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World Journal of Orthopedics

Contents

Monthly Volume 7 Number 6 June 18, 2016

REVIEW

343 Current concepts in the management of recurrent anterior gleno-humeral joint instability with bone loss

Ramhamadany E, Modi CS

MINIREVIEWS

355 Medial ulnar collateral ligament reconstruction of the elbow in major league baseball players: Where do we stand?

Erickson BJ, Bach Jr BR, Bush-Joseph CA, Verma NN, Romeo AA

361 Antimicrobial technology in orthopedic and spinal implants

Eltorai AEM, Haglin J, Perera S, Brea BA, Ruttiman R, Garcia DR, Born CT, Daniels AH

370 Orthopedic disorders of the knee in hemophilia: A current concept review

Rodriguez-Merchan EC, Valentino LA

ORIGINAL ARTICLE

Retrospective Study

376 Joint arthroplasty Perioperative Surgical Home: Impact of patient characteristics on postoperative outcomes

Phan DL, Ahn K, Rinehart JB, Calderon MD, Wu WD, Schwarzkopf R

Observational Study

383 Quantifying prosthetic gait deviation using simple outcome measures

Kark L, Odell R, McIntosh AS, Simmons A

SYSTEMATIC REVIEWS

392 Allograft tissue irradiation and failure rate after anterior cruciate ligament reconstruction: A systematic review

Dashe J, Parisien RL, Cusano A, Curry EJ, Bedi A, Li X

CASE REPORT

401 Posterolateral dislocation of the knee: Recognizing an uncommon entity

Woon CYL, Hutchinson MR

Contents

World Journal of Orthopedics
Volume 7 Number 6 June 18, 2016

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REVIEW

Current concepts in the management of recurrent anterior gleno-humeral joint instability with bone loss

Eamon Ramhamadany, Chetan S Modi

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Abstract

The management of recurrent anterior gleno-humeral joint instability is challenging in the presence of bone loss. It is often seen in young athletic patients and dislocations related to epileptic seizures and may involve glenoid bone deficiency, humeral bone deficiency or combined bipolar lesions. It is critical to accurately identify and assess the amount and position of bone loss in order to select the most appropriate treatment and reduce the risk of recurrent instability after surgery. The current literature suggests that coracoid and iliac crest bone block transfers are reliable for treating glenoid defects. The treatment of humeral defects is more controversial, however, although good early results have been reported after arthroscopic Remplissage for small defects. Larger humeral defects may require complex reconstruction or partial resurfacing. There is currently very limited evidence to support treatment strategies when dealing with bipolar lesions. The aim of this review is to summarise the current evidence regarding the best imaging modalities and treatment strategies in managing this complex problem relating particularly to contact athletes and dislocations related to epileptic seizures.

Key words: Shoulder dislocation; Bone loss; Latarjet; Hill-Sachs lesion; Remplissage

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Core tip: Managing recurrent anterior gleno-humeral instability with bone loss is challenging. Each case needs to be assessed on its own merits with consideration of both glenoid and humeral bone defects and their relative position to each other. Latarjet and iliac crest graft transfers are reliable for treating glenoid lesions. The treatment of humeral defects is controversial - the early results of Remplissage for small defects are promising; large defects may require bony reconstructions or partial resurfacing. The evidence remains limited when addressing bipolar lesions.

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INTRODUCTION

Shoulder instability can be defined as a symptomatic abnormal motion of the humeral head relative to the glenoid during active shoulder motion[1,2]. Traumatic anterior glenohumeral dislocations or subluxations can lead to recurrent instability, especially in young contact athletes and epileptic patients with humeral and/or glenoid bone loss[3]. Failure to identify and address the bone loss when planning treatment can result in unsuccessful soft tissue stabilization procedures being performed with recurrent dislocations[2,4]. This has been previously demonstrated by Burkhart and De Beer[2] where 89% of contact athletes who failed soft tissue stabilization procedures were found to have significant bone loss.

Bone loss in the context of glenohumeral instability includes glenoid, humeral or combined defects. Glenoid defects are mainly located in the antero-inferior glenoid between the 2 and 6 o'clock positions[5].

Humeral osseous defects in the context of anterior glenohumeral instability, referred to as Hill-Sachs lesions, occur where the posterolateral aspect of humeral head abuts against the anterior glenoid[6]. Posterior dislocations are associated with reverse Hill-Sachs lesions with an impaction fracture over the anteromedial aspect of the humeral head[3]. Co-existing osseous defects of the humerus and glenoid are termed bipolar lesions. Bipolar lesions can be defined as "on-track" or "off track", which describes the degree to which the humeral Hill-Sachs defect engages the glenoid defect in a position of 90 degrees of abduction and external rotation of the shoulder[7].

Epidemiology

A recent population-based study by Leroux *et al*[8] reported a 20% incidence of recurrent instability following a first time anterior shoulder dislocation in all adult patients. The highest risk group was young (< 20 years), male patients with an incidence density ratio of 98 per 100000 person-years. Other studies have also shown that young athletes and those that participate in high-energy contact sports are most likely to develop glenohumeral instability following an initial traumatic dislocation[9,10].

Epileptic patients present as a challenging subgroup due to a tendency to develop large bipolar lesions, especially if their condition is poorly controlled[11,12]. Bone loss in epileptic patients is also caused by underlying metabolic bone disorders with a reduced bone density seen in 20%-70% of patients taking antiepileptic medication[13].

Several studies have analysed the incidence of bone loss in shoulder instability. Edwards *et al*[14] reviewed plain films of chronic anterior shoulder instability and found an osseous lesion of glenoid in 78% and humeral impaction fracture in 73%. A series of two-dimensional (2D) computed tomography (CT) scans has shown glenoid bone loss in 86% of patients with glenohumeral instability[15]. Sugaya *et al*[16] found a glenoid osseous defect in 50% of patients with recurrent shoulder instability. The presence of a Hill-Sachs lesion consistent with humeral bone loss in recurrent shoulder instability is estimated to be between 38% and 88%[17,18].

There are few studies focusing on the incidence of bipolar bone loss in shoulder instability. However it should be noted that radiological studies have shown that the presence of an isolated glenoid or humeral defect increases the chances of an associated bipolar defect by a factor of 2.5 to 11[19,20].

CLINICAL PRESENTATION AND EXAMINATION

It is important to elicit a comprehensive history when assessing patients with recurrent glenohumeral instability. One must identify the age at which the instability began and the mechanism of injury, especially of the very first dislocation. Most commonly, patients identify a traumatic injury at young age but it is important to elicit whether there has been repeated injury or trauma, particularly in athletes or epileptic patients. The direction of initial dislocation and instability must be noted as well as the position of the arm at the time of injury. In cases of recurrent instability it is the key to document the level of force required to dislocate. Indeed, patients who dislocate during low energy activity such as turning in bed, reaching out for objects, putting a coat or seatbelt on, or whilst sleeping are likely to have a greater degree of concomitant bone loss and instability. The patient may describe mechanical symptoms such as locking whilst moving their shoulder suggesting an engaging bony defect on the humeral head or glenoid. The number of instability episodes per year should be noted and whether any dislocations or subluxations needed reducing in the Emergency Department or in the operating room. It is also important to record the patient's level of function and specific tasks performed causing apprehension. Enquiring about any underlying medical conditions such as epilepsy or collagen disorders is also vital information to obtain.

Key aspects of the examination include establishing intact cuff and neurological function and any associated stiffness that may be present in chronic conditions where degenerative joint changes may already have occurred. There are a number of special tests which can be performed to assess the degree of glenohumeral instability. The load and shift helps assesses the integrity of the glenoid. The humeral head is compressed into the glenoid fossa while an anterior and posterior translation force is applied. Following bone loss the resistance to this force is lost and it is possible to dislocate or subluxate the

humeral head[21]. The apprehension test assesses whether the patient experiences the sensation of instability when the shoulder is in the position of 90 degrees of abduction and varying degrees of external rotation. Patients with significant bone loss typically experience apprehension at lower degrees of abduction[22]. A reducing relocation force can then be applied to see if this reduces the pain. It is also important to assess for signs of laxity: One can examine for a sulcus sign, which suggests inferior shoulder laxity. This is achieved with traction of the humerus and measuring the gap between the lateral acromion and the humeral head and comparing with the unaffected side[23]. The Gagey hyper-abduction test looks for laxity in the inferior glenohumeral ligament and is useful to look for baseline laxity in the other/normal shoulder[24].

INVESTIGATION AND IMAGING

Plain radiographs

Initial investigations commence with plain radiographs of the shoulder. These include a true ("turned") antero-posterior (AP), axillary and scapula Y view. Other special plain films described include the West Point View, which can demonstrate a glenoid rim fracture. The presence of a Hill-Sachs lesion can be identified with the aid of the Stryker Notch view[22]. The Bernageau radiographic view has been described in order to calculate the degree of glenoid bone loss in glenohumeral instability[25]. It involves taking an X-ray with the shoulder in abduction and directing the beam at 20 degrees to the horizontal, so that the antero-superior border of the glenoid is in line with the anterior line of the scapula on the image. The diameter of the glenoid is measured and compared with the healthy side to estimate bone loss. A study by Pansard *et al*[26] however showed poor correlation with arthroscopic findings in affected individuals in a small retrospective cohort of patients with glenoid bone loss.

CT

Glenoid bone loss: Most imaging studies have focused on the evaluation of glenoid bone loss in shoulder instability. Current evidence suggests that 3D-CT is the gold standard imaging technique available to provide an accurate measure of the degree of bone loss. Chuang *et al*[27] showed good correlation between degree of bone loss using 3D-CT with arthroscopic assessment in 188 patients.

Bishop *et al*[28] performed a cadaveric study comparing the modalities of 2D-CT, 3D-CT and MRI to quantify bone loss and concluded that 3D-CT was the best modality to evaluate glenoid bone loss. 2D-CT relies upon orientating the beam directly perpendicular to the glenoid otherwise bone loss can be underestimated or overestimated.

There are also various different measurement techniques performed using 3D-CT to accurately quantify the glenoid defect. Several authors have concluded that the PICO measurement technique reliably produces an accurate and reliable measure of glenoid bone loss in shoulder instability[29-31]. The PICO method involves obtaining en-face 3D views of both the affected and normal glenoid. The healthy shoulder image is superimposed onto the affected side and the defect resembles the area of bone loss between the two. Bois concluded that 3D-CT was superior to 2D-CT and analysed three different 3D techniques to accurately quantify bone loss. The PICO method was found to be the most reliable measure of bone loss in 3D-CT[32,33]. However, the PICO technique has a number of drawbacks including the need to scan both shoulders increasing the radiation dose. Furthermore it is unsuitable for bilateral cases as relies on the presence of a "normal" shoulder.

Sugaya *et al*[16] reported good results in 100 patients using the "best fit circle principle". This assumes that inferior 2/3 of the glenoid resembles a "perfect circle", which has been supported by cadaveric studies[34]. The degree of bone loss can be calculated by finding the amount of surface area missing on the affected shoulder scan[17]. This method relies on scanning the affected shoulder alone and is currently the most widely used method.

Humeral bone loss: Studies evaluating imaging in humeral bone loss are limited. In a study of 104 patients 3D-CT was used to evaluate the parameters of the humeral Hill-Sachs defect. The use of CT with 3D reconstructions was able to accurately ascertain the size, shape and location of the defect and thereby can be predictive of humeral Hill-Sachs engagement[35]. Chen *et al*[36] reported that the degree of humeral bone loss can be reliably calculated by dividing the area of impaction by the total arc of the articular surface.

Ultrasonography and humeral bone loss

Ultrasound scanning has been shown to be able to detect the presence of humeral Hill-Sachs lesions[37]. It's advantageous as it is readily available, avoids radiation, and allows one to obtain dynamic multi-planar images[38]. Ultrasound scanning has also been shown to have a sensitivity and specificity comparable with CT arthrograms in identifying Hill-Sachs lesions[39]. However, its limitations include operator dependence and it cannot be used to quantify the size of the humeral head defect, and thus has a limited role in pre-operative planning.

Magnetic resonance imaging

Glenoid bone loss: Magnetic resonance imaging (MRI) scanning is advantageous to CT as it allows a detailed evaluation of the soft tissues around the shoulder as well as imaging the bone. Furthermore, it avoids the risks of radiation exposure. A study of 18 cadavers revealed that the accuracy of MRI in measuring glenoid defects was comparable to CT. They used the "best circle" method previously described and applied the technique to MR[40]. Moroder *et al*[41] however compared

CT with MRI in 83 patients in the pre-operative planning stage to evaluate bone defects in shoulder instability and reported that CT was found to be superior in their study.

Hijusmans' cadaveric study showed good accuracy of MR arthrograms when assessing glenoid bone loss[42]. This finding was supported in another study of 35 patients with glenoid bone loss where MR arthrograms were found to have good intra- and inter-observer reliability[43]. Both studies showed that MR arthrograms were comparable to 3D-CT. A study by Modi *et al*[44] with 103 patients reported that the sensitivity/specificity of MRA for glenoid bone loss was 0.58/1.00 and this increased to 0.75/1.00 when performing abduction external rotation views in addition to standard views.

Evidence to support the use of MRI is still limited and larger more significantly powered studies are required prior to it being considered equivocal to the current gold standard 3D-CT modality when trying to assess bone loss.

Humeral bone loss: Studies have reported on the ability of MRI to detect the presence of humeral Hill-Sachs lesions[45,46]. One study considered whether MRI could accurately predict the presence of a Hill-Sachs lesion diagnosed arthroscopically: In 83 patients, 90.6% specificity and 96.3% sensitivity were reported[46]. Evidence is limited on the ability of MRI to accurately quantify the degree of humeral bone loss. Further trials are required to evaluate this further.

MANAGEMENT

The management of bone loss in shoulder instability starts by understanding the role of patient demographics and functional demand. Failure of conservative management in glenohumeral instability has been found to be considerably higher in younger patients, especially athletes with high functional demand. A prospective study reported up to 90% recurrence rate in young athletes under 24-year-old following a first time shoulder dislocation[47]. Specifically, participation in contact sports was a significant patient factor in developing recurrent instability[48,49]. It is important to identify the chronicity of the shoulder problem, the functional restriction and quantification of the glenoid and humeral bone loss prior to treatment. Non-operative management in the context of bone loss in shoulder instability is reserved for high-risk surgical candidates, patients with low functional demands and those with poor compliance to rehabilitation protocols. In the specific case of patients with epilepsy, it is vital to achieve good seizure control prior to considering surgical intervention due to the high risk of surgical failure in this complex group of patients, especially as they often present with severe bipolar bone loss. We have attempted to present an algorithm, based upon the amount of glenoid and humeral bone loss, to guide management after considering the evidence currently available in the literature (Figure 1).

Glenoid bone loss

0%-25% bone loss: The literature suggests that patients with glenohumeral instability with up to 15% isolated glenoid bone loss can be treated with an arthroscopic soft tissue Bankart repair alone[50]. Initial trials favoured open stabilization over arthroscopic Bankart repair[51,52]. A systematic review by Brophy *et al*[53] reported instability following arthroscopic and open Bankart repairs to be comparable. However, a study by Rhee *et al*[54] reported a higher risk of failure with arthroscopic repair over open surgery in contact athletes although this was level 4 evidence.

