]. These include the use of bone marrow stimulation techniques pioneered by Pridie by introducing the concept of subchondral drilling^[4,5]. This was further developed by Steadman who introduced the notion of microfracture^[6]. A range of chondrocyte implantation techniques have also developed including autologous chondrocyte implantation (ACI), matrix-induced autologous chondrocyte implantation (MACI), mosaicplasty and osteochondral autologous transplantation (OATS)^[7-10].

In 2003 after funding issues were raised for two-

step procedures such as ACI and MACI partly in view of associated costs, a new one-step procedure was introduced for the repair of cartilage defects called autologous matrix-induced chondrogenesis (AMIC) that brings together microfracture with a collagen matrix scaffold^[11]. There is increasing interest in AMIC as it provides a cost-effective alternative to cell-based therapies for articular cartilage repair, and it is highly autologous in nature. Benthien and Behrens^[1] first described the AMIC procedure using an awl to perform perforations in the subchondral bone, and "partial autologous fibrin glue" (PAF) using commercially available fibrin glue to adhere Chondro-Gide® (Geistlich Biomaterials, Wolhausen, Switzerland) collagen membrane to the lesion. The TGFβ component of fibrin may contribute to the chondrogenic differentiation of mesenchymal stem cells (MSCs)^[10]. Since then the procedure has been described with variations in the drilling technique, scaffold and fixation.

The results with AMIC in the literature have been variable. As there are limited studies on AMIC, variability in the type of scaffold used^[12-15], the surgical procedure^[1,13,15-17], defect size and location, and patient variability may all contribute to variable results. In addition, we are not aware of the longevity of these results. We performed a systematic review of the literature identifying studies looking at AMIC to determine their clinical outcome, and address these three questions: (1) does the type of scaffold, surgical technique or rehabilitation regime affect outcome? (2) does the defect size and location, and patient factors affect outcome? and (3) does the outcome change with time?

MATERIALS AND METHODS

A systematic review of the published literature was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analysis Guidelines^[18]. This search was completed on November 30, 2016 using search databases MEDLINE, Google Scholar, Cumulative Index to Nursing and Allied Health Literature, AMED and EMBASE. No restrictions regarding publication date were applied during the literature search, due to the relatively new nature of AMIC and the limited number of related articles that have been published. Keywords used in the search include "autologous matrix-induced chondrogenesis" and "AMIC". The Cochrane library was also searched using the terms "autologous matrix-induced chondrogenesis" and "AMIC". Abstracts of the selected articles were reviewed to ensure they met the selection criteria, after which the full article was obtained. The bibliographies and in-text references of the retrieved articles were searched for any articles that may have been missed during the initial search. Unpublished or grey literature was identified using databases including System for Information on Grey Literature in Europe, the National

Technical Information Service, the National Research Register (United Kingdom), UKCRN Portfolio Database, the National Technical Information Service, the British Library's Integrated Catalogue, and Current Controlled Trials database. Published and unpublished material including university theses and dissertations, and conference proceedings in the English literature were also reviewed.

The inclusion criteria were clinical studies in English language looking at outcomes after AMIC in partial- and full-thickness focal chondral or osteochondral defects (ICRS grade III or IV) of any joint. Studies with a level of evidence I-IV as described by the Oxford Centre for Evidence-based Medicine^[19] were included. Studies not meeting these criteria, single-patient case studies, techniques, comments, letters, editorials, protocols and guidelines were excluded. Animal and cadaveric studies were also excluded.

The titles and abstracts of all citations were reviewed by the three authors (Shaikh N, Seah MKT and Khan WS). Full manuscripts of citations adhering to the inclusion criteria and those that were uncertain were downloaded. Reference lists of all full manuscripts and applicable review articles were reviewed to identify any further articles omitted from the initial search. The same investigators then reviewed all full manuscripts against the inclusion criteria and any disagreement on eligibility was resolved by discussion. The corresponding author of the paper was contacted if any queries arose. They were also consulted as to any additional citations that may address the research question.

Data was extracted from papers that satisfied the eligibility criteria. The variables that were determined for each study were study type, treatment period, study size, gender, mean age, patients lost to follow-up, mean and range of follow-up, joint involved, size, grade and location of lesion, inclusion and exclusion criteria, source of funding, surgical technique, previous and associated surgeries, rehabilitation and outcome scores. The extracted data was entered onto Microsoft Excel (Microsoft Corporation, Washington, DC) by one investigator (Shaikh N), and re-evaluated and verified by the other authors (Seah MKT and Khan WS). The investigators were blinded to the source or authors of the identified papers. Although the systematic review protocol was approved by the host institution, the systematic review protocol was not formally registered in a registry. A systematic review was performed rather than a meta-analysis in view of the lack of randomised controlled trials and consistent outcome measures, where the results could be combined to allow statistical analyses.

Study quality assessment

The Coleman Methodology Score (CMS)^[20] was used to evaluate the quality of the studies and to determine if the outcomes and claims made in particular studies

should be given more weighting than others. The ratings were also used as a guide to assess the level of confidence from which conclusions could be drawn from a particular study. CMS consists of two parts; Part A that focuses on the design of the study and Part B that relates to the study outcomes. This instrument uses a scaling system, in which the studies are assessed using 10 criteria. Part A has a maximum total score of 65, while Part B has a maximum total score of 35, giving a total score of 100. The total score can be graded as being excellent (85-100 points), good (70-84 points), fair (55-69 points) and poor (< 55 points). A higher total score suggests that the study has an efficient design and is better at avoiding the effects of chance, various biases and confounding factors. The categories used in the CMS were formed on the basis of the Consolidated Standards of Reporting Trials statement for randomized controlled trials^[21].

RESULTS

The results of the search using the databases retrieved 297 articles. Twenty-six articles were reviewed after excluding animal and pre-clinical studies, single-patient case reports, literature reviews and articles where the original text was in a language other than English. Of the 26 articles obtained, 10 were excluded as they represented level V evidence, review studies or technical notes, resulting in a total of 16 articles that were included in this systematic review (Figure 1)^[3,13,15-17,22-33]. Of the 16 included articles, 13 studies were prospectively conducted, 2 were retrospective, and only 1 was a randomized control trial.

There were more males than females included in the studies, with a ratio of approximately 2:1. The mean age was 36.2 years (range 15-50 years) and the mean follow-up period was 30 mo (range 6-62 mo). Ten of the 16 studies focussed on the knee, 3 on the ankle, and 3 on the hip (Table 1). Some of the studies mentioned sources of funding, but none that would trigger any concerns about conflict of interests or bias. A variety of treatment algorithms were used including different drilling techniques, scaffold used, method of fixation, associated surgery and the rehabilitation protocol (Table 2).

All of the studies adopted at least one form of established patient-reported outcome measure and 9 of the 16 studies obtained patient Magnetic resonance Observation of Cartilage Repair Tissue (MOCART) scores (Tables 3 and 4). For the 10 studies looking at the knee, all reported more than one clinical outcome measure. Five used the Visual Analogue Scale (VAS), 4 used the Lysholm score and the Knee injury and Osteoarthritis Outcome Score (KOOS), 3 used the International Knee Documentation Committee (IKDC) score, 2 used the International Cartilage Repair Society (ICRS) and the Cincinnati score, and 1 used the Tegner score and Kujala patellofemoral score.

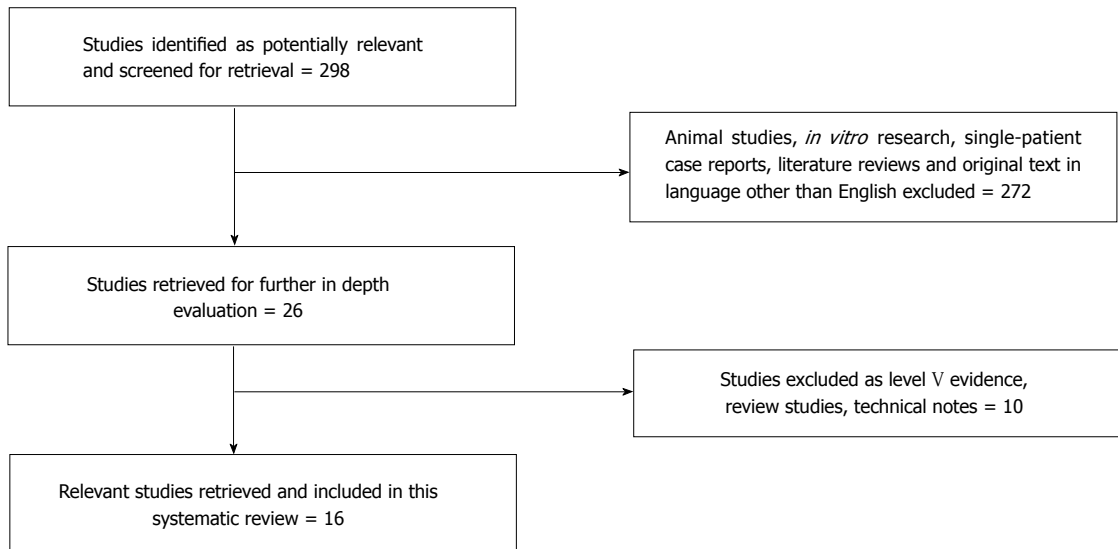


Figure 1 Illustration of the selection process for articles in this systematic review.

The three studies looking at the ankle joint used the American Orthopaedic Foot and Ankle Society (AOFAS) score and the VAS. One study also reported the Foot Function Index (FFI). Two of the hip studies reported the modified Harris Hip Score (mHHS). Four knee, four ankle and one hip studies also reported on MOCART scores. Although positive patient-reported outcomes were observed in all studies, MOCART scores did not always correlate with the patient-reported outcomes.

Kusano *et al.*^[22] found significant improvements in the IKDC and Lysholm scores, but the MOCART scores did not correlate with the positive clinical outcomes. The majority of patients displayed incomplete defect repair, damaged repair tissue, and inhomogeneous repair tissue structure, as well as subchondral lamina and subchondral bone that were not intact. The randomized control trial by Anders *et al.*^[3] assessed differences between a microfracture technique, a sutured AMIC technique, and a glued AMIC technique. In all three groups, positive patient outcomes and pain levels were observed at follow-up, with no significant differences between the groups. In assessing the magnetic resonance imaging (MRI) outcomes of patients in this study, results showed good defect filling in most patients, however homogenous repair tissue was only seen in 50% of the patients treated using the AMIC techniques, compared to 100% of the patients treated using traditional microfracture. Additionally, surface regeneration and integration of the lesion with the cartilage proved to be marginally inferior in patients that were treated using AMIC. The finding that MRI scores do not always correspond with patient-assessed outcomes is consistent with those observed in other studies. Dhollander *et al.*^[29] found favourable clinical outcome scores in patients undergoing AMIC at the patellofemoral joint but the radiological findings did not support these outcomes. All 10 patients

had subchondral lamina changes on MRI and 3 had osteophytes within 24 mo.

Does the type of scaffold, surgical technique or rehabilitation regime affect outcome?

There are three commercially available biodegradable membrane scaffolds that fill in the lesions until they are absorbed and replaced by repair tissue (Table 2). The three scaffolds are Chondro-Gide[®], Chondrotissue[®] (BioTissue, Zurich, Switzerland) and Hyalofast[™] (Fidia Advanced Biopolymers, Padua, Italy). Chondro-Gide[®] is a porcine-based membrane that is the original and most popular scaffold used in AMIC. This protein-based matrix has a bi-layer structure composed primarily of type I/III collagen. In cases where the AMIC Plus technique^[16] was implemented, a Platelet-rich plasma (PRP) gel (GPS[®] III System Advantages, Biomet) was applied to the surface of the lesion prior to the application of the membrane. Chondrotissue[®] is "sponge-like" matrix composed of polyglycolic acid treated with hyaluronan^[12,13]. In cases where Chondrotissue[®] was used, PAF was substituted with biodegradable pins^[13]. The Hyalofast[™] membrane is a partially-synthetic by-product of hyaluronic acid composed of an unstructured amalgamation of fibres. On degradation it releases hyaluronic acid into the defect site that may encourage chondrogenic differentiation of bone marrow-derived MSCs^[14]. Prior to commencing the AMIC procedure, bone marrow is aspirated from the iliac crest, and processed to obtain bone-marrow derived MSCs. This is used with autologous PRP obtained from the blood sample, and together the Hyalofast[™] membrane is immersed in this solution prior to being applied onto defect^[15]. Buda *et al.*^[15] performed the AMIC procedure on 20 patients using Hyalofast[™] membrane, and the improvements in the IKDC scores were greater than those seen with Chondro-Gide[®] membrane. The mean

Table 1 Study demographics, lesion location and grade, inclusion and exclusion criteria, and funding sources

Ref.	Treatment period	Patient numbers	Mean age (yr)	Mean follow-up in months (range)	Joint	Defect location and type	Grade of lesion	Lesion dimensions (cm ²)	Inclusions	Exclusions	Source of funding
Shetty <i>et al</i> ^[34]	4 yr	30				MFC, LFC, trochlea, patella	Grade III/IV	2-8		Malalignment of the knee exceeding 5° of valgus or varus. Generalized osteoarthritic changes in the knee	
Buda <i>et al</i> ^[15]	Apr 2006-May 2007	20 (12M, 8F)	15-50	29	Knees		Grade III/IV	Not specified		Diffuse arthritis, general medical conditions (e.g., diabetes, rheumatoid arthritis etc.), haematological disorders and infections	None
Gille <i>et al</i> ^[26]	2003-2005	27 (16M, 11F)	39	37 (24-62)	Knees	Medial femoral condyle 7, lateral femoral condyle 3, patella 9, trochlea 2, femoral condyle and patella 6	Grade IV	> 1	Clinical symptomatic chondral lesions at femoral condyle, patella or trochlea	Advanced osteoarthritis, rheumatic disease, total meniscectomy, BMI > 35, deviation of mechanical axis to the affected compartment	Not specified
Dhollander <i>et al</i> ^[16]	Jan 2008-Apr 2008	5 (3M, 2F)	18-50	24 (12-24)	Knees	Patella	Grade III/IV	2 (range 1-3)	Symptomatic focal patella cartilage defects	Untreatable tibiofemoral or patellofemoral malalignment, diffuse osteoarthritis, major meniscal deficiency or other general medical conditions	Not specified
Dhollander <i>et al</i> ^[13]	2008-2009	5 (4M, 1F)	29.8	24	Knees	Right 2 (40%), left 3 (60%) medial femoral condyle (2), lateral femoral condyle (2), trochlea (1)	Grade III/IV	Median 2.3, range 1.5-5	16-40 yr, single symptomatic focal cartilage defect on femoral condyles or patellofemoral joint	Untreated tibiofemoral or patellofemoral malalignment or instability, diffuse osteoarthritis, bipolar "kissing" lesions, major meniscal deficiency and other general medical conditions	Not specified
Kusano <i>et al</i> ^[22]	Aug 2003-Jul 2006	40 (23M, 17F)	35.6	28.8 (13-51)	Knees	Full thickness chondral defect in patella (20), femoral condyle (9), osteochondral defect in femoral condyle (11)	Grade III/IV	3.87		Defects in other locations, age > 50 yr, skeletally immature	Not specified

Leunig <i>et al</i> ^[23]	Mar 2009-Dec 2010	6 (5M, 1F)	22.7	Not specified (12-30)	Hips	Femoral head 5, acetabular 1, osteochondral 5	Grade III/IV	> 2	Full thickness chondral lesions > 2 cm ² or osteochondral lesions > 1 cm ² with defects in weight-bearing areas of acetabulum or femoral head, irreparable by osteotomy in age < 35 yr	Patients unwilling or unable to comply with post-operative rehabilitation protocols. Systematic inflammatory arthritis, advanced arthritis involving both femur and acetabulum, or age > 35 yr	Not specified
Pascarella <i>et al</i> ^[24]	2006-2008	19 (12M, 7F)		12-36	Knees	Right knee: Femoral condyle (medial 34%, lateral 14%), patella (9%) Left knee: Femoral condyle (medial 29%, lateral 14%)	Grade III/IV	3.6	Age 18-50 yr with single lesion	Osteoarthritis, axial deviations, ligamentous injuries, complete meniscal resection, allergy to collagen membrane components	Not specified
Anders <i>et al</i> ^[31]	Jan 2004-Mar 2010	38 (Not specified)	37	19 (6-24)	Knees		Grade III/IV	3.4	Age 18-50 yr, 1-2 lesions	> 2 defects, corresponding defects, bilateral defects, signs of osteoarthritis, other general diseases, history of complete meniscectomy, mosaicplasty, treatment with cartilage specific medication, chondroplasia patallae or patellar dysplasia	None
Gille <i>et al</i> ^[28]	Not specified	57 (38M, 19F)	37.3	24	Knees	Medial condyle (32), lateral condyle (6), trochlea (4), patella (15) Grouping based on lesion size: Group A 0-3 cm ² , Group B 3-6 cm ² , Group C 6-9 cm ²	Grade III (35), Grade IV (37)	3.4 (1-12)	Age 17-61 yr	Rheumatic disease, total meniscectomy, and revision surgery	Not specified
Valderrabano <i>et al</i> ^[17]		26 (18M, 8F)	33	31 (25-54)	Ankles	Osteo-chondral lesions of talus		1.68	First time osteochondral lesion or failure of previous lesion	Age > 55 yr, open ankle physis	Not specified
Wiewiorski <i>et al</i> ^[25]	2008-2010	23 (16M, 7F)	34	23 (11-49)	Ankles (talus)	Osteo-chondral lesions of talus	Osteo-chondral	1.49	Single lesion with history of ankle trauma		Not specified