In patients with 15%-25% bone loss, management is dependent on the level of functional demand of the patient. Balg *et al*[55] devised the instability severity index score, which identified six risk factors that may predict failure of an arthroscopic soft tissue Bankart repair. These included age < 20 years, participation in contact sports, competitive level, shoulder hyperlaxity, a Hill-Sachs lesion and a loss of contour of the glenoid rim. Scoring > 6/10 on this scale predicted a 70% failure of Bankart repair in such patients.

Thus in high demand patients or those with a significantly high instability index score, effort must be made to address the bony lesion. In the acute setting, where the glenoid bony fragment can be identified, early open reduction and internal fixation of the fragment is advised. Studies have shown that open reduction and fixation of a glenoid rim fracture with screws shows good outcomes at 1 year and a high rate of union[56,57]. Comminution and the inability to fix the fragment, necessitates a bony reconstruction procedure such as a Latarjet procedure[21]. In contrast, lower demand patients may be successfully managed with a soft tissue Bankart procedure alone.

> 25% bone loss: Significant bone loss has been described where the glenoid takes the appearance of an "inverted pear" shape. This corresponds to at least 25% bone loss. Burkhart *et al*[2] identified a 67% recurrent instability rate in such patients undergoing a soft tissue Bankart repair in contrast to 4% in those without bony deficiency.

In an acute setting, anatomical reduction may be achieved using open or arthroscopic reduction and internal fixation of the rim fragment. In cases where this is not possible reconstruction of the osseous defect is required. There are several ways this can be achieved including coracoid transfer procedures and the use of autografts or allografts to restore the bony anatomy of the glenoid.

Coracoid transfer procedures include the Bristow and Latarjet techniques. The Bristow procedure transfers the tip of the coracoid with its attached conjoined tendon to the anterior glenoid[58]. The Latarjet procedure involves transfer of approximately 3 cm of the coracoid in addition to the conjoined tendon hence provides a greater bony augment and allows fixation with two screws rather than one, as with the Bristow, increasing the stability and chance of successful union[59]. It also extends the

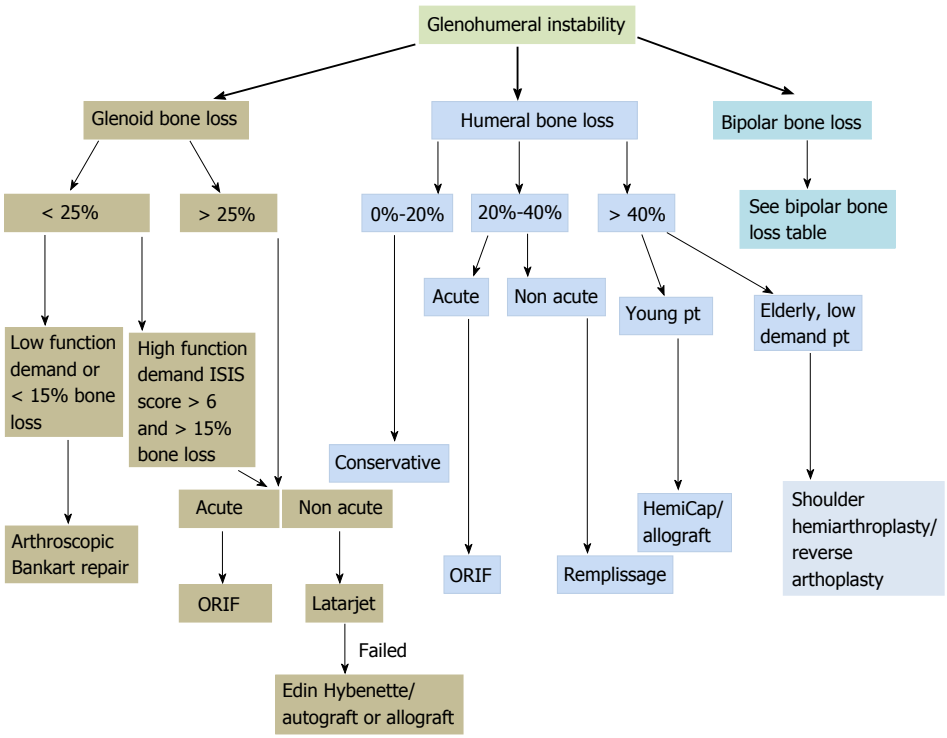

Figure 1 Management of glenoid and humeral bone loss in shoulder instability. ISIS: Instability severity index score; ORIF: Open reduction and internal fixation; pt: Patient.

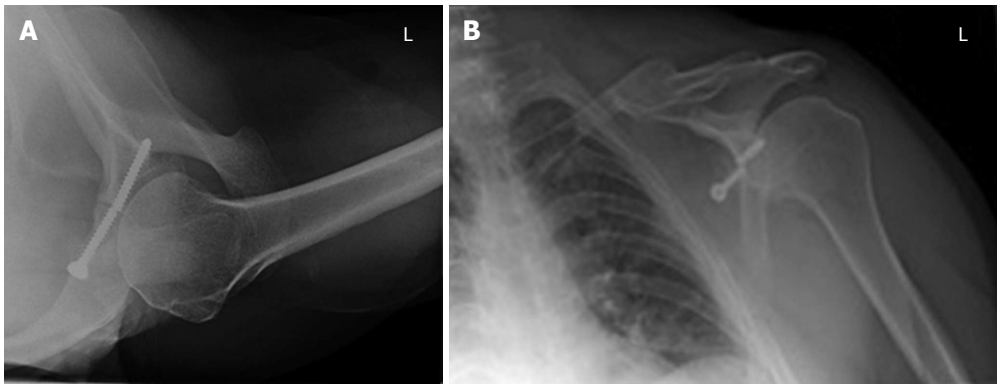

Figure 2 45-year-old gentleman with previous open latarjet procedure for left shoulder instability. Subsequent non-union of graft and failure of metalwork is seen on the axillary (A) and antero-posterior (B) radiographs.

concavity of the glenoid articular arc increasing the ability to resist off axis loads that allow the shoulder to subluxate or dislocate[60]. The transfer of the conjoined tendon with the graft also contributes to increased stability as it acts as a sling across the antero-inferior capsule when the shoulder is in abduction and external rotation. The original Latarjet procedure has been modified to preserve the inferior subscapularis muscle contributing to soft tissue stability. Furthermore the graft may be kept extra-articular by repair of the capsule to the native glenoid, which helps to stop the graft abrading the humeral surface[61].

Several studies have reported good outcomes with the Latarjet procedure, with low rates of recurrent instability, high patient satisfaction and return to sports[60,62]. Critics of the open Latarjet have focused on the loss of external rotation post procedure, which could have an adverse impact on overhead throwing athletes, and the development of osteoarthritis[63]. Other complications include infection, neurological injuries, non-union of the Latarjet graft and failure of metalwork (Figure 2).

A developing concept is an arthroscopic Latarjet procedure, which is a technically demanding procedure and should only be undertaken by the expert arthroscopist. Lafosse *et al*[64] reported no recurrence in 96 patients treated with an arthroscopic Latarjet with 91% of patients reporting an excellent subjective outcome on Disabilities of Arm, Shoulder and Hand score. Boileau *et al*[65] have advanced the technique by combining arthroscopic Latarjet with a Bankart repair (2B3 procedure). It is thought that repairing the residual capsular labrum contributes to shoulder stability and helps maintain proprioceptive fibres

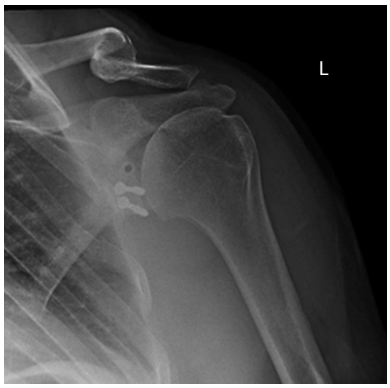

Figure 3 Failed latarjet procedure in Figure 1 treated with an Eden Hybinette procedure using an autologous iliac crest bone graft. The graft position and fixation with 2 screws is shown on the antero-posterior radiograph.

needed in athletes. Ninety-one percent of patients had no evidence of osteoarthritis with this technique, with all throwing athletes returning to sports, and only a mean 9 degree loss of external rotation on the operated side.

Glenoid reconstruction with autograft or allograft is another technique aimed at anatomically reconstructing the osseous defect. It addresses the bone defect but does not address the loss of stability caused by the laxity of the inferior glenohumeral ligament[66]. Griffin *et al*[3] has suggested that an autograft or allograft may be a used in cases of a failed Latarjet or in cases of concurrent coracoid fracture. It may also be of use in massive glenoid bone loss where the coracoid transfer is not enough bone stock to augment the defect.

The most commonly described autograft has been the Eden-Hybinette procedure. This involves using the inner table of the iliac crest as an autologous graft to augment the glenoid defect (Figure 3). Both intra and extra-articular grafts have been described. Studies have reported good outcomes in the use of iliac crest bone autograft in patients. However these studies are limited by small population groups and limited follow-up period[67-69]. The use of a distal clavicle arthroscopic autograft has also been reported[70].

Several studies have commented on the use of allografts for glenoid reconstructions. These include distal tibia[71] and femoral head allografts[72]. It has been proposed that the use of allografts may have several advantages over autografts including a more accurate restoration of the anatomical contour of the glenoid as well as the addition of a cartilaginous interface for articulation with the humeral head. Sayegh *et al*[73] conducted a systematic review into the use of allografts in addressing glenoid bone loss. This study concluded a recurrence rate of instability of 7.1% following allograft procedure with excellent subjective clinical outcome. The review included a collection of small population studies hence the effectiveness and limitations of this treatment are yet to be fully understood.

It has been proposed that low demand patients may still be managed successfully with arthroscopic Bankart stabilization. Kim *et al*[74] showed that in a study of 36 non-athletic individuals with low functional demand, arthroscopic stabilization produced a satisfactory outcome in patients with glenoid bone loss of 20%-30%. However in patients with excessive joint laxity, arthroscopic stabilization is unreliable with a recurrent instability rate of 23%. These findings are also supported by a study of 21 patients with 20%-30% bone loss by Mologne *et al*[75]. One must be cautious with these findings, however, as both studies are poorly powered statistically with limited follow-up duration.

Humeral bone loss

0%-20% bone loss: Current concepts suggest that a humeral bone defect of 0%-20% can be managed conservatively. A trial of immobilization followed by physiotherapy focusing on dynamic shoulder stabilizers is warranted. In most individuals this will be a suitable management strategy, especially in the elderly and low demand patients[76] (Figure 1).

It is important to understand however high demand athletes, such as baseball players, who require stability throughout extremes of motion may require surgery at a lower threshold of bone loss.

20%-40% bone loss: Various different surgical strategies have been described for managing humeral bone loss > 20%. In cases where a humeral defect has been detected within 3-4 wk of injury, anatomical fixation of the defect has been described. This involves disimpaction of the humeral defect by elevating it with a bone tap until anatomy of the head is restored. The defect can then be held with cortical screws and defect be filled with cancellous bone graft. Unfortunately there is noticeable lack of evidence in the literature focusing on this technique's outcome and indication[77,78].

The Remplissage technique has recently become more popular for the treatment of engaging Hill-Sachs lesions. This involves a tenodesis of the infraspinatus tendon and posterior capsule into the humeral head defect rendering the defect extra-articular and thus preventing engagement with the glenoid rim[79]. It is now usually performed arthroscopically and can be combined with a Bankart repair to address combined humeral and glenoid defects where glenoid bone loss is < 25%. Open techniques involve mobilizing the tendon free from its attachment on the greater tuberosity and suturing it into the defect over the lateral humeral cortex. In larger defects up to 40% it is advisable to osteotomise the greater tuberosity with the infraspinatus tendon and to fix the bone and tendon transfer into the defect with fully threaded cancellous screws[80].

The reported outcomes of arthroscopic remplissage are promising. Purchase, Sahajpal *et al*[80] reported a recurrent instability rate of 7% at 2 years post surgery with no significant loss in range of motion. Other studies report a loss of external rotation between 1.9 to 8 degrees[81,82]. A 90% return to sport has been reported following the procedure. A systematic review comparing remplissage, weber osteotomy and allograft procedures

Table 1 Management of bipolar bone loss in shoulder instability

	Bipolar bone loss			
	Non engaging humeral Hill-Sachs "on-track"	Engaging humeral Hill-Sach "off-track" < 40% loss	Engaging humeral Hill-Sachs "off track" large defect > 40% loss. Young pt	Engaging humeral Hill-Sachs "off track" large defect > 40% Elderly pt
Glenoid bone loss < 25%	Arthoscopic Bankart repair	Remplissage ± Bankart	HemiCap ± Bankart	Shoulder hemiarthroplasty
Glenoid bone loss > 25%	Latarjet procedure	Latarjet + remplissage	Latarjet + HemiCap	Reverse shoulder replacement

pt: Patient.

for humeral bone loss found that remplissage had the better outcome scores and fewer complications[83].

Historically proximal rotational humeral osteotomy, described by Weber *et al*[84] in 1969, was used to treat young adults with moderate to severe Hill-Sachs lesions with aim of restoring stability. This involved a subcapital humeral osteotomy with medial rotation of humeral head by 25 degrees and imbrication of subscapularis tendon and anterior capsule. As a result the humeral defect could not engage the glenoid through the arc of motion. However the procedure is associated with high complication rates and has fallen out of favour[85,86].

> 40% bone loss: In young patients with large humeral defects (> 40% bone loss), osseous allograft reconstruction has been described as a useful strategy to avoid the need for prosthetic replacement. The data in the literature on this technique is very limited and further work is needed to evaluate the efficacy and limitations of technique. Miniaci *et al*[85,86] used fresh frozen cryopreserved humeral head allografts in 18 patients. The graft is size and side matched to reconstruct the humeral head following chevron osteotomy of the Hill-Sachs defect. At 50 mo there were no episodes of instability and an 89% return to work. Two patients had partial graft failure and three showed early evidence of osteoarthritis. Another strategy has been the use of femoral head allografts. In a study of 13 patients there was a high Constant score 86.8 at 54 mo with one case of osteonecrosis noted[87].

An emerging technique in the treatment of young patients with bone loss > 40% has been the use of a partial resurfacing prosthesis such as the HemiCAP® (Arthrosurface, Franklin, MA, United States). This uses a spherical cobalt chrome component to fill the Hill-Sachs defect and restore joint congruity. The technique requires patients to have at least 60% normal bone stock, hence is contraindicated in those with osteoporotic bone[88]. The largest case series performed by Raiss *et al*[89] only involved 10 patients. They performed uncemented partial resurfacing in locked anterior dislocation patients with significant humeral bone loss and found an increase Constant score of 41 points post operatively with two re-operations for dislocation and glenoid erosion. Other case reports have been discussed in the context of bipolar bone loss where the engaging humeral defect was treated with this technique[90,91].

The lack of significant evidence in the literature suggests that there is no consensus strategy as to how to treat young patients with large degrees of humeral bone loss. Shoulder hemiarthroplasty is advocated in low demand or elderly patients with osteopenic bone and young adults in whom the strategies discussed above are not appropriate. Indeed in those patients with concomitant glenoid wear it may be sensible to consider a total shoulder replacement[92].