Dhollander <i>et al</i> ^[29]	April 2009-May 2011	10 (8M, 2F)	37.2 ± 7.1	24	Knee	Patella (8), trochlea (2)	Grade III/IV	4.2 ± 1.9	Patients aged 18-50 yr with a focal patellofemoral defect and clinical symptoms (pain, swelling, locking, giving way)	Untreatable tibio-femoral or patellofemoral mal-alignment or instability, diffuse osteoarthritis or bipolar "kissing" lesions, major meniscal deficiency and other general medical conditions (diabetes, rheumatoid arthritis)	Not specified
Mancini <i>et al</i> ^[30]	November 2004-June 2007	31	36.4 ± 10.3	60	Hip	Acetabular chondral defects	Grade III/IV	2-4	Patients 18-50 yr of age with acetabular chondral lesions with radiological Tönnis degree < 2 followed up to 5 yr	Concomitant chondral kissing lesion, systemic rheumatoid diseases, dysplasia, femoral neck axial deviations, coxa profunda, protrusio acetabuli	Not specified
Fontana <i>et al</i> ^[31]	November 2004-March 2011	55	39.1 (18 to 55)	36-60	Hip	Acetabular ± femoral head chondral defects	Grade III/IV	2-8	Patients 18-55 years of age with acetabular ± femoral head chondral lesions with radiological Tönnis degree < 2 followed up for 3-5 yr	Rheumatoid arthritis, dysplasia, axial deviation of the femoral neck, coxa profunda, protrusio acetabuli	Not specified but Girolamo is a paid consultant for Geistlich
Kubosch <i>et al</i> ^[32]	Not specified	17	38.8 ± 15.7	39.5 ± 18.4	Ankle	Osteo-chondral lesions of talus	Grade III/IV	2.4 ± 1.6	First-time diagnosis or failure of a previous operative treatment	Arthritis of the ankle joint, kissing lesions and rheumatoid arthritis	Not specified

BMI: Body mass index.

KOOS score at follow-up in this study were significantly greater than those reported by Dhollander *et al*^[16,29] using Chondro-Gide® and in Dhollander *et al*^[13] using Chondrotissue. The clinical outcomes achieved in Buda *et al*^[15]'s study were partly supported by the MOCART scores, with a majority of patients displaying complete defect repair, complete integration to surrounding cartilage, intact repair tissue surface, and isointense signal intensity, while other MRI measures showed poor results despite positive patient-assessed outcomes. The remainder of the studies in this review used Chondro-Gide® and resulted in patient outcomes that were posi-

tive and comparable.

Several drilling techniques were adopted in the studies. In 6 of the 16 studies, an awl was used to perforate the subchondral surface of the bone as originally described^[1]. Seven studies substituted an awl with a microdrill, with or without Kirchner wires^[23,24]. Pascarella^[24] carried out a slightly modified AMIC procedure with the intention of increasing the number of MSCs to produce healthy regenerative cartilage. Perforations were performed rather than microfractures, and the covering of the focus of the lesion with a biological collagen patch enriched with bone marrow

Table 2 Treatment algorithms

Ref.	Drilling technique	Scaffold/fixation	Associated surgery	Joint	Rehab
Buda <i>et al</i> ^[15]	No drilling	Hyalofast + PRP	3 osteotomy	Knees	NWB 4 wk, run 6 mo, RTS 12 mo
Gille <i>et al</i> ^[26]	Awl/sharp cannula	ChondroGide Fibrin glue	2 realignments, 1 capsular shift	Knees	Immobilization 1 wk, passive motion 6 wk, NWB 6 wk
Dhollander <i>et al</i> ^[16]	Microdrill	ChondroGide + PRP Sutures	3 osteotomy + 1 medial patello-femoral ligament reconstruction	Knees	NWB 2 wk, brace 0-90° for 4 wk, full ROM at 8 wk, Low impact sports 12 mo
Dhollander <i>et al</i> ^[13]	Microdrill	Chondrotissue Pin	1 osteotomy	Knees	NWB 2 wk, 0-90° 4 wk, full range 8 wk, RTS 12 mo
Kusano <i>et al</i> ^[22]	Awl	ChondroGide Suture/fibrin glue	28 osteotomy	Knees	PWB 6 wk, 0-60° 4wk
Leunig <i>et al</i> ^[23]	Kirchner wire	ChondroGide, fibrin glue	3 osteoplasty, 2 femoral neck lengthening, drilling of acetabular defects	Hips	PWB 6-8 wk, passive motion 6-8 h for 6-8 wk
Pascarella <i>et al</i> ^[24]	Kirchner wire	ChondroGide Fibrin glue		Knees	
Anders <i>et al</i> ^[3]	Awl	ChondroGide Suture/fibrin glue		Knees	PWB and lymphatic draining massage 3-6 wk, FWB at 4-6 mo, RTS 3-18 mo
Gille <i>et al</i> ^[28]	Awl	ChondroGide Fibrin glue	2 patella realignments, 3 corrective osteotomies, 6 partial menisectomies, 1 ACL reconstruction	Knees	
Valderrabano <i>et al</i> ^[17]	Microdrill	ChondroGide Fibrin glue	16 osteotomy	Ankles	PWB, ROM of < 200 passive motion machine, lymphatic drainage massage 6wks, FWB 6-12 wk, Light sports 12 wk, RTS 5-6 mo
Wiewiorski <i>et al</i> ^[25]	Microdrill	ChondroGide Fibrin glue		Ankles (talus)	PWB and lymphatic draining massage 6 wk, FWB 12 wk
Dhollander <i>et al</i> ^[29]	Slow speed 1.2 mm diameter	ChondroGide Vicryl 6/0	No	Knees (Patellofemoral joint)	NWB for 2 wk, FWB at 10 wk, full range of motion at 8 wk, low impact sports 12 mo
Mancini <i>et al</i> ^[30]	Awl/sharp cannula	ChondroGide Fibrin glue	All patients had cam-type and/or pincer-type impingement, and underwent arthroscopic femoral head-neck resection arthroplasty and/or arthroscopic acetabular rim trimming and labral reattachment to the acetabular rim with suture anchors	Hips	PWB (30% of body weight) for 4 wk, impact sports 3 mo, complete RTS 6 mo
Fontana <i>et al</i> ^[31]	Awl/sharp cannula	ChondroGide Fibrin glue	All patients had cam-type and/or pincer-type impingement, and underwent arthroscopic femoral head-neck resection arthroplasty and/or arthroscopic acetabular rim trimming and labral reattachment to the acetabular rim with suture anchors	Hips	PWB for 7 wk, light sporting activities 4 wk, low impact sports 6 mo, complete RTS 12 mo
Kubosch <i>et al</i> ^[32]	Not specified	ChondroGide Fibrin glue	All patients also underwent autologous cancellous bone grafting to the site	Ankles (talus)	Ankle immobilisation for 2 wk, PWB for 6 wk
Shetty <i>et al</i> ^[34]	Microdrill	Tiseel Coltrix (atelocollagen)	-	Knees	PWB for 6 wk, gradual increase to FWB by next 6 wk

PRP: Platelet-rich plasma; ACL: Anterior cruciate ligament; PWB: Partial weight bearing; NWB: Non-weight bearing; FWB: Full weight bearing; ROM: Range of motion; RTS: Return to sport.

[illegible]

KOOS: Knee injury and Osteoarthritis Outcome Score; IKDC: International Knee Documentation Committee; VAS: Visual Analogue Scale; AOFAS: American Orthopaedic Foot and Ankle Society; ICRS: International Cartilage Repair Society; mHHS: Modified Harris Hip Score; FFI: Foot Function Index; MOCART: Magnetic resonance Observation of Cartilage Repair Tissue.

blood drawn through the knee itself. The aim of the study was simply to show that the modified AMIC procedure was a viable alternative to current surgical practices. The IKDC and Lysholm scores showed a similar trend to that observed by Kusano *et al.*^[22], with the mean IKDC score increasing from 30 to 83 in 24 mo, and the mean Lysholm score increasing from 54 to 98. MRI scores showed a significant reduction of the defect area, although detailed MRI evaluations were not available. Similarly Valderrabano^[17] introduced a modified AMIC procedure that involved the addition of spongiosa bone harvested from the iliac crest to increase the number of MSCs being recruited. This graft is inserted into the lesion and the membrane placed on top. They reported significant improvement in the mean AOFAS scores from 62 to 89 for 26

Table 4 Summary of detailed magnetic resonance imaging evaluation results if provided from studies that reported Magnetic resonance Observation of Cartilage Repair Tissue scores

Scoring measure	Outcome	Number and percentage of patients that achieved a particular result for each category of the MOCART scoring system															
		Buda <i>et al</i> ^[15]		Dhollander <i>et al</i> ^[16]		Dhollander <i>et al</i> ^[13]		Kusano <i>et al</i> ^[22]		Leunig <i>et al</i> ^[23]		Valderrabano <i>et al</i> ^[17]		Wiewiorski <i>et al</i> ^[25]		Dhollander <i>et al</i> ^[29]	
		No. of Pts.	% of Pts.	No. of Pts.	% of Pts.	No. of Pts.	% of Pts.	No. of Pts.	% of Pts.	No. of Pts.	% of Pts.	No. of Pts.	% of Pts.	No. of Pts.	% of Pts.	No. of Pts.	% of Pts.
Degree of defect repair	Complete	14	70%	0	0%	1	20%	3	19%	4	100%	9	35%	8	35%	2	20%
	Hypertrophy	4	20%	2	40%	2	40%	3	19%	0	0%	13	50%	12	52%	2	20%
	Incomplete	2	10%	3	60%	2	40%	10	63%	0	0%	4	15%	3	13%	6	60%
Integration to the Surrounding Cartilage	Complete	16	80%	4	80%	1	20%	8	50%	4	100%	9	35%	8	35%	4	40%
	Incomplete	2	10%	0	0%	4	80%	4	25%	0	0%	9	35%	0	0%	2	20%
	Defect visible	2	10%	1	20%	0	0%	4	25%	0	0%	8	31%	15	65%	4	40%
Surface of the Repaired tissue	Intact	14	70%	0	0%	1	20%	2	13%	3	75%	17	65%	15	65%	3	30%
	Damaged	6	30%	5	100%	4	80%	14	88%	1	25%	9	35%	8	35%	7	70%
	Homogeneous	6	30%	0	0%	0	0%	0	0%	1	25%	7	27%	6	26%	4	40%
Structure of the Repaired tissue	Inhomogeneous	14	70%	5	100%	5	100%	16	100%	3	75%	19	73%	17	74%	6	60%
	Isointense	13	65%	0	0%	2	40%	1	6%	2	50%	4	15%	3	13%	1	10%
	Hyperintense	7	35%	5	100%	2	40%	15	94%	1	25%	18	69%	17	74%	6	60%
DPFSE	Hypointense	0	0%	0	0%	1	20%	0	0%	1	25%	4	15%	3	13%	3	30%
	Intact	6	30%	0	0%	0	0%	3	19%	1	25%	9	35%	8	35%	0	0%
	Not intact	14	70%	5	100%	5	100%	13	81%	3	75%	17	65%	15	65%	10	100%
Subchondral lamina	Intact	6	30%	0	0%	1	20%	4	25%	2	50%	3	12%	3	13%	6	60%
	Not intact	14	70%	5	100%	4	80%	12	75%	2	50%	23	88%	20	87%	4	40%
	Adhesions	20	100%	5	100%	5	100%	15	94%	3	75%	26	100%	23	100%	10	100%
Effusion	Yes	0	0%	0	0%	0	0%	1	6%	1	25%	0	0%	0	0%	0	0%
	No	17	85%	5	100%	3	60%	6	38%	4	100%	25	96%	22	96%	7	70%
	Yes	3	15%	0	0%	2	40%	10	63%	0	0%	1	4%	1	4%	3	30%

patients. MRI findings however showed that only 35% of participants displayed complete filling of the defect, and less than half of the participants returned to their previous level of activity. There were also slight variations depending on the region that needed to be operated upon. The study by Anders *et al*^[3] assessed differences in efficacy and safety between a microfracture technique, a sutured AMIC technique, and a glued AMIC technique. Although the sutured AMIC group showed the greatest improvement in mean Cincinnati scores, there were no significant differences between the groups.

In more than half of the studies, additional surgery was required on at least one subject in the study. The most common additional procedure required was osteotomy and bony realignment. All patients who underwent AMIC at the hip joint underwent additional surgery, mostly for impingement. In the study carried out by Kusano *et al*^[22] looking at the knee joint, patients treated with AMIC alone were compared with patients who had an associated procedure such as an osteotomy. No significant differences in outcomes were noted.

Post-operative rehabilitation regimes varied for the various studies, and were influenced by the location and extent of the lesion. Three studies^[3,17,25] included lymphatic drainage massage as part of their rehabilitation process. The post-operative regime generally involved a period of reduced weight-bearing that may include immobilisation of the joint, followed by a periodic increase in weight-bearing and range of motion. Full-weight bearing commenced from 6 wk to 6 mo. Return to sports periods also lacked consistency, with subjects being able to return to sports after as little as 12 wk^[17], and as much as 18 mo^[3].

Does the defect size and location, and patient factors affect outcome?

For all of the studies investigated, the AMIC procedure was carried out on subjects that had either grade III or grade IV type lesions, although the three ankle-based

Table 5 Coleman methodology scores for the 15 reviewed studies reporting on autologous matrix-induced chondrogenesis

Ref.	Coleman methodology score																Total, max = 100
	Part A, maximum = 65						Part B, maximum = 35										
	1	2	3	4	5	6	1			2			3				
Buda <i>et al</i> ^[15]	0	4	0	10	10	5	2	2	3	3	5	4	3	3	5	5	64
Gille <i>et al</i> ^[26]	4	4	7	10	10	5	2	2	3	3	5	4	3	3	5	5	75
Dhollander <i>et al</i> ^[16]	0	4	10	10	10	5	2	2	3	3	5	0	3	0	5	5	67
Dhollander <i>et al</i> ^[13]	0	4	10	10	10	5	2	2	3	3	5	4	3	3	5	5	74
Kusano <i>et al</i> ^[22]	4	4	10	0	10	5	2	2	3	3	5	0	3	3	5	5	64
Leunig <i>et al</i> ^[23]	0	4	10	0	10	5	2	2	3	3	5	4	3	0	5	0	56
Pascarella <i>et al</i> ^[24]	0	4	10	10	0	5	0	2	3	0	5	0	3	0	5	5	52
Anders <i>et al</i> ^[3]	4	0	0	10	10	5	2	2	3	3	5	0	3	0	5	0	52
Gille <i>et al</i> ^[28]	7	4	10	0	0	0	2	2	3	3	5	0	3	0	5	5	49
Valderrabano <i>et al</i> ^[17]	0	4	10	10	10	5	2	2	3	3	5	0	3	0	5	5	67
Wiewiorski <i>et al</i> ^[25]	0	4	10	10	10	0	2	2	3	0	0	0	3	3	5	5	57
Dhollander <i>et al</i> ^[29]	0	4	10	0	10	5	2	2	3	3	5	0	3	3	5	5	60
Mancini <i>et al</i> ^[30]	4	7	0	10	5	5	2	2	3	0	5	0	3	3	5	5	59
Fontana <i>et al</i> ^[31]	7	7	0	10	5	5	2	2	3	0	5	0	3	3	5	5	62
Kubosch <i>et al</i> ^[32]	0	7	10	0	0	5	2	2	3	3	5	0	3	3	5	5	53
Shetty <i>et al</i> ^[34]	4	7	10	0	0	5	2	2	3	3	5	0	3	3	5	0	52

studies^[17,25] did not specify the grade of lesions. The studies focussed on both osteochondral and chondral defects of the joints. Although the lesions varied from 1-8 cm², the mean lesion size for all studies ranged from 1.5-3.6 cm². In the ankle based studies all AMIC procedures were conducted on the talus, and a majority of the knee based studies involved the AMIC procedure being carried out on the femoral condyle.