Bipolar humeral and glenoid bone loss

The management of bipolar or combined humeral and glenoid bone loss in the context of shoulder instability is an evolving concept. This degree of bone loss is usually seen after multiple traumatic dislocations and epileptic seizures. The key factors are the degree of bone loss involved but also whether the humeral Hill-Sachs lesion engages or not. The significance of the interaction between the humeral and glenoid defect can best be understood using the glenoid track principle. Yamamoto *et al*[93] described the glenoid track as the zone of contact between the humeral head and the glenoid at 90 degrees of shoulder abduction relative to the trunk. The region corresponds to 83% of diameter of the glenoid and represents a distance from the medial point of the contact area to the medial margin of the rotator cuff insertion on the humerus[94]. Thus glenoid bone loss decreases the size of the glenoid track (Table 1).

If the humeral Hill-Sachs bone lesion lies within the diameter of the glenoid track, there is bone support adjacent to this and the lesion is described as being "on-track". If the defect lies outside this region, there is no adjacent bone support and the lesion is "off track". If the Hill-Sachs lesion is "off-track" it gives rise to a more unstable shoulder in the context of bipolar bone loss. An updated definition of an engaging humeral bone lesion can be defined as one that lies outside of the glenoid track[50].

The concepts described can help determine the management of bipolar bone loss in shoulder instability. We have previously discussed the treatment of both glenoid and humeral bone loss individually. Di Giacomo *et al*[7] has proposed an algorithm for combined bone loss. Fundamental to this is whether the humeral bone lesion is "on track" or not. Bipolar defects with an "on-track" humeral defect may be treated by addressing the glenoid defect alone. Hence < 25% glenoid bone loss can be managed with arthroscopic Bankart repair and > 25% bone loss with a Latarjet procedure.

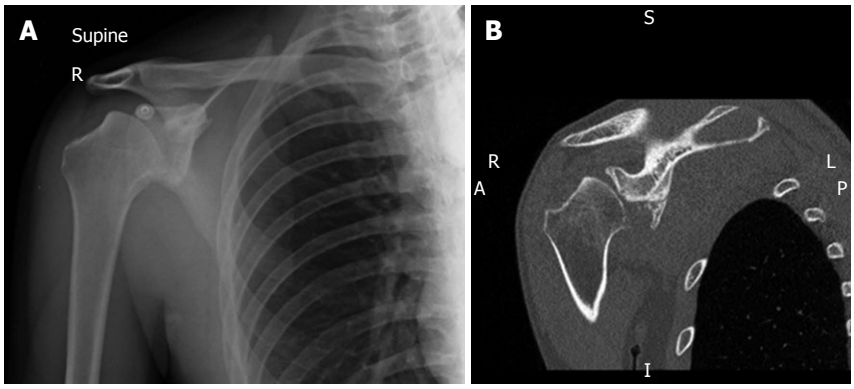

Figure 4 Antero-posterior radiograph (A) and computed tomography scan (B) of a 25-year-old epileptic with massive bipolar bone loss. He was found to have > 25% glenoid bone loss and > 40% humeral bone loss pre-operatively.

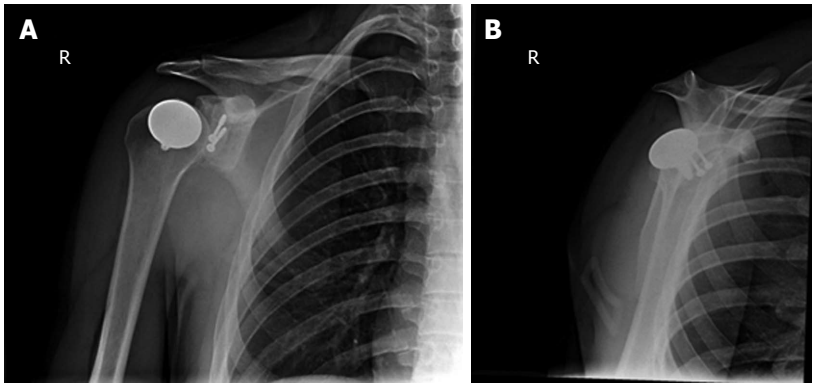

Figure 5 Antero-posterior (A) and scapular Y (B) views of an epileptic patient with massive bipolar bone loss treated with a humeral HemiCap and Latarjet procedure.

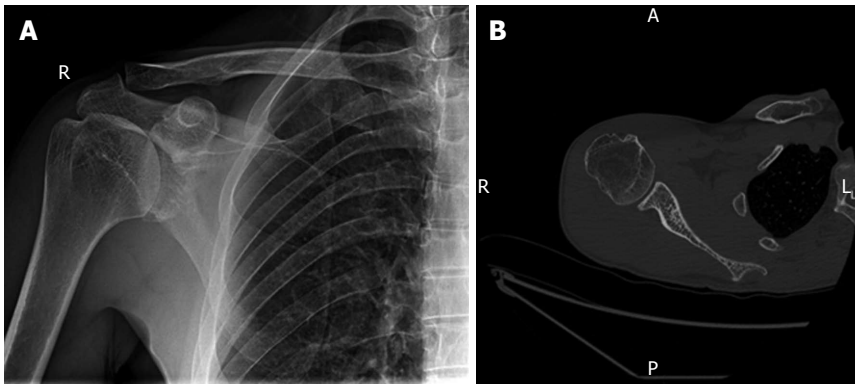

Figure 6 42-year-old manual worker with anterior shoulder instability with < 25% glenoid bone loss and an engaging Hill-Sachs lesion. He was managed successfully with an arthroscopic Remplissage and Bankart repair. Pre-operative antero-posterior radiographs (A) and computed tomography (B) images are demonstrated.

Patients with an "off-track" humeral bone defect require both the glenoid and the humeral defect to be addressed. Ranne *et al*[25] described successfully combining an open Latarjet and Remplissage in a patient with severe bipolar bone loss. This may be a reasonable option in those with > 25% glenoid bone loss with engaging humeral defects. In cases with significant > 40% humeral bone loss and > 25% glenoid loss, treatment with a combination of an open Latarjet with a partial resurfacing/replacement or allograft reconstruction procedure would address both the glenoid and humeral bone loss respectively (Figures 4 and 5). Those, however, with a lesser degree of glenoid bone loss < 25% with an "off-track" humeral Hill-Sachs may be successfully treated with a combined arthroscopic Bankart and Remplissage procedure (Figure 6).

In the case of failure of such procedures, the only available options for salvage surgery may be to consider shoulder fusion in younger patients (Figure 7), and reverse shoulder arthroplasty is older, lower demand

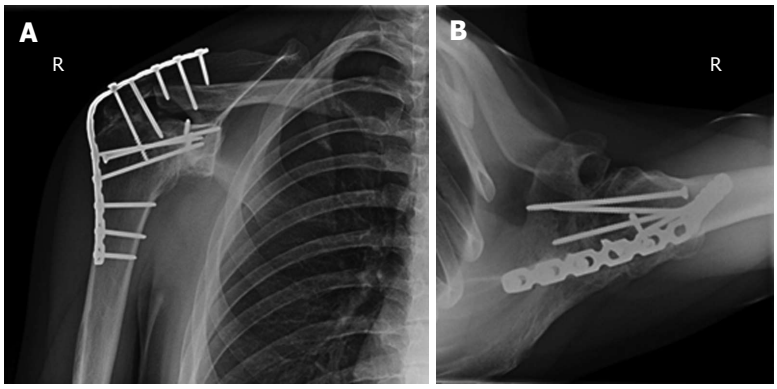

Figure 7 Antero-posterior (A) and axillary view (B) radiographs six months following shoulder fusion after failure of a combined HemiCap and Latarjet procedure in an epileptic patient with massive bipolar bone loss.

patients to restore stability and maintain some function.

CONCLUSION

Bone loss in shoulder instability is a challenging problem to orthopaedic clinicians. In this review we have addressed the current concepts in identifying and treating such patients using best current evidence available. Currently the literature is limited and further high level evidence studies are needed to further investigate the benefit of different surgical strategies, particularly in the area of combined humeral and glenoid bone loss.

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MINIREVIEWS

Medial ulnar collateral ligament reconstruction of the elbow in major league baseball players: Where do we stand?

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Abstract

The ulnar collateral ligament (UCL) is a vital structure to the overhead athlete, especially the baseball pitcher. For reasons not completely understood, UCL injuries have become increasingly more common in major league baseball (MLB) pitchers over the past 10 years. UCL reconstruction (UCLR) is the current gold standard of treatment for these injuries in MLB pitchers who wish to return to sport (RTS) at a high level and who have failed a course of non-operative treatment. Results following UCLR in MLB pitchers have been encouraging, with multiple RTS rates now cited at greater than 80%. Unfortunately, with the rising number of UCLR, there has also been a spike in the number of revision UCLR in MLB pitchers. Similar to primary UCLR, the etiology of the increase in revision UCLR, aside from an increase in the number of pitchers who have undergone a primary UCLR, remains elusive. The current literature has attempted to address several questions including those surrounding surgical technique (method of exposure, graft choice, management of the ulnar nerve, concomitant elbow arthroscopy, *etc.*), post-operative rehabilitation strategies, and timing of RTS following UCLR. While some questions have been answered, many remain unknown. The literature surrounding UCLR in MLB pitchers will be reviewed, and future directions regarding this injury in these high level athletes will be discussed.

Key words: Ulnar collateral ligament; Ulnar collateral ligament reconstruction; Tommy John; Major league baseball; Pitcher; Baseball

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Core tip: The number of ulnar collateral ligament (UCL) tears in major league baseball athletes is increasing with time. UCL reconstruction (UCLR) has become the gold standard for treatment of UCL tears. The outcomes of this surgery in elite level athletes is encouraging, with return to sport rates typically > 80%. Results following revision UCLR are less encouraging. Currently, there is no standardized rehabilitation protocol or timing to return to sport. Future research into graft choice,

surgical technique, management of the ulnar nerve, and rehabilitation protocols must be done to achieve the best possible results in this elite group of athletes.

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INTRODUCTION

The ulnar collateral ligament (UCL) is one of the most important structures about the elbow in the overhead athlete, especially the baseball pitcher[1,2]. While the UCL is not commonly stressed during activities of daily living, the baseball pitch imparts a significant amount of stress on the UCL, specifically the posterior band of the anterior bundle as it is this part of the UCL that sees the most stress at higher degrees of elbow flexion, causing the UCL to approach failure with each pitch[3-5]. Without the secondary osseous and soft tissue restraints about the elbow, the UCL would fail after each pitch as the valgus force generated at the elbow with each pitch is approximately 64 nmol/L, while the ultimate load to failure of the native and reconstructed UCL is 34.29 nmol/L, and 30.55 nmol/L, respectively[3].

Diagnosis of UCL tears is accomplished through patient history, physical exam maneuvers, and diagnostic imaging[6]. Baseball pitchers who sustain tears to the UCL often report a decrease in velocity as well as a loss of accuracy in the time leading up to their injury[7]. Some patients will have concomitant ulnar nerve symptoms, such as numbness/tingling of the pinky and ulnar half of the ring finger, weakness of the first dorsal interosseous muscle, and others. On physical exam, these patients can have pain along the course of the UCL. They may also have an increase in elbow valgus laxity compared to the contralateral arm, although this can be physiologic in baseball pitchers[8]. Special physical exam maneuvers, including the moving valgus stress test and milking maneuver, are often positive in these patients as these tests stress the UCL in the position of throwing[6,9,10]. Although anteroposterior, lateral, and external oblique radiographs are useful to rule out calcifications in the UCL as well as other pathology, magnetic resonance imaging (MRI) with or without arthrography is the current imaging modality of choice to diagnose a UCL tear[11,12]. It seems that the increase in diagnosis of UCL tears is likely secondary to sports specialization in adolescents leading to an increase in the true number of UCL tears rather than an overdiagnosis on MRI like has been shown with superior labral tears[13-15].

Should the UCL fail, the current gold standard treatment option for elite level overhead athletes who wish to return to sport (RTS) at a high level after failing non-operative management is an UCL reconstruction (UCLR). Although repair of the UCL has been described with encouraging results for properly indicated adolescents, the results of repair have reproducibly been inferior to UCLR in major league baseball (MLB) athletes, and so UCLR has become to standard of care[7,16,17]. UCLR was initially described by Jobe *et al*[18] in the literature in 1986, although the index surgery was performed on September 25, 1974 on then Los Angeles Dodgers pitcher, Tommy John.

The initial technique by Jobe *et al*[18] called for an elevation of the flexor pronator mass with a submuscular transposition of the ulnar nerve and a figure of eight graft configuration in which the graft was sutured to itself. Results of the initial Jobe technique demonstrated that greater than 60% of elite throwing athletes were able to RTS at their pre-surgical level of participation[16]. However, 21% of these patients had a post-operative ulnar neuropraxia, all of which resolved by seven years[16]. Following this initial description, concern arose over the treatment of the flexor pronator mass, as well as the routine submuscular transposition of the ulnar nerve. Therefore, since the initial description by Dr. Jobe, many modifications have been made to improve patient outcomes and decrease complications following UCLR; these modifications include a split in the flexor pronator mass, subcutaneous ulnar nerve transposition, and varying ways to secure the graft both on the ulna as well as humerus[7,19-24].

EPIDEMIOLOGY OF UCLR IN MLB

Several studies have shown a recent increase in the number of UCL tears, and more specifically, the number of UCLR in MLB pitchers[2,25-27]. Recent studies have also shown an increase in the number of UCLR performed in adolescent athletes, specifically those between the ages of 15-19 years[28]. When evaluating MLB players, as expected, UCLR is significantly more common in MLB pitchers than any other position. When Conte *et al*[2] surveyed 5088 professional baseball players, there was a 16% prevalence of UCLR amongst pitchers compared to only 3% amongst all other position players. Interestingly, this survey study by Conte *et al*[2] found that 25% of al MLB pitchers admitted to a history of UCLR, while 15% of minor league pitchers had undergone UCLR. No difference was seen in the prevalence of UCLR between pitchers born in the United States *vs* those born in Latin America countries[2]. Erickson *et al*[25,26] showed a significant increase in the number of UCLR in MLB pitchers from 2000 to 2012 (P = 0.014), and further studies have demonstrated that the number has continued to rise in 2013 and 2014[2]. Interestingly, there was no statistically significant increase in the number of UCLR in MLB pitchers between the 1980s and 1990s[25]. MLB pitchers who underwent primary UCLR played an average of 5.27 ± 4.34 seasons prior to surgery[25]. Furthermore, pitchers who grew up in warm weather climates were more likely to undergo UCLR earlier in their MLB career than

those from cold weather climates[26]. While the increase in UCLR has been clearly documented, the reason for this increase remains unknown. There have been no prospective studies in the literature to date that have definitively shown what the cause of this increase in the number of UCLR is.

Several studies have, however, demonstrated risk factors for elbow injuries in adolescent athletes including pitching more than 100 innings per year, high pitch counts, pitching on consecutive days, pitching for multiple teams, pitching while fatigued, pitching year round, pitching with higher velocity, pitching with supraspinatus weakness, geography, pitching with a glenohumeral internal rotation deficit, and most recently pitching with a loss of total arc of motion, especially decreased external rotation[26,29-38]. While these risk factors have been well established, there have been no studies to date that have been able to show a risk reduction in the number of UCLR by implementing programs to limit these risk factors. This is an area that requires further attention in the coming years as there does not appear to be an end in sight to the growing number of UCLR, and injury prevention must be at the forefront of current research to protect both MLB and adolescent pitchers[39].

Although the increase in the number of primary UCLR in MLB pitchers is worrisome, a more pressing concern is the increase in the number of revision UCLR in these athletes[2,40-42]. Wilson *et al*[42] evaluated 271 professional baseball pitchers who underwent primary UCLR and found that 40 (15%) required at least one revision UCLR during their pitching career while three pitchers required a second revision. The revision surgery occurred an average of 5.2 ± 3.2 years following the index UCLR, although there was a wide range from 1-13 years. As pitchers are beginning to undergo UCLR at earlier ages, it begs the question if the longevity of these athletes is going to decrease with time. Some would argue that a pitcher has a finite number of innings he can throw. If adolescent athletes are throwing year round and not following the rules set forth for their protection regarding inning and pitch count limits, these athletes could begin to undergo their index UCLR at earlier ages, causing the likelihood of a revision UCLR to rise, thereby limiting the ultimate number of years they can pitch in MLB.

OUTCOMES FOLLOWING PRIMARY AND REVISION UCLR IN MLB PITCHERS

Primary

There have been many studies that have looked at publically available data to determine the outcomes following UCLR in MLB pitchers as it relates to RTS as well as overall performance upon RTS[25,43]. Erickson *et al*[25] evaluated all MLB pitchers from 1974 to 2012 who underwent UCLR using publically available data, team injury reports, *etc.*, and compared this group to a matched control group of healthy MLB pitchers. The authors found a total of 179 pitchers who underwent UCLR having pitched at least one game in MLB. Of these 179 pitchers, 148 (83%) were able to RTS and pitch in at least one MLB game following UCLR, 174 (97.2%) were able to RTS in either the major or minor leagues, and only 5 pitchers (2.8%) were unable to pitch again in the major or minor leagues. The pitchers were able to RTS at an average of 20.5 ± 9.72 mo following their UCLR and pitched for an average of 3.9 ± 2.84 years after their RTS. The number of years pitched after RTS may have been falsely low as 56 of these pitchers were still active in MLB at the time the study was conducted.

When the authors evaluated the performance of these MLB pitchers upon RTS they found that pitchers pitched fewer innings in season following their UCLR and had fewer wins and losses per season compared to before surgery[25]. Furthermore, pitchers had a significantly lower earned run average (ERA) and walks plus hits per inning pitched (WHIP) following surgery than beforehand. WHIP is a sabermetric that is calculated by summing a pitcher's total walks and hits for one season and dividing the sum by the number of innings pitched that season. A later study conducted by Jiang *et al*[43] evaluated 28 MLB pitchers between 2008-2010 who underwent UCLR to determine if pitching velocity, as well as performance variables changed compared both to pre-operative levels upon RTS in MLB as well as control group of healthy MLB pitchers. The authors found a statistically significant decrease in mean pitch velocity of both the fastball and changeup in each post-injury year compared to pre-injury velocities. The average decrease in fastball velocity for post-UCLR years 1-3 was 1.3, 1.0, 1.0 miles per hour (mph) respectively. The average decrease in changeup velocity for post-UCLR years 1-3 was 1.2, 1.3, 1.0 mph respectively. Furthermore, a decrease in curveball velocity was seen in post UCLR years 2 and 3 that averaged 1.0 and 1.7 mph respectively. However, despite these differences between pre and post UCLR pitching velocities in the group of pitchers who underwent UCLR, there was no significant difference in mean pitch velocity for any pitch, in any year following UCLR in cases *vs* matched controls[43]. Hence, this could mean that pitchers who sustain UCL tears and undergo UCLR are throwing faster than their peers at baseline. Lansdown *et al*[44] performed a similar study and found similar results; pitchers who underwent UCLR had a significant decrease in mean fastball velocity (91.3 mph *vs* 90.6 mph) (P = 0.003), with the greatest decrease in velocity seen in pitchers older than 35 years of age (91.7 to 88.8 mph) (P = 0.0048). Despite the belief from players, parents, and coaches as shown by Ahmad *et al*[45] that UCLR will improve a pitchers velocity, these two studies clearly demonstrate a small but significant decrease in velocity following UCLR.

Revision

While the results following primary UCLR in MLB pitchers are reliable, the results following revision UCLR in the same patient population are not as encouraging[40]. Marshall *et al*[40] evaluated 33 MLB pitchers who under-

went revision UCLR and compared these pitchers to matched controls to determine if differences existed in performance upon RTS. The authors found that 65.5% of pitchers who underwent revision UCLR were able to return to RTS in MLB while 84.8% were able to RTS in either the major or minor leagues; both rates are lower than RTS rates following index UCLR of 83% for MLB and 97.2% for either major or minor leagues[25]. Interestingly, when Liu *et al*[46] also evaluated 31 MLB pitchers following revision UCLR surgery, the authors found that while 65% were able to RTS in the MLB for one game or more, only 42.8% were able to pitch 10 or more games in MLB. Similar to the reported length of recovery following primary UCLR of 20.5 mo, the average time to RTS following revision UCLR was 20.76 mo[25,46].

When compared to pre-injury performance levels, following revision UCLR pitchers pitched fewer innings, had fewer wins and losses, and let up more walks per nine innings. The only performance parameter that improved was the number of runs allowed per nine innings declined following revision surgery. Furthermore, pitchers who were able to RTS following revision UCLR pitched significantly fewer seasons than matched controls (2.6 *vs* 4.9 seasons)[46]. Following revision UCLR, pitchers had no difference in ERA and WHIP when compared to controls[40]. Unfortunately, following revision UCLR pitchers threw significantly fewer innings, gave up significantly more walks, and had significantly fewer wins (although they also had significantly fewer losses) compared to controls[40].

FUTURE DIRECTIONS

Although there have bee numerous studies that have reported on the RTS rate and outcomes of MLB pitchers following both primary and revision UCLR, there have been no prospective studies in this athlete cohort that have evaluated RTS rate or success upon RTS as it relates to surgical technique, graft choice, management of the ulnar nerve, concomitant arthroscopy, rehabilitation protocol, and timing of RTS[25,40,44,46]. In order to improve outcomes, it is necessary to determine if these variables influence outcomes in MLB pitchers. One topic that has received recent attention is when to allow pitchers to throw for the first time following UCLR. While some protocols wait five months or more, some allow throwing as early as three to four months. Unfortunately, no data exists on the ideal timing, so these protocols have not yet been standardized to efficiently and safely return these pitchers to sport.

Furthermore, large, prospective studies must be designed to follow elite pitchers starting at the Little League level through their career. Although only a small percentage of these athletes will become MLB pitchers, it would be extremely valuable to see if implementing some of the rules and regulations aimed at decreasing elbow injuries were effective, and likewise to see if pitchers who did not adhere to the regulations were at higher risk for undergoing UCLR later in life. This would also give the orthopaedic community an idea if pitchers do in deed have a finite number of innings their body will allow them to pitch, thereby proving to coaches and parents the importance of limiting excessive pitching at early ages.

CONCLUSION

Recent times have seen an increase in the number of UCLR in MLB pitchers. While evidence has shown a greater than 80% RTS rate following UCLR, the RTS rate following revision UCLR is not as high. Further large scale, prospective studies are necessary to help dictate treatment algorithms in these high level athletes.

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MINIREVIEWS

Antimicrobial technology in orthopedic and spinal implants

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Abstract

Infections can hinder orthopedic implant function and retention. Current implant-based antimicrobial strategies largely utilize coating-based approaches in order to reduce biofilm formation and bacterial adhesion. Several emerging antimicrobial technologies that integrate a multidisciplinary combination of drug delivery systems, material science, immunology, and polymer chemistry are in development and early clinical use. This review outlines orthopedic implant antimicrobial technology, its current applications and supporting evidence, and clinically promising future directions.

Key words: Antimicrobial; Coated implants; Antibiotic; Antiseptic; Nano-silver; Photoactive

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Core tip: Infections can hinder orthopedic implant function and retention. Current implant-based antimicrobial strategies largely utilize coating-based approaches in order to reduce biofilm formation and bacterial adhesion. Several emerging antimicrobial technologies that integrate a multidisciplinary combination of drug delivery systems, material science, immunology, and polymer chemistry are in development and early clinical use. This review outlines the latest orthopedic implant antimicrobial technologies-including updates on chitosan

coatings, photoactive-based coatings, electrospinning technology, integrated biofilms-highlighting the current applications, supporting evidence, and clinically-promising future directions.

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BACKGROUND

Orthopedic implants are commonly used in spine surgery, arthroplasty, arthrodesis, as well for applications in treating fractures and nonunions[1]. Typically formulated from titanium, stainless steel, cobalt-chromium, or polyethylene polymers, orthopedic implants can serve as niduses for infection and may hinder infection clearance due to biofilm formation on the implant surface[2]. Orthopedic implant-associated infections are challenging complications which can lead to delayed healing, implant loosening, implant removal, amputation, or even death[3].

In many infections, bacteria will form a biofilm on the implant, increasing their resistance to antibiotics and resulting in infection persistence despite aggressive surgical debridement and prolonged antibiotic treatments[4,5]. A biofilm is an aggregated mass of bacteria that can form on the surface of an orthopedic implant, providing the ideal environment for bacteria to flourish. Such bacterial growths are difficult to eliminate and present a serious challenge in implant development[6,7]. In the United States, orthopedic implants are associated with an approximate 5% infection rate, representing 100000 infections per year[8]. This frequency represents a notable economic burden on both patients and health care providers. Although exact figures are elusive, even with the existence of antibiotic prophylactic it is estimated that implant infections increase the overall cost of hospitalization up to 45% on average[9,10].

ANTIMICROBIAL COATED IMPLANTS

Current antimicrobial strategies have largely focused on coating-based approaches-each of which aims to prevent infection by mitigating biofilm formation[11]. Key coatings include antibiotic, antiseptic, nano-silver, and photoactive-based coatings[11].

Antibiotic-based coatings

Antibiotic coatings allow for local delivery of antibiotics with a sustained release based on the drug carrier pharmacokinetics[12]. While various antibiotics have been studied (*e.g.*, amoxicillin, vancomycin, cephalothin, and tobramycin), the most widely studied antibiotic for such coatings has been gentamicin[11]. Common biocompatible drug carriers for the coatings include polymethylmethacrylate (PMMA), poly(lactic-co-glycolic acid) (PLGA), poly(lactic acid), polyethylene glycol, and poly(D,L)lactide (Figure 1)[7]. Hydroxyapatite (HA) was recently shown to be an effective drug carrier of gentamicin[13,14].

Neut *et al*[15] demonstrated the wide-spectrum antibacterial efficacy of a gentamicin coating *in vitro* through investigating infection prophylaxis of *Staphylococcus aureus* (*S. aureus*) in cementless total-hip arthroplasty. In a rabbit model, Alt *et al*[16] found that the gentamicin-HA composite provided a statistically significant reduction in infection rate when compared to uncoated total joint replacements. In patient trials, gentamicin-coated implants have displayed promising preliminary results (Figure 1)[17-20]. Limitations of antibiotic coatings include the use of fixed, predetermined antibiotics; limited duration of drug elution; and the risk of developing drug resistance[21].

To overcome the limited duration of drug elution, Ambrose *et al*[22-24] developed antibiotic-impregnated bioresorbable microspheres for sustained release of antibiotics over several weeks-which have been shown to reduce infection rates in animal models. Antiseptic-based coatings have emerged to address antibiotic coatings fixed bactericidal spectrum and possible drug resistance limitations. Antibiotic-based coatings are currently the most commonly utilized local antimicrobial clinical delivery method due to the well characterized nature of the antimicrobial agents. These coatings are limited by antibiotic classes, which are compatible with the chemistry of the coating matrix. Asides from pharmacokinetic limitations, antibiotic-based coatings represent the most accepted antimicrobial option available.

Antiseptic-based coatings

In contrast to antibiotic coatings, which are formulated to work against specific bacterial strains, antiseptic-based coatings are intended to combat a wide range of bacteria by way of more general chemical agents. For this reason antiseptic coatings are less likely to induce bacterial resistance compared to antibiotics[25,26]. Common antiseptics include chlorhexidine and chloroxylenol, which are thought to act through the interaction of their natural cationic nature with the anionic phosphate residue of the lipid molecules in bacterial cell membranes. This ionic adsorption damages cell membranes and limits bacterial adhesion (Figure 2)[27,28]. In 1998, Darouiche[8] first demonstrated the effectiveness of antiseptic coatings on titanium cylinders studied *in vitro* with human serum before DeJong *et al*[29] tested chlorhexidine and chloroxylenol in a goat model, finding that these two antiseptics reduced external fixator pin tract infections. Ho *et al*[30] demonstrated *in vivo* efficacy of antiseptic coatings in humans by reducing vascular and epidural catheter infection with application of a chlorhexidine-impregnated dressing. Due to their broad spectrum efficacy, antiseptic-based coatings are not without some level of generalized toxicity. Because of their general toxicity, antiseptic based

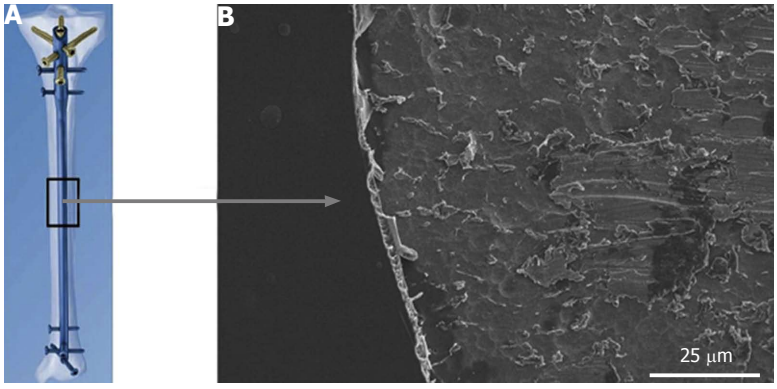

Figure 1 Diagram of tibial nail with gentamicin coating (A), visualized on metal implant using scanning electron microscopy (B)[20].