Kusano *et al*^[22] compared 40 defects; 11 were Osteochondral Femoral Condyle lesions (ocF), 20 were Chondral Patella lesions (cP), and nine were Chondral Femoral Condyle lesions (cF). The ocF group had the lowest mean age at 25.9, while the mean age for the other groups was just below 40. Only 36% of patients in the ocF group had an osteotomy compared with 90% in the cP group and 67% in the cF group. The cF group had a significantly smaller mean lesion size (2.3 cm²), compared with 4.2 and 4.4 cm² in the other groups. The patient outcome scores were consistent across the groups. Although the cP group reported the highest mean pre-operative scores, the ocF group showed the greatest improvement at follow-up, and the cF group showed the least improvement. As there were inconsistencies between the three groups relating to age and size of lesion, it is difficult to draw a definitive conclusion from these results. Gille *et al*^[26] followed up patients for 48 mo and failed to identify any significant effect of lesion size on Patient outcome scores. They did however find that outcomes were better for femoral condyle defects than patella defects, and the two patients who had cartilage defects greater than 8 cm² did not benefit from the procedure. Fontana *et al*^[31] compared AMIC with microfracture at the hip joint in patients undergoing impingement surgery, and only found a better five-year clinical outcome for the AMIC group for lesions greater than 4 cm².

Interestingly Fontana *et al*^[31] only found the five-

year results to be better for the AMIC group in males, and not females. Looking at the remaining studies, males generally reported higher outcome scores but showed similar levels of improvement to females after treatment. In the study carried out by Kusano *et al*^[22], the results suggested that younger patients generally experience greater improvements than older patients. Gille *et al*^[26] reported on patient outcome scores at 48 months, and failed to identify any significant effect of age, weight, gender, and previous surgery on patient outcome, but younger patients did generally display better recovery rates than older patients.

Does the outcome change with time?

Mancini *et al*^[30] and Fontana *et al*^[31] reported five-year follow-up in patients undergoing AMIC at the hip joint but all patients underwent additional impingement surgery. The authors report improved outcome scores that were achieved at six months and generally maintained till final follow-up at five-years. Gille *et al*^[26] reported on ICRS, Cincinnati, and Lysholm patient-assessed scores at 24, 36, and 48 mo for patients undergoing AMIC at the knee joint with less than 10% of patients undergoing additional procedures. Patient recovery tended to peak at 24 mo before declining. The mean Cincinnati score peaked at 74 at 24 mo, and steadily declined to 62 (36 mo) and 37 (48 mo). For all scoring systems, the patient outcomes deteriorated more rapidly once they passed the 36 mo follow-up. The randomized control trial by Anders *et al*^[3] compared a microfracture technique, a sutured AMIC technique, and a glued AMIC technique. None of the patients underwent any additional procedures. In all three groups, improvements in pain scores and patient outcomes, including Cincinnati scores, were observed at both 12 and 24 mo follow-up. Between 12 and 24 mo follow-up, 12 patients showed further

Table 6 Coleman methodology scores - mean, range and standard deviation for each section

Section score (maximum)	Mean	Range	SD
Part A (65)			
Study size	2.1	0-7	2.6
Minimum follow-up	4.5	0-7	1.7
Number of different surgical treatment included	7.3	0-10	4.3
Study design	6.3	0-10	4.8
Description of surgical technique	6.9	0-10	4.3
Post-Op management described	4.4	0-5	1.7
Total part A	31.4	21-40	5.7
Part B (35)			
Outcome measures clearly defined	1.9	0-2	0.5
Timing of outcome clearly stated	2	2	0
Use of reliable outcome criteria	3	3	0
General health measure inc.	2.2	0-3	1.3
Subjects recruited	4.7	0-5	1.2
Inv. independent of surgeon	1	0-4	1.7
Written assessment	3	3	0
Completion of assessment by patients with minimal investigator assistance	1.9	0-3	1.5
Selection criteria reported and unbiased	5	5	0
Recruitment rate reported	4.1	0-5	2
Total part B	28.9	23-35	3.9
Total, maximum = 100	60.2	49-75	7.7

improvement in Cincinnati scores, 12 showed little or no change, and 3 showed a decline.

Methodological quality assessment

CMS was used to assess the methodological quality of the studies carried out using the AMIC procedure (Tables 5 and 6). The mean CMS and standard deviation (SD) achieved was 60.7 ± 7.9 (range 49-75) out of 100. The mean CMS and standard deviation (SD) achieved in Part A was 31.8 ± 5.9 , and in Part B was 28.9 ± 4.1 .

DISCUSSION

AMIC enables the transplantation of a scaffold with MSCs in one step, avoiding the need for laboratory cell number expansion and a second procedure^[26]. In our review, 15 studies between 2003 and 2015 that used AMIC for the repair of articular cartilage defects in patients were systematically reviewed. AMIC is still a relatively new procedure and more mid-term and long-term outcomes are awaited. The mean CMS suggesting that the overall quality of the studies was fair. Studies scored poorly for number of patients, length of follow-up, study design and independence of the investigator and the surgeon. For Part A, the overall mean CMS was 31.8 out of 65 points (49%), whereas for Part B the overall mean CMS was 28.9 out of 35 (72%). This indicates that overall, the studies were more competent in defining their outcome criteria and procedures, and that greater improvements need to be made regarding study design and procedures. Although blinding of participants has ethical implications, blinding of clinicians recording the outcome measures was not practised commonly. In scoring systems that require completion by an investi-

gator, it is recommended that the investigation be carried out by an independent investigator to ensure accurate responses from the patient avoiding risk of bias through patient-investigator relationships. Several authors contributed to multiple studies included in this review introducing a risk of bias in both study design and reporting of outcomes across the studies.

The studies included in this review were not directly comparable due to differences in study design, lesions, surgical technique, follow-up and outcome measures. Although the AOFAS score was used in all three ankle studies and the mHHS in two of the three hip studies, there were no consistent scoring systems used for the knee studies. Nevertheless, a pattern of positive patient outcomes can be seen across all of the studies. Future studies should incorporate a universal method of rating patient outcomes for each joint location, allowing direct comparison of results. There also is a need to determine whether MRI assessment is a reliable tool as the studies in our review suggest that it does not necessarily correspond with patient outcome measures. Nevertheless, we recommend that all studies should continue to carry out an MRI assessment while further evidence on its relevance is sought.

Many of the studies included patients that required additional surgical procedures including osteotomies. For a patient undergoing more than one surgical procedure it would be difficult to determine the effect of each procedure in relieving pain and improving joint function. There is a distinct lack of consensus regarding post-operative management and the structure of rehabilitation programmes. Rehabilitation programs can have a significant influence on patient outcomes and recovery rates. Although it is difficult to develop a universal rehabilitation program due to the large number of variables such as patient demographics, and

lesion size and location, this needs to be considered when comparing outcomes between different studies. Due to the variation in studies it is not possible to determine if the type of scaffold, surgical technique or rehabilitation regime affect the outcome.

Limited studies suggest that femoral condyle lesions do better than patellar lesions, and osteochondral defects do better than chondral lesions. Defect sizes did not generally have an effect on the patient's outcome unless the defect was $> 8 \text{ cm}^2$, in which case it had a detrimental effect on outcomes. There is limited evidence that younger patients experience greater improvements than older patients and display better recovery rates. It has been shown *in vitro* that bone marrow stem cells from older patients have reduced chondrogenic potential compared with younger patients, potentially decreasing the effectiveness of AMIC in older patient groups.

Follow-up period is an important factor in assessing the real effectiveness and reliability of the AMIC procedure. Since the treatment method is relatively new, there is a lack of long-term patient outcome data available. A longer follow-up period allows the proper assessment of long term outcomes for a procedure. Although five-year follow-up was available for two studies^[30,31], the patients had all undergone additional procedures making any improvements difficult to attribute to the AMIC procedure alone. It was demonstrated in the study conducted by Gille *et al.*^[26] and Gudas, Gudas *et al.*^[27] that declines in clinical outcomes can be observed as early as 18 to 24 mo after undergoing surgical treatment without additional procedures. Patient assessed outcomes by Gille *et al.*^[26] declined significantly between the 24 mo and 48 mo post-operative period, indicating that there may be concerns regarding durability of the repaired cartilage after undergoing the AMIC procedure. In the randomized control trial by Anders *et al.*^[3] improvements in pain scores and patient outcomes, including Cincinnati scores, were observed at 12 mo follow-up. Between 12 and 24 mo follow-up, although 12 patients showed further improvement in Cincinnati scores, 12 showed little or no change, and 3 showed a decline. This supports the observation by other studies, and their 5-year follow-up results are awaited.