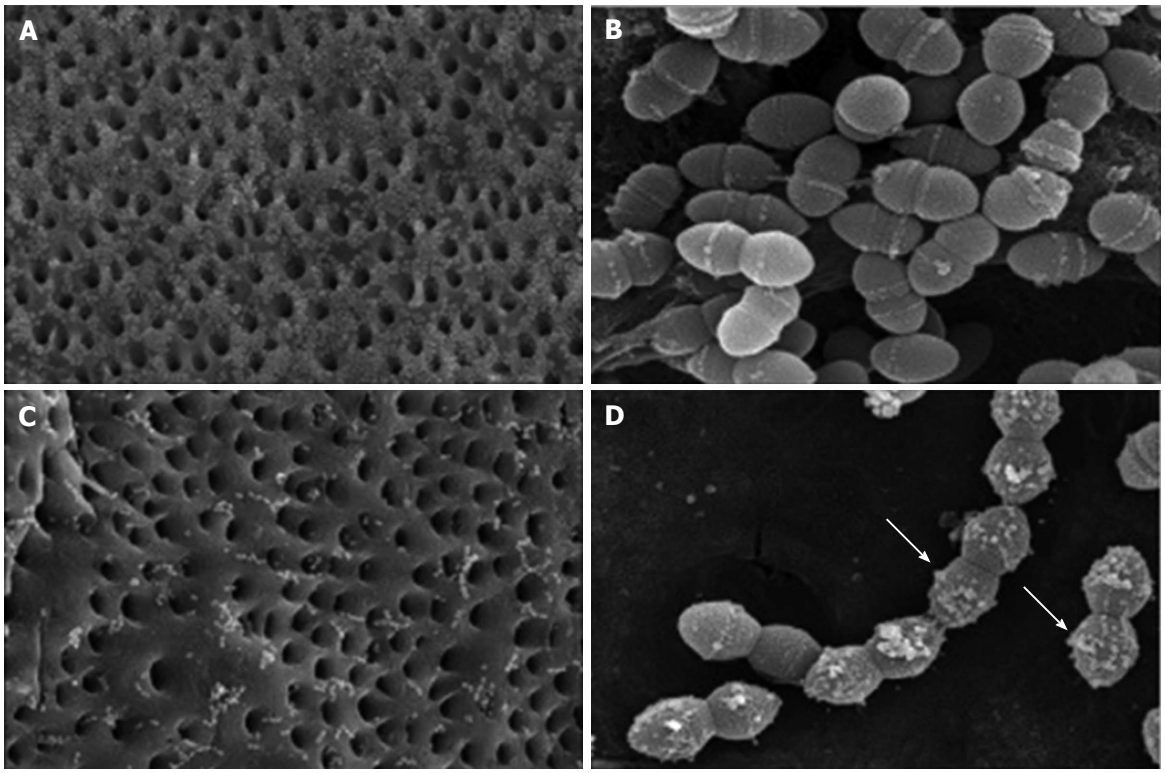

Figure 2 Scanning electron microscopy images of *Enterococcus faecalis*-infected dentin blocks treated with saline and chlorhexidine. Blocks treated with saline solution for 10 min show many adhering *Enterococcus faecalis* (A, × 1500) with normal shape (B, × 20000). The group soaked with 2% chlorhexidine shows fewer adhering bacteria (C, × 1500) and chlorhexidine particles attached to bacterial membranes (D, × 20000, white arrows)[28].

coatings are more commonly utilized as topical dressings.

Chitosan coatings

Chitosan is a polymer of chitin that exhibits active anti-microbial properties. Recent pre-clinical studies have provided evidence that several composites of chitosan may act as effective antimicrobial agents suited for titanium orthopedic implants. Yang *et al*[31] tested a vancomycin-chitosan composite by monitoring the proliferation of human osteoblast cells *in vitro* using methyl thiazole tetrazolium and cell adhesion using FEMSEM. They found that vancomycin-chitosan coated implants displayed lesser biofilm formation, a result corroborated by *in vivo* experiments in a rabbit model[31].

In fact, some results indicate that a simple mixtures of 2%-3% chitosan and 2% cinnamon oil may also hold antimicrobial properties against *Staphylococcus epidermidis* (*S. epidermidis*) on titanium implants[32]. Most recently, Qin *et al*[33] revealed preliminary *in vitro* results suggesting that chitosan-casein phosphopeptides coatings could provide antimicrobial benefits for cobalt matrix orthopedic implants. Other studies have suggested that chitosan alone may not be sufficiently potent as an antimicrobial agent and suffers from poor release kinetics. More current studies have focused on the synergistic use of chitosan and antibacterial agents with more promising results. As yet we are not aware of any clinical trials incorporating chitosan-based coats.

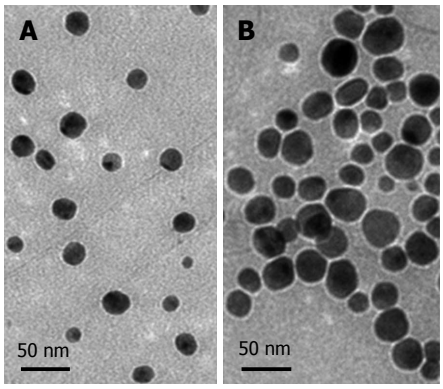

Figure 3 Silver nanoparticles of two sizes: Small (A) and Large (B), visualized *via* transmission electron microscopy[42].

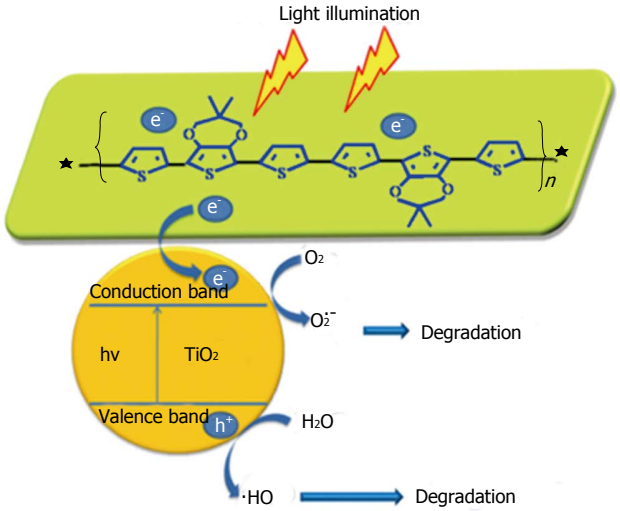

Figure 4 Schematic illustration of proposed photocatalytic and antibacterial mechanisms of a nanocomposite photocatalytic coating[55]. TiO_2: Titanium oxide.

Nano-silver coatings

The antimicrobial properties of silver particles are well-established[34-38]. Silver particles have several known mechanisms of action including binding to thiol groups of enzymes, cell membranes, and nucleic acids, resulting in structural abnormalities, a damaged cell envelope, and inhibition of cell division[39-41]. Silver nanoparticles (Figure 3)[42] are typically incorporated into titanium surfaces or polymeric coating to control the release rate and duration of the bioactive silver[11,43-45]. Electrical currents are established when silver nanoparticles (cathode) embedded in a titanium matrix (anode) are exposed to electrolytes[45] - this galvanic coupling can cause changes in bacterial membrane morphology and DNA, leading to cell death[37]. Silver-based coatings have antimicrobial efficacy against a broad spectrum of pathogens, including *Escherichia coli*, *S. aureus* and *S. epidermidis*[46-48]. Using an *in vivo* model for osteomyelitis, Tran *et al*[48] inoculated *S. aureus* into fractured goat tibias and found after 5 wk silver-doped coated intramedullary nails led to better clinical and histology outcomes than the controls fixed with uncoated nails.

Early clinical studies have shown promising results with regard to reducing periprosthetic infections. Wafa *et al*[49] retrospectively compared 85 patients with silver-coated tumor prostheses to 85 tumor patients with non-silver tumor prostheses. The authors found that the average infection rate among silver-coated implant patients was 10.6% lower than that of their uncoated counterparts. In a similar prospective study by Hardes *et al*[50], silver-coated prosthetic tumor implants were shown to have an 11.7% lower infection rate over a five-year period than uncoated implants. Despite these encouraging clinical results, clinical use of silver-coated implants has been limited by concerns of mammalian bone cell cytotoxicity[51,52]. While this cytotoxic level is much lower than the anti-microbial threshold used for implant coatings, there is evidence to suggest that prolonged exposure to even low doses of nano-silver may result in mild toxicity in rats[53]. The long-term implications of such toxicity are yet undetermined. Because of its long history of usage, and relatively low toxicity, silver-based antimicrobial coatings represent a very promising tool against antibiotic-resistant pathogens. The effectiveness of the technology has been shown to be largely dependent on the ability of the coating matrix to provide efficacious release kinetics and formulation of silver nanoparticles or ions.

Photoactive-based coatings

Photocatalyst coatings are composed of titanium alloys and display bactericidal effects *via* membrane degradation after activating exposure to ultraviolet irradiation (Figure 4)[54,55]. Titanium oxide (TiO_2) is a commonly used photocatalytic agent due to its strong oxidizing power, lack of toxicity, and long-term chemical stability[56]. Villatte *et al*[56] demonstrated TiO_2-based photoactive coatings were able to withstand mechanical stress from inserting stainless steel pins in cow femurs, had antibacterial effectiveness against *S. aureus* and *S. epidermis* cultures, and has the added benefit of low cost and easy scalability. Photocatalysts as antimicrobial agents in orthopedic implants remain to be tested *in vivo.*

NON-COATING TECHNOLOGY

Antibiotic-loaded bone cement

In addition to coatings, several other antimicrobial orthopedic implant technologies are being evaluated. Antibiotic-loaded bone cement (ALBC), such as PMMA, is widely used by orthopedic surgeons to help secure arthroplasty implants, to fill bone voids, and to treat vertebral compression fractures (Figure 5)[57,58]. ALBC has been in use since first being developed in 1970 as a potential method for *in situ* drug release[59]. Despite its widespread use, the antimicrobial efficacy of ALBC is debated[60,61]. Due to irregular release of antibiotic, only 5%-8% of the drug typically elutes properly[62]. Therefore, the high doses needed for a therapeutic effect have been shown to produce pathogen resistance[57].

Figure 5 Antibiotic loaded bone cement beads strung on braided stainless steel[58].

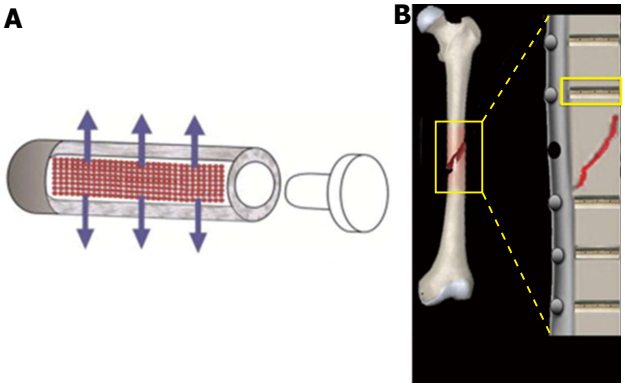

Figure 6 Fixation pins with tubular reservoirs for controlled drug release. Diagrams highlighting the principle design of fixation pins: A: Scheme of a drug releasing fixation pin. Note the permeation through the porous wall (arrows)[64]; B: Scheme of implanted fixation pins, each capable of eluting local antibiotics around fixation site[65].

Antibiotic-loaded reservoirs

A novel system utilizes antibiotic-loaded reservoirs within the steel implant itself to enable a more controlled, localized release of drug when compared to coatings[63]. Initial *in vivo* testing by Gimeno *et al*[64] demonstrated that sheep infected with a biofilm-forming *S. aureus* strain showed no signs of infection of pre-placed tibia implants 7-9 d post introduction of *S. aureus*. Gimeno *et al*[65] subsequently proposed a design detailing fixation pins with tubular reservoirs for loading of antibiotics, allowing for more controlled release of the antibiotic based on number and size of release orifices (Figure 6).

Modified surface characteristics

Modifying implant surface characteristics have are also been investigated as a means of reducing biofilm. For example, mixtures of polyethylene oxide and protein-repelling polyethylene glycol have shown significant bacterial inhibition when applied implant surfaces[66,67]. Singh *et al*[68] demonstrated that modifying surface roughness (Figures 7[69] and 8) of a material at the nanoscale level could provide antibacterial properties. Surface

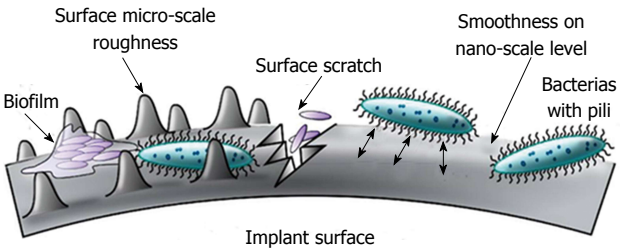

Figure 7 Interaction between surface roughness and bacterial adhesion[69].

characteristic modification has been shown to interfere with osseointegration of the implants, challenging its clinical application[70]. Other studies have shown that certain pathogens are able to adhere, proliferate, and form biofilms more readily on rough surfaces. The data available suggests there is threshold where modified surface microtopography can be an effective means of reducing biofilm, or encouraging bacterial growth.

Electrospinning

Electrospun matrices of PLGA nano-fibers have recently been proposed as a promising antimicrobial approach to orthopedic implant-associated infections[71]. In electrospinning, ultrafine fibers with nanometer diameters form a matrix with a very high surface-area-to-volume ratio[72]. Produced by syringe-pumping various drug and polymer solutions in the presence of a high electrical field potential[73], the resulting drug loaded, non-woven PLGA membranes are flexible, porous, and enable controlled drug release (Figure 9)[71,74]. Like coating, the matrices adhere directly to orthopedic implants.

Integrated biofilms

Özçelik *et al*[75] proposed a novel polyelectrolyte multilayer film approach using combined antimicrobial and immunomodulatory strategies (Figure 10). Composed of polyarginine and hyaluronic acid, the film inhibits the production of inflammatory cytokines, combats bacteria using a nanoscale silver coating, and opens the opportunity for bacteria-specific customization *via* embedded antimicrobial peptides. Although development of such films is far from clinical practice, microfilms are a promising look into the benefits of combining existing approaches for limiting implant-related complications to develop the composite technology of the future.

CONCLUSION

Several imperfect options exist for reducing the risk of orthopaedic implant infections. Despite technological advancement, orthopedic implant-associated infections remain as an important clinical problem, necessitating additional improvement. With promising technology on the horizon, it seems that the answer for reduced infection may not lie in solely one device or technology but in the synergy of many.

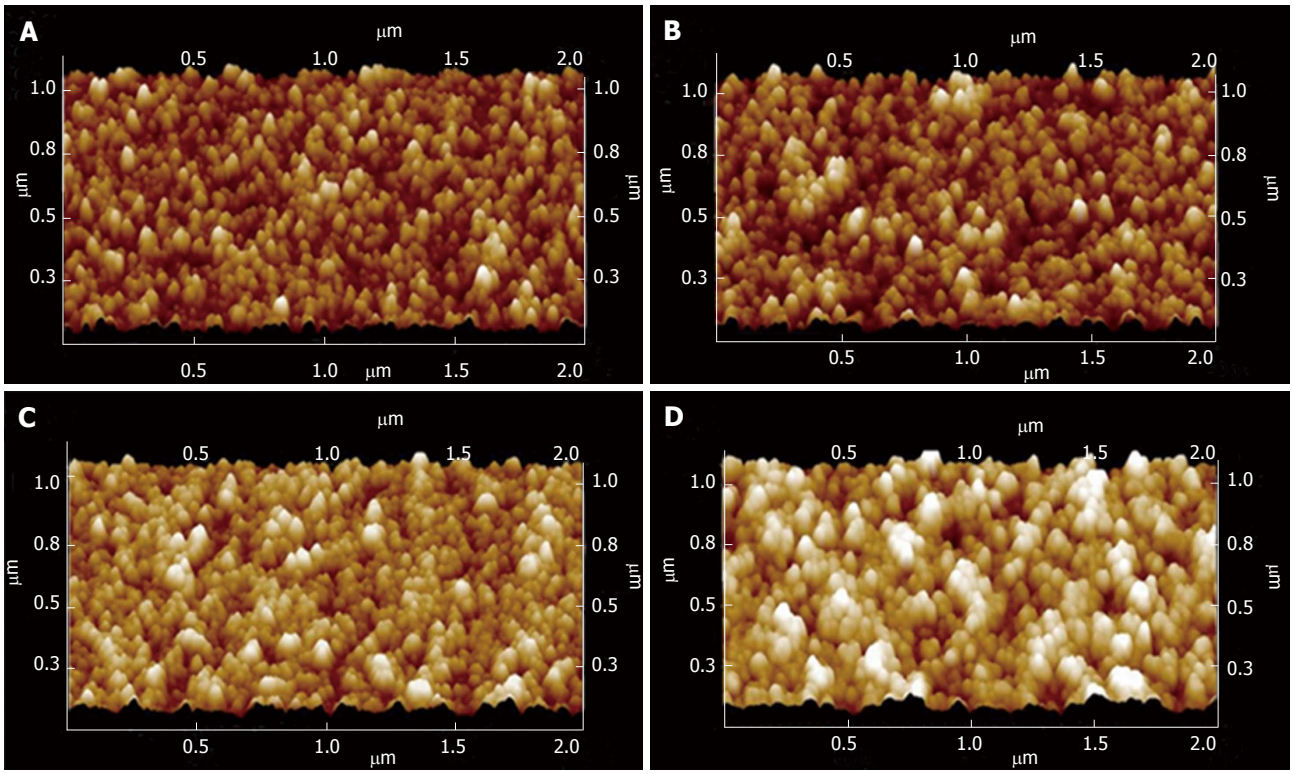

Figure 8 Atomic force microscopy of different surface film topography of increasing thickness (A: 50 nm; B: 100 nm; C: 200 nm; D: 300 nm)[68].