The published literature reviewed suggests that AMIC in cartilage repair is a safe and effective treatment option that improves patient outcome measures and reduces pain. MRI findings however do not necessarily correspond with patient outcome measures. Most studies reported promising results, with no mention of further surgical corrections being needed in the follow-up period. Medium- and long-term results for AMIC procedures without additional surgeries are awaited. Earlier studies suggest that AMIC results may peak at around 24 mo.

The CMS results suggest that the clinical trials evaluated in this systematic review were of fair to reasonable quality; with 8 of the 15 studies achieving

total CMS scores ranging from 60 to 80. The main weaknesses across the studies were the total number of participants and the patient follow-up periods. Improvements in these areas will significantly increase the reliability of the patient outcome measures, while allowing investigators to draw more definitive conclusions. More high level studies with larger sample sizes, and extensive and robust validated outcome measures should be conducted to evaluate the medium- and long-term effect of the AMIC procedure.

COMMENTS

Background

The results with autologous matrix-induced chondrogenesis (AMIC) in the literature have been variable. As there are limited studies on AMIC, variability in the type of scaffold used, the surgical procedure, defect size and location, and patient variability may all contribute to variable results. In addition, we are not aware of the longevity of these results.

Research frontiers

AMIC is a one-step procedure that brings together microfracture with a collagen matrix scaffold. There is increasing interest in AMIC as it provides a cost-effective alternative to cell-based therapies for articular cartilage repair, and it is highly autologous in nature.

Innovations and breakthroughs

The published literature reviewed suggests that AMIC in cartilage repair is a safe and effective treatment option that improves patient outcome measures and reduces pain. MRI findings however do not necessarily correspond with patient outcome measures. Most studies reported promising results, with no mention of further surgical corrections being needed in the follow-up period. Medium- and long-term results for AMIC procedures without additional surgeries are awaited.

Applications

More high level studies with larger sample sizes, and extensive and robust validated outcome measures should be conducted to evaluate the medium- and long-term effect of the AMIC procedure.

Terminology

Mesenchymal stem cells (MSCs): These cells reside in bone marrow and many adult tissues. MSCs are multipotent stromal cells capable of self-renewal and differentiation *in vitro* into a variety of cell lineages, including chondrocytes, osteoblasts, and adipocytes. They are therefore seen as an optimal regenerative cellular therapeutic for musculoskeletal regeneration.

Peer-review

This is a well-designed and written systematic review.

REFERENCES

- 1 Benthien JP, Behrens P. The treatment of chondral and osteochondral defects of the knee with autologous matrix-induced chondrogenesis (AMIC): method description and recent developments. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 1316-1319 [PMID: 21234543 DOI: 10.1007/s00167-010-1356-1]
- 2 Buckwalter JA, Mankin HJ. Articular cartilage: degeneration and osteoarthritis, repair, regeneration, and transplantation. *Instr Course Lect* 1998; **47**: 487-504 [PMID: 9571450]
- 3 Anders S, Volz M, Frick H, Gellissen J. A Randomized, Controlled Trial Comparing Autologous Matrix-Induced Chondrogenesis (AMIC®) to Microfracture: Analysis of 1- and 2-Year Follow-Up Data of 2 Centers. *Open Orthop J* 2013; **7**: 133-143 [PMID: 23730377 DOI: 10.2174/1874325001307010133]

- 4 **Pridie K.** A method of resurfacing osteoarthritic knee joints. *J Bone Joint Surg Br* 1959; **3**: 618-619 [DOI: 10.1186/ar4301]
- 5 **Müller B, Kohn D.** Indication for and performance of articular cartilage drilling using the Pridie method. *Orthopade* 1999; **28**: 4-10 [PMID: 10081038]
- 6 **Steadman JR, Rodkey WG, Briggs KK.** Microfracture to treat full-thickness chondral defects: surgical technique, rehabilitation, and outcomes. *J Knee Surg* 2002; **15**: 170-176 [PMID: 12152979]
- 7 **Brittberg M.** Autologous chondrocyte implantation--technique and long-term follow-up. *Injury* 2008; **39** Suppl 1: S40-S49 [PMID: 18313471 DOI: 10.1016/j.injury.2008.01.040]
- 8 **Behrens P, Bitter T, Kurz B, Russlies M.** Matrix-associated autologous chondrocyte transplantation/implantation (MACT/MACI)--5-year follow-up. *Knee* 2006; **13**: 194-202 [PMID: 16632362 DOI: 10.1016/j.knee.2006.02.012]
- 9 **Lahav A, Burks RT, Greis PE, Chapman AW, Ford GM, Fink BP.** Clinical outcomes following osteochondral autologous transplantation (OATS). *J Knee Surg* 2006; **19**: 169-173 [PMID: 16893154]
- 10 **Gille J, Meisner U, Ehlers EM, Müller A, Russlies M, Behrens P.** Migration pattern, morphology and viability of cells suspended in or sealed with fibrin glue: a histomorphologic study. *Tissue Cell* 2005; **37**: 339-348 [PMID: 16009388 DOI: 10.1016/j.tice.2005.05.004]
- 11 **Benthien JP, Behrens P.** Autologous matrix-induced chondrogenesis (AMIC). A one-step procedure for retropatellar articular resurfacing. *Acta Orthop Belg* 2010; **76**: 260-263 [PMID: 20503954]
- 12 **Patrascu JM, Freymann U, Kaps C, Poenaru DV.** Repair of a post-traumatic cartilage defect with a cell-free polymer-based cartilage implant: a follow-up at two years by MRI and histological review. *J Bone Joint Surg Br* 2010; **92**: 1160-1163 [PMID: 20675765 DOI: 10.1302/0301-620x.92b8.24341]
- 13 **Dhollander AA, Verdonk PC, Lambrecht S, Almqvist KF, Elewaut D, Verbruggen G, Verdonk R.** The combination of microfracture and a cell-free polymer-based implant immersed with autologous serum for cartilage defect coverage. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 1773-1780 [PMID: 22068269 DOI: 10.1007/s00167-011-1763-y]
- 14 **Hegewald AA, Ringe J, Bartel J, Krüger I, Notter M, Barnewitz D, Kaps C, Sittlinger M.** Hyaluronic acid and autologous synovial fluid induce chondrogenic differentiation of equine mesenchymal stem cells: a preliminary study. *Tissue Cell* 2004; **36**: 431-438 [PMID: 15533458 DOI: 10.1016/j.tice.2004.07.003]
- 15 **Buda R, Vannini F, Cavallo M, Grigolo B, Cenacchi A, Giannini S.** Osteochondral lesions of the knee: a new one-step repair technique with bone-marrow-derived cells. *J Bone Joint Surg Am* 2010; **92** Suppl 2: 2-11 [PMID: 21123588 DOI: 10.2106/jbjs.j.00813]
- 16 **Dhollander AA, De Neve F, Almqvist KF, Verdonk R, Lambrecht S, Elewaut D, Verbruggen G, Verdonk PC.** Autologous matrix-induced chondrogenesis combined with platelet-rich plasma gel: technical description and a five pilot patients report. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 536-542 [PMID: 21153540 DOI: 10.1007/s00167-010-1337-4]
- 17 **Valderrabano V, Miska M, Leumann A, Wiewiorski M.** Reconstruction of osteochondral lesions of the talus with autologous spongiosa grafts and autologous matrix-induced chondrogenesis. *Am J Sports Med* 2013; **41**: 519-527 [PMID: 23393079 DOI: 10.1177/0363546513476671]
- 18 **Moher D, Liberati A, Tetzlaff J, Altman DG.** Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009; **151**: 264-29, W64 [PMID: 19622511 DOI: 10.7326/0003-4819-151-4-200908180-00135]
- 19 **Obrensky WT, Pappas N, Attallah-Wasif E, Tornetta P, Bhandari M.** Level of evidence in orthopaedic journals. *J Bone Joint Surg Am* 2005; **87**: 2632-2638 [PMID: 16322612 DOI: 10.2106/jbjs.e.00370]
- 20 **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]
- 21 **Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, Gøtzsche PC, Lang T.** The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med* 2001; **134**: 663-694 [PMID: 11304107]
- 22 **Kusano T, Jakob RP, Gautier E, Magnussen RA, Hoogewoud H, Jacobi M.** Treatment of isolated chondral and osteochondral defects in the knee by autologous matrix-induced chondrogenesis (AMIC). *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 2109-2115 [PMID: 22198419 DOI: 10.1007/s00167-011-1840-2]
- 23 **Leunig M, Tibor LM, Naal FD, Ganz R, Steinwachs MR.** Surgical technique: Second-generation bone marrow stimulation via surgical dislocation to treat hip cartilage lesions. *Clin Orthop Relat Res* 2012; **470**: 3421-3431 [PMID: 22773396 DOI: 10.1007/s11999-012-2466-5]
- 24 **Pascarella A, Ciatti R, Pascarella F, Latte C, Di Salvatore MG, Liguori L, Iannella G.** Treatment of articular cartilage lesions of the knee joint using a modified AMIC technique. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 509-513 [PMID: 20012016 DOI: 10.1007/s00167-009-1007-6]
- 25 **Wiewiorski M, Miska M, Kretzschmar M, Studler U, Bieri O, Valderrabano V.** Delayed gadolinium-enhanced MRI of cartilage of the ankle joint: results after autologous matrix-induced chondrogenesis (AMIC)-aided reconstruction of osteochondral lesions of the talus. *Clin Radiol* 2013; **68**: 1031-1038 [PMID: 23809267 DOI: 10.1016/j.crad.2013.04.016]
- 26 **Gille J, Schuseil E, Wimmer J, Gellissen J, Schulz AP, Behrens P.** Mid-term results of Autologous Matrix-Induced Chondrogenesis for treatment of focal cartilage defects in the knee. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1456-1464 [PMID: 20127072 DOI: 10.1007/s00167-010-1042-3]
- 27 **Gudas R, Stankevicius E, Monastyreckiene E, Pranys D, Kalesinskas RJ.** Osteochondral autologous transplantation versus microfracture for the treatment of articular cartilage defects in the knee joint in athletes. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 834-842 [PMID: 16552548 DOI: 10.1007/s00167-006-0067-0]
- 28 **Gille J, Behrens P, Volpi P, de Girolamo L, Reiss E, Zoch W, Anders S.** Outcome of Autologous Matrix Induced Chondrogenesis (AMIC) in cartilage knee surgery: data of the AMIC Registry. *Arch Orthop Trauma Surg* 2013; **133**: 87-93 [PMID: 23070222 DOI: 10.1007/s00402-012-1621-5]
- 29 **Dhollander A, Moens K, Van der Maas J, Verdonk P, Almqvist KF, Victor J.** Treatment of patellofemoral cartilage defects in the knee by autologous matrix-induced chondrogenesis (AMIC). *Acta Orthop Belg* 2014; **80**: 251-259 [PMID: 25090800]
- 30 **Mancini D, Fontana A.** Five-year results of arthroscopic techniques for the treatment of acetabular chondral lesions in femoroacetabular impingement. *Int Orthop* 2014; **38**: 2057-2064 [PMID: 24951948 DOI: 10.1007/s00264-014-2403-1]
- 31 **Fontana A, de Girolamo L.** Sustained five-year benefit of autologous matrix-induced chondrogenesis for femoral acetabular impingement-induced chondral lesions compared with microfracture treatment. *Bone Joint J* 2015; **97-B**: 628-635 [PMID: 25922456 DOI: 10.1302/0301-620X.97B5.35076]
- 32 **Kubosch EJ, Erdle B, Izadpanah K, Kubosch D, Uhl M, Südkamp NP, Niemeyer P.** Clinical outcome and T2 assessment following autologous matrix-induced chondrogenesis in osteochondral lesions of the talus. *Int Orthop* 2016; **40**: 65-71 [PMID: 26346373]
- 33 **Taichman RS.** Blood and bone: two tissues whose fates are intertwined to create the hematopoietic stem-cell niche. *Blood* 2005; **105**: 2631-2639 [PMID: 15585658 DOI: 10.1182/blood-2004-06-2480]
- 34 **Shetty AA, Kim SJ, Bilagi P, Stelzeneder D.** Autologous collagen-induced chondrogenesis: single-stage arthroscopic cartilage repair technique. *Orthopedics* 2013; **36**: e648-e652 [PMID: 23672920 DOI: 10.3928/01477447-20130426-30]