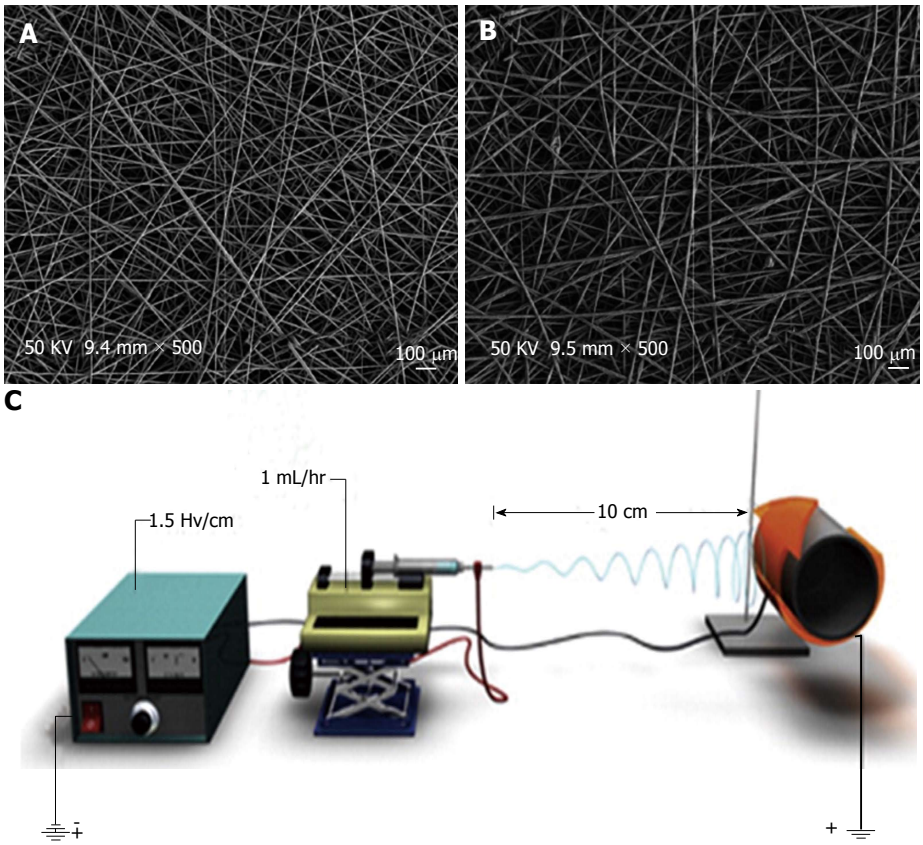

Figure 9 Micrograph and apparatus perspective of electrospinning technology. Scanning electron microscopy micrographs of PLGA electrospun coatings containing (A) vancomycin and (B) no drug[74]; C: Schematic of a charged electrospinning apparatus spinning a PLGA coating onto an implant device[71]. PLGA: Poly(lactic-co-glycolic acid).

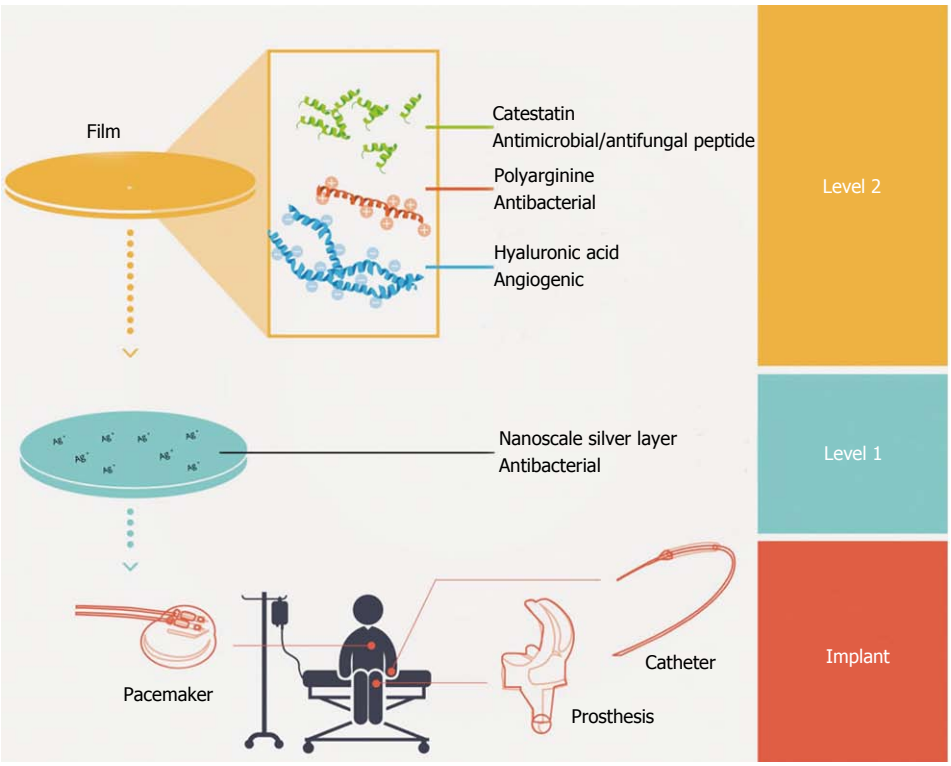

Figure 10 Integration of antimicrobial biofilms into the implant process[75].

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MINIREVIEWS

Orthopedic disorders of the knee in hemophilia: A current concept review

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Abstract

The knee is frequently affected by severe orthopedic changes known as hemophilic arthropathy (HA) in patients with deficiency of coagulation factor Ⅷ or Ⅸ and thus this manuscript seeks to present a current perspective of the role of the orthopedic surgeon in the management of these problems. Lifelong factor replacement therapy (FRT) is optimal to prevent HA, however adherence to this regerous treatment is challenging leading to breakthrough bleeding. In patients with chronic hemophilic synovitis, the prelude to HA, radiosynovectomy (RS) is the optimal to ameliorate bleeding. Surgery in people with hemophilia (PWH) is associated with a high risk of bleeding and infection, and must be performed with FRT. A coordinated effort including orthopedic surgeons, hematologists, physical medicine and rehabilitation physicians, physiotherapists and other team members is key to optimal outcomes. Ideally, orthopedic procedures should be performed in specialized hospitals with experienced teams. Until we are able to prevent orthopedic problems of the knee in PWH will have to continue performing orthopedic procedures (arthrocentesis, RS, arthroscopic synovectomy, hamstring release, arthroscopic debridement, alignment osteotomy, and total knee arthroplasty). By using the aforementioned procedures, the quality of life of PWH will be improved.

Key words: Hemophilia; Knee; Orthopedic problems; Prevention; Surgical treatment

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Core tip: Hemophilia is an inherited bleeding disorder due to deficiency of factor Ⅷ (hemophilia A) or factor Ⅸ (hemophilia B) resulting in insufficient thrombin generation leading to recurrent intra-articular hemorrhages (hemarthroses). Prevention of hemarthroses with intravenous infusions of the deficient protein from infancy to adulthood (primary prophylaxis) should be considered to achieve optimal outcomes. If factor replacement therapy (FRT) is insufficient, or if patients are not adherent to the prescribed regimen, recurrent hemarthroses results in chondrocyte apoptosis (cartilage

degeneration) and hypertrophy of the synovium (synovitis). Many surgical interventions are available for the knee joint. For example, to treat synovitis recalcitrant to FRT, there are two primary orthopedic modalities: Radiosynovectomy and arthroscopic synovectomy. This article reviews the pathogenesis, diagnosis and treatment of hemophilic arthropathy of the knee.

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INTRODUCTION

Hemophilic arthropathy (HA) in one or more joints, mainly ankles, elbows and knees affects about 90% of people with hemophilia (PWH) by 20-30 years of age (Figure 1). Recurrent bleeding into joints (hemarthroses) results in progressive, proliferative and degenerative articular changes. To prevent these complications, regular factor replacement therapy (FRT) with the deficient protein from an early age (primary prophylaxis) is the key to prevent synovitis and HA. However, despite primary prophylaxis, some PWH suffer from clinical bleeding due to an insufficient dosing regimen or non-adherence while others may experience subclinical joint bleeding. Although the pathogenesis of HA is not fully understood[1], it is generally assumed that primary prophylaxis prevents bleeding and HA[2,3].

There are multiple strategies for implementing primary prophylaxis in young children with severe hemophilia including once-weekly injections which has the advantage of avoiding the implantation of a central venous access device in very young children. Unfortunately, this regimen fails to prevent joint bleeding in all but a few children and most develop HA[4].

Prophylaxis must begin early in life because even infrequent or a short durations of blood in contact with cartilage can cause chondrocyte apoptosis that can eventually lead to HA. Once developed, HA can be addressed with basic surgical procedures including radiosynovectomy (RS), chemical synovectomy (CS), arthroscopic synovectomy (AS), arthroscopic joint debridement and total knee arthroplasty (TKA)[5,6].

RESEARCH

A literature review of knee disorders in patients with hemophilia was performed using MEDLINE (PubMed) and the Cochrane Library. The keywords used were "knee" and "hemophilia". The time period of the searches was from the beginning of the availability of the search engines until 31 December 2015. A total of 767 articles were found, of which 56 were selected and reviewed because they were deeply focused on the topic. The flow diagram of the study is shown in Figure 2.

PATHOGENESIS

Chronic hemophilic synovitis (CHS) and cartilage destruction are the main findings of HA, both phenomena due to severe or recurrent hemarthroses. The precise pathogenesis of CHS and HA remains poorly understood. *Ex vivo* studies with canine cartilage suggest that a 4-d duration of blood exposure produces loss of cartilage matrix[7]. Experimental studies have also demonstrated that after a major hemarthrosis the joint cavity is filled with a dense inflammatory infiltrate, and the tissues become brown-stained due to hemosiderin deposition following the breakdown of erythrocytes[8,9]. Vascular hyperplasia takes place resulting in tenous and friable vessels prone to bleed creating a viscous cycle of bleeding-vascular hyperplasia-bleeding. The articular surface becomes rugose with pannus formation and the subchondral bone becomes dysmorphic. After about one month, cartilage and bone erosions are evident.

It has been reported that the loading of the affected joint may play a role in the mechanism of cartilage degeneration in hemophilia[10]. Other authors have found that molecular changes induced by iron in the blood could explain the increase in cell proliferation in the synovial membrane (synovitis)[11]. Valentino *et al*[12] found in an experimental murine model that hemorrhage induced by a controlled, blunt trauma injury leads to causes joint inflammation, synovitis and HA.

DIAGNOSIS

The diagnosis of CHS is usually made following examination of the knee with typical signs of joint swelling and warmth but with or without painful symptoms and reductions in motion of the knee. Ultrasonography (US) can be used to demonstrate hypertrophy of the synovium and the presence of fluid[13,14]. However, validation of US for the assessment of HA has not been established yet[15-17]. Magnetic resonance imaging is the gold standard for the diagnosis of synovitis.

ORTHOPEDIC TREATMENT

CHS

Celecoxib: Rattray *et al*[18] reported that celecoxib is effective in treating hemophilic synovitis, although the mechanism for this effect remains to be determined and these findings require controlled trials to be confirmed.

RS: RS is the optimal choice for treatment of patients with CHS, even in patients with anti-factor antibodies (inhibitors)[19-23]. The current recommendation is to use Yttrium-90 for the knees and Rhenium-186 for elbows and ankles and is supported by more than 40-years of experience with RS by the authors, who believe that the procedure is safe, easy to perform and economical technique for the management of CHS.

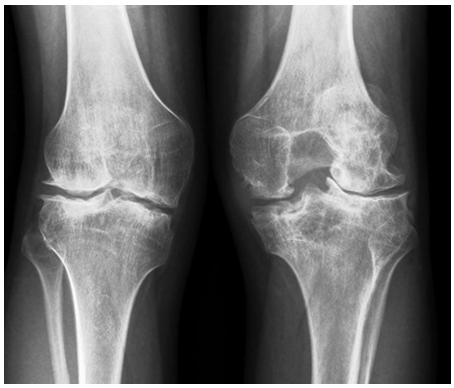

Figure 1 Severe bilateral hemophilic arthropathy of the knee in a 37-year-old male.

CS: Many chemical agents have been proposed to scar the synovium of patients with CHS including oral D-penicillamine[24]. A short-term period (3-6 mo) of treatment at a dose of 5-10 mg/kg per day for children and less than 750 mg/d for adults (one hour before breakfast) was recommended. The efficacy of this treatment needs further clinical trial data before it will gain widespread use. Oral D-penicillamine may be especially useful in patients with inhibitors. Another method to perform CS is by means of intra-articular injections of rifampicin[25] or oxytetraycline[26]. Alternative, RS is a favorable alternative to oral D-penicillamine and to rifampicin or oxytetracycline for synovectomy, because its efficacy has been proven over the last 40 years[27].

AS: The goal of AS is to reduce the number of hemarthroses in order to maintain the range of motion of the knee joint. However, AS cannot prevent joint degeneration[28-32].

Advanced HA

Open and arthroscopic debridement: Both open and arthroscopic debridement with synovectomy has been used in PWH between 20 and 40 years of age, with improvement in pain lasting several years, delaying the need of a TKA[33-35].

Hamstring release: Fixed knee flexion contracture is a common complication in PWH and hamstring tenotomy in association with posterior capsulotomy may be used to improve ambulation by reducing the contraction[36,37].

External fixation for flexion contracture: More drastic measures have also been used to reduce flexion contractures. For example, Kiely *et al*[38] reported the case of a 13-year-old boy with hemophilia who underwent Ilizarov external fixator with improvement of his knee flexion contracture. In this case, progressive extension reduced the contracture from 50 to 5 degrees.

Osteotomies around the knee: Malalignment of the lower limb is common in hemophilia patients and osteotomy around the knee (proximal tibia, distal femur) has resulted in improvements in gait and reduction in painful symptoms[39-42].