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Painless swollen calf muscles of a 75-year-old patient caused by bilateral venous malformations

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Abstract

A 75-year-old man presented with knee pain due to medial osteoarthritis of the knee in the orthopedic outpatient clinic. Conservative treatment was started with steroid infiltration. Besides his knee complaint reported a bilateral painless swollen calf muscle without traumatic cause, and also without any pain at night, fever or medical illness. On physical examination the soleus muscle had a swollen aspect in both calfs. The skin appeared normal without deformities and the arterial pulsations were intact. An X-ray did not show abnormalities in the tibia. Magnetic resonance imaging of the legs revealed bilateral multiple saccular intramuscular venous malformations involving the soleus muscle. Intramuscular venous malformations in skeletal muscles are rare, especially when the occurrence is bilateral. Bilateral venous malformations have the potential to be missed because of the intramuscular localization. Symptoms of intramuscular venous malformation can be often mild and overlap with non-exercise related compartment syndrome, claudication, lymphedema and post thrombotic syndrome or muscle strains.

Key words: Venous malformations; Bilateral intramuscular venous malformation; Swollen calf muscles

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Core tip: Intramuscular venous malformations involving in the skeletal muscles are rare, especially when occurrence of these lesions is bilateral. These lesions are easily missed due to intramuscular localization. We report a rare presentation of these lesions arising from the soleus muscle on both sides in a 75-year-old man, diagnosed with magnetic resonance imaging of the

legs. When the lesions are asymptomatic conservative treatment is preferred. When the appearance is symptomatic surgical resection or sclerotherapy can be an option.

Piekaar RSM, Zwitser EW, Hedeman Joosten PPA, Jansen JA. Painless swollen calf muscles of a 75-year-old patient caused by bilateral venous malformations. *World J Orthop* 2017; 8(7): 602-605 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v8/i7/602.htm> DOI: <http://dx.doi.org/10.5312/wjo.v8.i7.602>

INTRODUCTION

A vascular malformation is an aberrant morphogenetic type of blood or lymphatic vessel. The origin of vascular malformations is an abnormal embryonic development of the vascular build-up after the endothelial stage. The malformation consists of an arteriovenous, capillary, venous or lymphatic type. Also combined structures are described^[1]. This subdivision is based on the type of vessel involvement. When a lymphatic vessel is involved the anomaly is called a lymphangioma. Abnormal connections between arteries and veins will lead arteriovenous shunting with a cluster of vessels, the nidus. The most common shown type of vascular malformation is the venous malformation. These are mostly situated in the skin and subcutaneous tissues and are present at birth, although clinical manifestation will usually become apparent later in life^[2,3]. Intramuscular venous malformations on the other hand are rare especially when the occurrence is bilateral, and these have the potential to be missed because of the intramuscular localization^[1,2]. In this report we have described a patient with bilateral extensive intramuscular venous malformations involving the soleus muscles with an asymptomatic presentation.

CASE REPORT

A 75-year-old man was seen in our orthopedic outpatient clinic with osteoarthritis of the right knee. He experienced morning stiffness, pain on the medial side of his right knee after walking and he had difficulties with full flexion of his knee. Conservative treatment was started with steroid infiltration, 4 cc lidocaine mixed with 1 cc depomedrol. Besides these complaints the patient reported a bilateral painless swollen calf muscle. The patient had noticed these swellings of the calf muscle a few years ago without any traumatic history. He had no pain at night and no fever or medical illness. The past medical history of the patient was uneventful.

On physical examination the soleus muscle was swollen on both sides. The swelling was localized on the right leg over the whole soleus muscle, 10 by 3 cm.



Figure 1 Frontal view of the lower legs. On physical examination the soleus muscle was a bit swollen on both sides, with a dimpling in both legs (right more than left).

On the left lower leg the swelling was about 3 by 3 cm over the medial part of the soleus muscle. A dimpling in both legs (right more than left) at the medial calf area was seen while standing (Figure 1). There was full strength in all lower leg muscles and the reflexes were normal on examination. The rest of the examination was unremarkable, the overlying skin appeared normal without deformities, erythema or warmth and the arterial pulsations were intact. Laboratory test results did not show any abnormalities. An X-ray did not show any bony irregularities in the tibia.

Magnetic resonance imaging (MRI) of the legs revealed bilateral multiple saccular intramuscular venous malformations involving the soleus muscle (Figure 2). There was no nidus seen on MRI so an arteriovenous form of the malformation was not plausible. Due to its asymptomatic presentation no angiogram or ultrasonography was performed to further specify the lesion. After consultation of the vascular surgeon we did not perform surgical resection or focal sclerotherapy because of the asymptomatic nature of the lesions. After explanation of the possible muscle damage from resection and because of the fact that our patient had no disabilities in daily living, we agreed upon conservative management. At three mo follow up the swollen calf muscles were still asymptomatic and examination did not show any change of the venous malformations. We continued the conservative treatment focused on the osteoarthritis of the knee with good result.