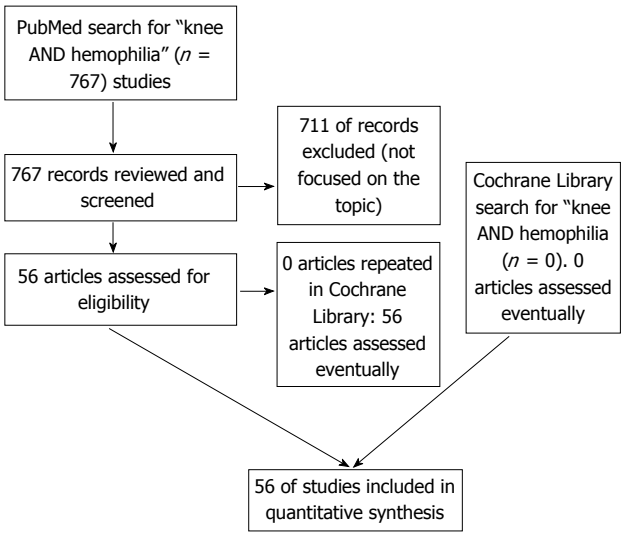

Figure 2 Flow chart of our search strategy.

TKA: Unfortunately, many patients with knee HA continue to deteriorate resulting in life-altering knee pain. For these individuals, TKA is the treatment of choice and has resulted in dramatic improvements in patients with severe HA[43-49]. Therefore, TKA is an excellent option for the treatment of advanced HA of the knee (Figure 3). However the procedure is not without risk as the rate of infection after TKA is 7% on average.

HEMATOLOGICAL PERIOPERATIVE TREATMENT

In major orthopedic procedures the preoperative levels of the deficient factor should be maintained at 80%-100%. In the postoperative period factor level must be over 50% in the two weeks and 30% later on, at least until wound healing (removal of staples)[50,51]. Continuous infusion of the deficient factor is better than bolus infusion[52,53] however mechanical malfunction of the venous line and pump must be guarded against. In patients with inhibitors there are two potential hematological treatments: Recombinant factor Ⅶ activated or Factor Eight Inhibitor Bypassing Agent[54-57].

CONCLUSION

The best treatment for PWH is primary prophylaxis replacing the deficient clotting factor with early institution of regular injections of concentrates of factor Ⅷ or Ⅸ. In this way, not only is bleeding into the joints prevented but also the development of synovitis and articular degeneration (HA). For CHS recalcitrant to aggressive factor replacement, RS must be considered the first option and alternatively, AS. Surgery in PWH has a high

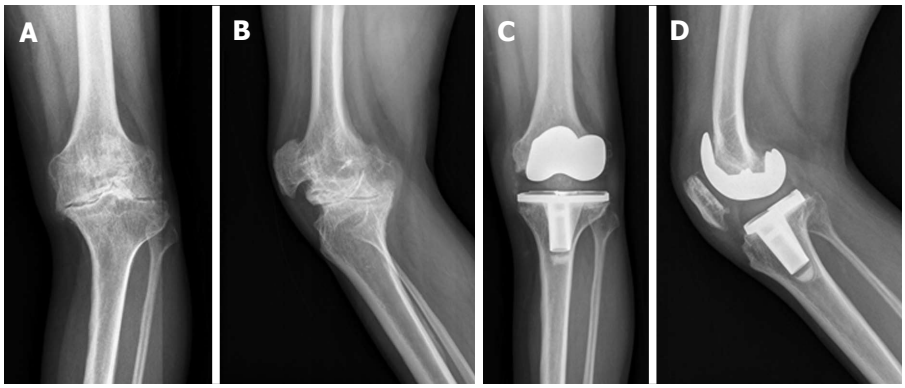

Figure 3 Severe painful hemophilic arthropathy of the left knee in a 41-year-old male. A cemented total knee arthroplasty (NexGen, Zimmer, United States) was performed with a satisfactory result: A: Anteroposterior preoperative radiograph; B: Lateral preoperative view; C: Anteroposterior radiograph 5 years later; D: Lateral view at 5 years. The quality of life of this patient improved significantly.

risk of bleeding and infection. This kind of surgery must be performed with FRT in a specialized center. This way we will improve the quality of life of PWH minimizing the risk of complications.

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ORIGINAL ARTICLE

Retrospective Study

Joint arthroplasty Perioperative Surgical Home: Impact of patient characteristics on postoperative outcomes

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Data sharing statement: All technical data is available from the corresponding author at schwarzk@gmail.com. Consent was not obtained for data sharing but the presented data is anonymized and the risk of identification is low.

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Abstract

AIM: To determine the impact of different characteristics on postoperative outcomes for patients in a joint arthroplasty Perioperative Surgical Home (PSH) program.

METHODS: A retrospective review was performed for patients enrolled in a joint arthroplasty PSH program who had undergone primary total hip arthroplasty (THA) and total knee arthroplasty (TKA). Patients were preoperatively stratified based on specific procedure performed, age, gender, body mass index (BMI), American Society of Anesthesiologists Physical Classification System (ASA) score, and Charleston Comorbidity Index (CCI) score. The primary outcome criterion was hospital length of stay (LOS). Secondary criteria including operative room (OR) duration, trans-

fusion rate, Post-Anesthesia Care Unit (PACU) stay, readmission rate, post-operative complications, and discharge disposition. For each outcome, the predictor variables were entered into a generalized linear model with appropriate response and assessed for predictive relationship to the dependent variable. Significance level was set to 0.05.

RESULTS: A total of 337 patients, 200 in the TKA cohort and 137 in the THA cohort, were eligible for the study. Nearly two-third of patients were female. Patient age averaged 64 years and preoperative BMI averaged 29 kg/m^2. The majority of patients were ASA score Ⅲ and CCI score 0. After analysis, ASA score was the only variable predictive for LOS (P = 0.0011) and each increase in ASA score above 2 increased LOS by approximately 0.5 d. ASA score was also the only variable predictive for readmission rate (P = 0.0332). BMI was the only variable predictive for PACU duration (P = 0.0136). Specific procedure performed, age, gender, and CCI score were not predictive for any of the outcome criteria. OR duration, transfusion rate, post-operative complications or discharge disposition were not significantly associated with any of the predictor variables.

CONCLUSION: The joint arthroplasty PSH model reduces postoperative outcome variability for patients with different preoperative characteristics and medical comorbidities.

Key words: Perioperative Surgical Home; Arthroplasty; Length of stay; American Society of Anesthesiologists Physical Classification System; Body mass index

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Core tip: The Perioperative Surgical Home (PSH) model is designed to improve healthcare delivery and reduce medical costs. In this study, patients in a joint arthroplasty PSH program were stratified based on preoperative characteristics and comorbidities to determine if these variables would impact postoperative results. Our results suggest that a joint arthroplasty PSH program may improve postoperative consistency and limit the influence of different patient attributes on surgical outcome. Arthroplasty patients with preoperative characteristics traditionally considered risk factors for negative outcomes, such as a high body mass index or an elderly age, may benefit from enrollment in a PSH program.

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INTRODUCTION

The relative increase in the elderly population, combined with changing indications for younger patients, is predicted to result in a growing number of patients undergoing total joint arthroplasty (TJA)[1-3]. This will likely result in a diverse surgical population, with different medical comorbidities and characteristics, which can potentially lead to equally variable results. Standardizing and streamlining the operative experience and minimizing procedural and patient variables will thus be essential to ensure optimal and predictable outcomes.

The Perioperative Surgical Home (PSH) has been promoted as a patient-centered model to improve health, healthcare delivery, and reduce medical costs[4-6]. A multidisciplinary team led by the primary surgeon and anesthesiologist engages with the patient, starting from the moment the decision for surgery is made all the way through to the post-operative 30-d recovery phase, to yield the best possible results and optimize value for both the patient and the healthcare system. PSH is ideally designed to enhance the perioperative experience, regardless of preoperative patient conditions, and has been implemented in different patient populations with beneficial results[7].

The purpose of this study was to examine the results of a TJA PSH protocol designed and adopted at our institution. Preoperative stratification and postoperative outcomes for patients undergoing primary total knee (TKA) and primary total hip (THA) arthroplasty were analyzed to determine the effects of PSH. Our hypothesis was that the joint arthroplasty PSH will lead to equivalent or improved perioperative outcomes regardless of our patients' preoperative comorbidity burden.

MATERIALS AND METHODS

After institutional review board approval was obtained, a retrospective review was performed of joint arthroplasty PSH patients undergoing elective primary TKA and THA at our institution from October 2012 through February 2015. The structure of the PSH protocol is detailed in Figure 1. All surgeries were performed by the senior author. Exclusion criteria included revision, bilateral, and acute post-traumatic arthroplasty. During surgery, all TKA patients were supine and underwent a medial parapatellar approach with the use of a tourniquet, while THA patients were lateral decubitus and underwent either a posterolateral or modified lateral surgical approach.

Patient charts were pulled from the PSH data mart for analysis. Preoperative variables that were stratified included: Specific procedure, age, gender, body mass index (BMI), Charleston Comorbidity Index (CCI), and American Society of Anesthesiologists Physical Classification System score (ASA). The primary outcome criteria measured was length of stay (LOS); secondary outcomes included operating room (OR) duration, trans-

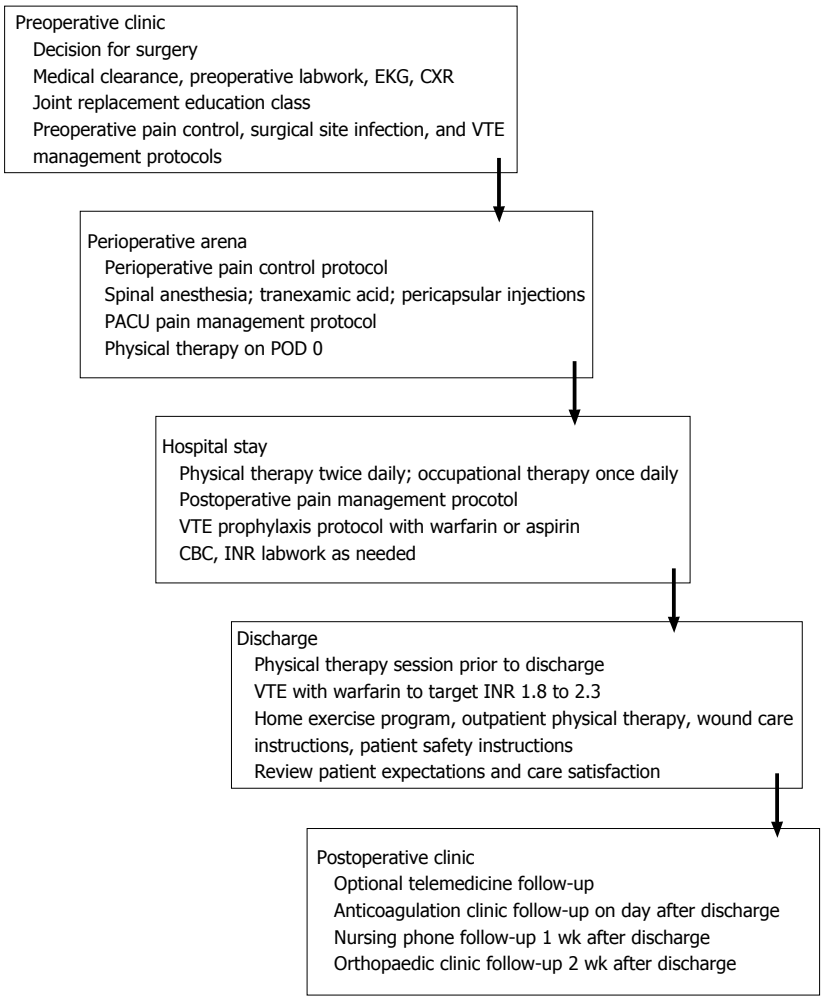

Figure 1 Total joint arthroplasty Perioperative Surgical Home protocol. PACU: Post-anesthesia care unit; EKG: Electrocardiogram; CXR: Chest X-ray; VTE: Venous thromboembolism; POD: Postoperative day; CBC: Complete blood count.

fusion rate, Post-Anesthesia Care Unit (PACU) stay, readmission rate, post-operative complications, and discharge disposition up to 30-d post-surgery.

Statistical analysis

For the primary and secondary outcomes, the predictor variables were entered into a generalized linear model with appropriate response (Linear for scalar measures, Gamma for counts or time, logit for binary outcomes like readmissions) and assessed for predictive relationship to the dependent variable. Significance level was set to 0.01 to correct for multiple comparisons. Demographics and variable summaries were presented as mean ± SD, or as percentage for binary outcomes. Statistics were performed with Microsoft Excel (Microsoft, Redmond, WA); SPSS (IBM, Armonk NY), and R (R-Project, https://www.r-project.org/).

RESULTS

Our cohort included 337 patients, 200 undergoing TKA and 137 undergoing THA. The average age was slightly over 60 years of age and almost two-thirds of patients were female. The most common preoperative medical comorbidity was hypertension, while the majority of patients were rated as ASA Ⅲ and CCI 0 when evaluating for overall medical condition. Complete patient demographics are shown in Table 1. The average total OR time was slightly over three hours and the average PACU stay was slightly over two hours. The average hospital length of stay was two and a half days. The rate of hospital readmission was minimal. Complete surgical outcomes are shown in Table 2.

With regards to the primary outcome, age, BMI, and ASA score were all predictive of LOS. Specific procedure performed, gender, and CCI scores were non-significant. ASA score was strongly predictive of LOS (P = 0.0011) as shown in Figure 2; on average each increase in ASA score above 2 increased LOS by 0.5 d. Age was only weakly predictive (P = 0.0021), with older patients having a slightly shorter LOS. Similarly, BMI was weakly predictive (P = 0.0003), with higher BMI patients having slightly shorter LOS.

With regards to secondary outcomes, ASA score was the only variable predictive of readmission rate (P = 0.0332). With a 0.6% readmission rate, however, the power for this outcome was low. BMI was the only variable predictive of increased PACU duration (P =

Table 1 Patient demographics and comorbidities

Number	337
Age (yr)	63.7 ± 13.8
Gender (M/F)	123/214
Procedure (THA/TKA)	137/200
BMI (kg/m^2)	29.4 ± 6.2
Congestive heart failure	6 (1.8%)
Chronic obstructive pulmonary disease	25 (7.4%)
Diabetes mellitus	59 (17.5%)
Hypertension	198 (58.8%)
History of myocardial infarction	17 (5.0%)
American Society of Anesthesiologist score	Ⅰ-0 (0.0%)
	Ⅱ-67 (19.9%)
	Ⅲ-255 (75.7%)
	Ⅳ-15 (4.5%)
Charlson Comorbidity Index score	0-226 (67.1%)
	1-85 (25.2%)
	2-24 (7.1%)
	6-2 (0.6%)

THA: Total hip arthroplasty; TKA: Total knee arthroplasty; BMI: Body mass index; M: Male; F: Female.

Table 2 Surgical outcomes

OR duration (min)	189 ± 60
PACU duration (min)	138 ± 80
Transfusion rate	32 (9.5%)
Length of stay (d)	2.5 ± 0.8
Severe postoperative nausea and vomiting	15 (4.5%)
Emergency department visits	7 (2.1%)
Readmissions	2 (0.6%)

PACU: Post-anesthesia care unit; OR: Operative room.