DISCUSSION

Vascular anomalies are common in the general population, and the major of vascular malformations occur in the upper and lower extremities. The origin of the development of vascular malformations lies in an abnormal embryonic root thus they are present at birth, although not always evident^[1]. The precise pathogenesis is still though. These anomalies exist of an arteriovenous, capillary, venous and lymphatic type. Also combined structures are described^[1]. Venous malformations are a type of vascular malformations



Figure 2 Magnetic resonance imaging of both legs. A: Sagittal plane magnetic resonance imaging (MRI) of both legs reveals bilateral multiple saccular intramuscular venous malformations involving the musculus soleus; B: Transverse plane MRI of both legs reveals bilateral multiple saccular intramuscular venous malformations involving the musculus soleus.

that is seen more often by changes in skin color and focal edema^[3]. These are mostly the malformations situated in the skin and subcutaneous tissues^[2]. As an uncommon cause of tumor the venous malformation can also occur in skeletal muscles of the lower extremities. Asymptomatic intramuscular venous malformations are rare, especially when the occurrence is bilateral^[1,2]. The venous malformations we presented in our patient had a bilateral appearance in both calf muscles, the soleus muscle, although the left lower extremity was less severe in comparison with the right side.

Intramuscular venous malformations can provoke contractures of the involved muscles^[4,5]. A study by Hein *et al.*^[3] shows that most of the intramuscular venous malformations are noted in youth and remain manifest during lifetime. Symptoms of intramuscular venous malformation can be often mild and overlap with non-exercise related compartment syndrome, claudication, post thrombotic syndrome or muscle strain. Other possible diagnosis of swollen lower extremities can be lymphedema with or without hyperkeratosis and papillomatosis^[6]. Besides this other vascular anomalies such as arteriovenous or lymphatic malformations can fit in the differential diagnosis of these swellings.

To determine the nature of the vascular malformation MRI is the most accurate tool and it is superior to the other modalities such as ultrasound. On MRI, venous malformations have a T1-hypointense or T1-isointense signal with a T2-hyperintense signal^[3]. In this case there were no nidi or connections between arteries and veins visible on the MRI so arteriovenous malformations were not plausible. The lymphatic system was shown without any abnormalities.

Surgical treatment for venous malformations is mostly not necessary and conservative therapy is preferred. Pain, bleeding due to lesions of the skin or cosmetic issues can make treatment indicated though after failure of nonoperative management. When the appearance is intramuscular, venous malformations can result in painful contractures of the involved

muscles. In these cases operative treatment can be necessary. The main operative treatment is surgical resection or sclerotherapy (percutaneous embolization). Percutaneous approach is the recommended treatment due to the minor connections to the normal venous system^[7]. This kind of treatment often required for larger extensive intramuscular lesions was not indicated in this instance. If sclerotherapy is impossible due to the extent or location more invasive therapy by performing excision of the lesion is possible. If surgical resection is planned it is important to visualize hidden deep truncular anomalies previously to the operation. Otherwise surgery can result in large defects with venous insufficiency and cosmetic deformities as undesirable results. The patient in our case had neither symptoms nor disabilities in daily living as a result of the intramuscular venous malformations whereby conservative treatment, focused on the osteoarthritis of the knee was chosen.

Previously some case indicated focal lesions in the muscle were presented by toe walking and a case reported the presence of extensive intramuscular venous malformation in the lower extremity as well^[4,5,8]. But, to our knowledge, a bilateral form of these intramuscular venous malformations in the soleus muscles was never reported before.

Venous malformations are the most common type of vascular anomalies. Although an asymptomatic tumor of the lower extremity can have many causes, a painless swollen calf muscle can be caused by the presence of intramuscular venous malformations. Bilateral asymptomatic appearances of these intramuscular venous malformations are rare and have the potential to be missed because of the intramuscular localization. The intramuscular localization is easily found by using MRI. Treatment is only necessary when the swelling is symptomatic.

Learning points: (1) intramuscular venous malformations in the skeletal muscles are rare, especially when the occurrence is bilateral; (2) bilateral venous malformations have the potential to be missed because

of the intramuscular localization; (3) symptoms of intramuscular venous malformation can be often mild and overlap with non-exercise related compartment syndrome, claudication, post thrombotic syndrome or muscle strain; and (4) in this case we have reported a bilateral venous malformation manifestation in calf muscles.

COMMENTS

Case characteristics

A 75-year-old man with osteoarthritis of the knee presented with asymptomatic bilateral painless swollen calf muscles, which were firstly noticed a few years ago without any previous traumatic cause.

Clinical diagnosis

Bilateral painless swollen soleus muscles, with a dimpling (right more than left) while standing.

Differential diagnosis

Non-exercise related compartment syndrome, muscle strain, claudication, lymphangioma, lymphedema, post-thrombotic syndrome or other vascular anomalies such as arteriovenous or lymphatic malformations.

Laboratory diagnosis

All laboratory test results were within the normal limits.

Imaging diagnosis

X-ray of the both legs did not show abnormalities in the bones. Magnetic resonance imaging of both legs revealed bilateral multiple saccular intramuscular venous malformations involving the musculus soleus, nidus of the arteries and the veins in an arteriovenous form of the malformation were not found.

Pathological diagnosis

Biopsy was not performed so pathological findings could not be given.

Treatment

Because of asymptomatic appearances of the bilateral swollen calf muscles conservative treatment was started in our case. Main treatment for symptomatic venous malformations is surgical resection or sclerotherapy (percutaneous embolization).

Related reports

The precise etiopathogenesis of vascular malformations is still unclear, but the origin of the development lies in an abnormal embryonic root. Venous malformations are frequently shown and are simply diagnosed when situated

in the skin or in the subcutaneous tissues. Uncommon localizations of these entities are those in the skeletal muscles. Bilateral appearances of venous intramuscular malformations in the lower extremities are commonly confused with other causes of tumor in the legs.

Term explanation

Asymptomatic bilateral intramuscular venous malformation is a rare type of vascular anomalies of which the origin lies in an abnormal embryonic development.

Experiences and lessons

Bilateral intramuscular venous malformations in the skeletal muscles are rare, with mild symptoms, and have the potential to be missed because of the intramuscular localization.

Peer-review

A straightforward, simple case report with a reasonable review of the literature. The interest is from the differential diagnosis and the concomitant other pathology of knee arthritis.

REFERENCES

- 1 **Mulliken JB**, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg* 1982; **69**: 412-422 [PMID: 7063565 DOI: 10.1097/00006534-198203000-00003]
- 2 **Villavicencio JL**, Scultetus A, Lee BB. Congenital vascular malformations: when and how to treat them. *Semin Vasc Surg* 2002; **15**: 65-71 [PMID: 11840428 DOI: 10.1053/svas.2002.30450]
- 3 **Hein KD**, Mulliken JB, Kozakewich HP, Upton J, Burrows PE. Venous malformations of skeletal muscle. *Plast Reconstr Surg* 2002; **110**: 1625-1635 [PMID: 12447041 DOI: 10.1097/00006534-200212000-00001]
- 4 **Domb BG**, Khanna AJ, Mitchell SE, Frassica FJ. Toe-walking attributable to venous malformation of the calf muscle. *Clin Orthop Relat Res* 2004; **420**: 225-229 [PMID: 15057102 DOI: 10.1097/0003086-200403000-00032]
- 5 **Babiker MO**, Yeo TH, Goodwin S. A venous malformation presenting as toe walking. *Pediatr Neurol* 2015; **52**: 133-134 [PMID: 25439487 DOI: 10.1016/j.pediatrneurol.2014.09.001]
- 6 **Warren AG**, Brorson H, Borud LJ, Slavin SA. Lymphedema: a comprehensive review. *Ann Plast Surg* 2007; **59**: 464-472 [PMID: 17901744 DOI: 10.1097/01.sap.0000257149.42922.7e]
- 7 **Steiner F**, FitzJohn T, Tan ST. Surgical treatment for venous malformation. *J Plast Reconstr Aesthet Surg* 2013; **66**: 1741-1749 [PMID: 24012651 DOI: 10.1016/j.bjps.2013.07.033]
- 8 **Jung HC**, Kim DH, Park BK, Park MK. Extensive intramuscular venous malformation in the lower extremity. *Ann Rehabil Med* 2012; **36**: 893-896 [PMID: 23342327 DOI: 10.5535/arm.2012.36.6.893]

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