0.0136), with higher BMI leading to slightly longer PACU stay. Specific procedure performed, age, gender, and CCI score were not predictive for any of the secondary outcome criteria. OR duration, transfusion rate, post-operative complications or discharge disposition were not significantly associated with any of the predictor variables.

DISCUSSION

TKA and THA are common orthopaedic procedures that provide reliable and beneficial outcomes for the majority of patients[8,9]. However, despite advancements in surgical implants, technique, and management, a minority of patients continue to do comparatively poorly[10,11]. The expected significant increase in the patient population eligible for TJA will only increase the overall number of patients that have suboptimal outcomes. The goal of this study was to examine if TJA patients, managed under a new surgical home care model, perioperative outcomes were equivalent or better as compared to national standards.

The PSH has been endorsed by the American Society of Anesthesiologists as a model to decrease the variability in perioperative care[4]. PSH starts in the office, where immediately after a decision for surgery is made,

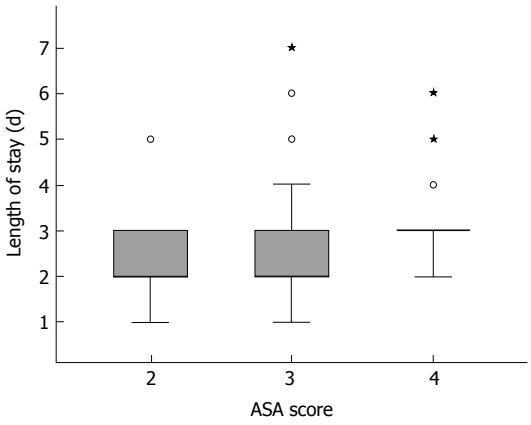

Figure 2 Box plots showing American Society of Anesthesiologists score was strongly predictive of length of stay (P = 0.0011) as shown in the figure; on average each increase in American Society of Anesthesiologists score above 2 increased length of stay by 0.5 d.

both surgical and anesthesiology teams are in constant communication with the patient. Perioperative factors such as surgical technique, anesthetic delivery, pain control, and discharge disposition are addressed to help formulate an operative plan and set expectations. During surgery, perioperative variables are minimized due to consistent protocol based surgical and anesthesiology performance; potential pitfalls are avoided by adhering to the operative plan and perioperative pathways and deviating only when necessary. After surgery, dedicated inpatient ancillary staff, including nurses and therapists, assist the surgical and anesthesiology teams to provide a smooth transition to discharge. Patients follow-up with the surgical and anesthesiology teams to ensure postoperative continuity of care. By having a patient-centered team assuring continuity of care throughout the surgical period and applying evidence-based medicine in a consistent and standardized manner, PSH is designed to minimize errors, reduce unnecessary costs, and improve patient outcomes. Studies examining the benefits of PSH are currently limited, likely due to only a recent increase in popularity. However, PSH has been implemented in cardiac and vascular patients[12] as well as in a Veterans Affairs population[13] with success, and results are expected to be forthcoming as more institutions adopt the PSH model.

In the current orthopaedic literature, only 2 significant studies have been published analyzing patients in a PSH model. Boraiah *et al*[14] recently published a study examining the utility of a scoring system, the Readmission Risk Assessment Tool, for TJA patients in their PSH model and noted that preoperative patient stratification could predict readmission rates. However, the benefits of PSH on patient outcomes were not directly examined. The results of PSH implementation have recently been published after adoption of a TJA protocol at our institution, with postoperative outcome measures comparable to national benchmarks[6]. However, this study did not stratify patients preoperatively to determine if the outcomes were due to PSH or if there was an

inherent selection bias that played a role. The current study is a follow-up to that first initial analysis to examine if the benefits of the PSH model could be isolated and specified, and to predict if similar outcomes could be achieved among patients with a differing preoperative comorbidity burden.

Preoperative stratification took into account different variables, all of which have been examined previously in the literature. An increased patient age has been shown to result in higher hospital LOS[15-17], readmission rates[15,18-20], increased complication rate[16,21,22], and disposition to an extended care facility[16]. Interestingly, a relatively young age at time of surgery has also been shown to increase readmission rates[11,20]. Male gender resulted in a higher readmission rate in most studies[11,19,23,24] while female gender was the predictor of readmission in another[25], and associated with a longer LOS[26]. Male gender also predicted a higher complication rate[24]. Obesity resulted in a longer hospital LOS[17,27,28], readmission rate[19,20,23,27], and complication rate[21,22,28]. An underweight status has also been shown to increase the rate of readmission[20]. A higher ASA score predicted a longer LOS[26], higher rate of readmission[23,25,29], and complication rate[29]. A higher CCI score predicted higher rate of readmission[30] and a higher complication rate[31].

In the current study, the influence of preoperative variables appeared to be minimized as patients underwent TJA in a PSH care model. As contrasted to the previously mentioned studies, patient gender, procedure type, and CCI score did not have any significant correlation with peri-operative outcome criteria, including LOS, PACU duration, discharge disposition, complication rate, and readmission rate. This does not imply that these variables do not play a role in patient outcomes. Rather, it suggests that within a PSH care model, the effects of these variables on the outcomes in TJA patients are reduced. This is likely due to standardization of the entire continuum of perioperative care that includes close follow-up of patients by a dedicated PSH team, and incorporation of evidence-based clinical pathways. These processes help reduce the variability in the delivery and quality of care typically found within a traditional care model. The effect of age was also diminished. Similarly, preoperative BMI also had a diminished effect with outcome criteria, aside from PACU duration.

The effects of both age and BMI on LOS, while very weak, were the opposite of what has been previously reported in other studies (both increasing age and BMI led to marginally but statistically significant shorter LOS). We hypothesize that this may be because younger, thinner patients who are having total joint replacements are more likely to have other physical or social factors contributing to their need for replacement which may contribute to longer LOS (for example narcotic dependence), as opposed to older or heavier patients who are more likely to have uncomplicated primary osteoarthritis joint degeneration.

Higher ASA scores were strongly predictive for an increase in hospital LOS, with each point increase above 2 resulting in an increased stay of 0.5 d. Similarly, higher ASA scores were strongly predictive for patient readmission rates. There was not a strong correlation between ASA scores and other outcome criteria, which is surprising because a large number of readmissions are due to post-operative complications. Also surprising is that CCI scoring did not result in a similar correlation to LOS and readmission rates. Like the ASA model, CCI is designed to evaluate overall patient comorbidity and as such it would be expected that stratification of both would lead to comparable outcomes. It is possible that the ASA score intrinsically includes the information contained in CCI such that using both in the same model becomes redundant. The ASA score is also more discriminating between the full range of mild to severe comorbidity, whereas the CCI tends to discriminate better between moderate and severe comorbidity only.

There were several limitations to the study that may have affected the results. The study was retrospective in nature, which may have led to inadvertent biases. However, preoperative exclusion criteria and stratification was stringently designed in order to limit any bias. The surgeries were all performed by one surgeon, which may have skewed outcomes but also limited surgical variation. This was supported by using standard surgical approaches and the same implant system for all patients. Although samples sizes were not small, a larger patient population would have increased the power of the study. Patient outcomes were included only up to the 30-d postoperative period and changes afterwards were not incorporated into outcome analysis. Finally, patients readmitted elsewhere would not have been captured within our study, although such a limitation is not unique to our study. Our joint replacement PSH was designed to encompass perioperative patient care up to 30-d after surgery; as such we felt it appropriate to end data collection at this time point.

The PSH is a patient-centered care model designed to provide coordinated care through shared decision-making and standardization using evidence-based medicine. Through physician-led multidisciplinary care, this care model aims to add value and help achieve Institute for Healthcare's Triple Aim of improving patient-care experience and population health at a reduced cost. Our study suggests that patient factors, which have historically influenced TJA results, such as age, gender, CCI scores, and BMI, may be minimized. To the best of our knowledge, this is the first study examining the outcomes of TJA patients in a PSH model. Further prospective studies are needed in order to support our results.

COMMENTS

Background

Perioperative Surgical Home (PSH) is a patient-centered program designed to improve clinical efficiency, optimize surgical results, and decrease the financial burden on healthcare. The increasing number of patients who will undergo total joint arthroplasty (TJA) makes this subset of the medical population ideal for enrollment in a PSH protocol.

Research frontiers

PSH has been used selectively with beneficial results in different patient populations in the last decade. Optimizing patient outcome after TJA has been a focus of analysis since these surgeries were invented and recent studies have highlighted different factors, such as age, weight, gender, and procedure performed, that have an influence on outcomes.

Innovations and breakthroughs

To our knowledge, this study is the first of its kind stratifying TJA PSH patients preoperatively based on different characteristics and comorbidities and identifying associations with postoperative outcomes. The results suggest that a majority of patients with different preoperative variables may have equivalent outcomes due to perioperative optimization in a PSH protocol.

Applications

The study shows the efficacy and safety for TJA patients enrolled in a PSH protocol and suggests that preoperative differences may be minimized through this patient-centered model.

Terminology

PSH: Patient-centered multidisciplinary team led by the lead surgeon and anesthesiologist.

Peer-review

The manuscript is well written and the use of English is good.

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ORIGINAL ARTICLE

Observational Study

Quantifying prosthetic gait deviation using simple outcome measures

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Abstract

AIM: To develop a subset of simple outcome measures to quantify prosthetic gait deviation without needing three-dimensional gait analysis (3DGA).

METHODS: Eight unilateral, transfemoral amputees and 12 unilateral, transtibial amputees were recruited. Twenty-eight able-bodied controls were recruited. All participants underwent 3DGA, the timed-up-and-go test and the six-minute walk test (6MWT). The lower-limb amputees also completed the Prosthesis Evaluation Questionnaire. Results from 3DGA were summarised using the gait deviation index (GDI), which was subsequently regressed, using stepwise regression, against the other measures.

RESULTS: Step-length (SL), self-selected walking speed (SSWS) and the distance walked during the 6MWT (6MWD) were significantly correlated with GDI. The 6MWD was the strongest, single predictor of the GDI, followed by SL and SSWS. The predictive ability of the regression equations were improved following inclusion of self-report data related to mobility and prosthetic utility.

CONCLUSION: This study offers a practicable alternative to quantifying kinematic deviation without the need to conduct complete 3DGA.

Key words: Gait deviation; Prosthesis; Amputation;

Functional outcomes; Regression; Receiver operating characteristic curve

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Core tip: The number of available outcome measures and multi-dimensionality of functional status complicate appropriate selection. This study assists clinicians in choosing apposite measures by exploring the relationship between various measures and demonstrating that often expensive and unavailable measures can be estimated using a combination of readily available self-report and performance-based measures.

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INTRODUCTION

The multitude of available outcome measures and the multi-dimensional concept of functional status complicate the selection of appropriate outcome measures for use with lower-limb amputees (LLAs).

Numerous outcome measures are used with LLAs[1], and are generally classified as either self-report or performance-based. Self-report measures have been used in abundance with lower limb amputees and include the generic short-form 36[2] and amputee-specific prosthesis evaluation questionnaire (PEQ)[3]. Ease of administration make self-report measures attractive clinical tools, but answers are highly subjective and affected by a multitude of factors[4]. But, they provide a patient perspective, which in itself is an important part of functional status. Self-report measures also involve the patient in the decision-making process, which has been associated with improved patient outcome[5]. More objective than self-report measures are performance-based measures, which assess the ability to perform everyday tasks. These can be divided into clinical- or laboratory-based and real-world measures[6]. In contrast to self-report and real-world measures (for example, step-counters and accelerometers), which account for real-world experiences over a period of time, laboratory-based measures assess performance on defined tasks in an artificial environment and within a limited time period. Examples of laboratory-based measures used with LLAs include walking tests, such as the six-minute walk test and tests involving sit-to-stand and turning, such as the timed-up-and-go test (TUGT)[1]. Three-dimensional gait analysis (3DGA) is another such example. It is considered the assessment of choice for gait because it measures gait dynamics in detail with a high level of reliability[7,8]. Its low level of use with the LLA population has been attributed to its financial, personnel and time cost[9].

The correlation between outcome measures, including 3DGA, remains relatively unknown, particularly within the LLA population. Research into older people found that gait speed predicted self-perceived physical functioning[10], but the relationships between self-administered, interview-administered and performance-based measures was inconsistent and the strength of correlation ranged from weak to moderate[11,12]. Amongst diabetics and LLAs, research has shown that self-reported activity levels do not correlate with performance-based measures[6,13]. Relationships between 3DGA and other outcome measures have been investigated in the context of paediatric cerebral palsy, where gait analysis has demonstrated moderate to strong correlation with measures derived from observational gait analysis[14-17] and parent-report measures[18,19]. Gait velocity however was representative of functional capacity in children with cerebral palsy[20]. Archer *et al*[21] investigated the relationship between clinical factors, such as range of motion and strength, and observed gait deviation following lower extremity trauma, however excluded LLAs. Establishing the correlation between these outcome measures is important in order to: Assist in the development of appropriate research methods; assist in the interpretation of research results; advocate for resources to develop assessment facilities; and, identify the most appropriate assessments for individuals and populations. This paper will help establish the utility of selected measures in predicting gait deviation and contribute to the selection in research and clinical applications of cost-effective alternatives to 3DGA for the lower limb amputee population.

The aims of this study were to examine correlations between a selection of common outcome measures used to assess gait deviation and function in individuals with LLA, and to quantify kinematic deviation using a subset of these common outcome measures. This study was designed with the premise that 3DGA is the "gold standard" for measuring gait pathology, and it was hypothesised that simple outcome measures can be used to quantify overall kinematic deviation.

MATERIALS AND METHODS

Participants

Ethics approval was obtained (University of New South Wales Human Research Ethics Committee, UNSW HREC 07247), and 20 unilateral LLAs and 28 able-bodied participants were recruited using direct mail to a number of support groups. Informed consent was obtained prior to participation in this study. Exclusion criteria for the LLA group included multiple amputations, upper limb amputations, amputations at a level other than transfemoral or transtibial, less than six months consistent prosthesis use, use of walking aids other than walking sticks, or cognitive disabilities. Able-bodied participants were included to create a normative

database similar in age and body mass index to the LLA group. The exclusion criterion for the able-bodied participants was known gait pathology. Individuals aged less than 18 years were excluded.

Procedure

Participants underwent 3DGA wearing their everyday prosthesis (with shoes) and using regular walking aids (if normally used) at UNSW's Gait and Biomechanics Laboratory using an eight-camera Vicon 612 motion capture system (Oxford Metrics). Initial contact was detected by one of two embedded force plates (Kistler) located at the midpoint of the 15-m walkway. Markers were placed according to a modified Helen Hayes marker set[22] with additional markers placed over the anterior portion of the pelvis to address anterior pelvic marker dropout during the gait cycle[23]. Participants were recorded at a comfortable self-selected walking speed (SSWS), and at least six successful trials were collected for each limb. Success was defined by a complete foot strike of at least one of the in-ground force plates.

Following 3DGA, participants completed two performance-based tests - TUGT and the 6MWT as described in the literature[24,25]. Both measures have demonstrated validity for use with LLAs[26,27]. Practices were permitted for the TUGT, which was conducted three times. Participants completed a self-report measure, the PEQ, in rest periods throughout the test protocol. Able-bodied participants underwent the same protocol, but did not complete the PEQ.

Statistical analysis

Lower limb kinematics and temporospatial data were calculated using the Plug-In-Gait model (Vicon, Oxford Metrics). Step-length (SL) and SSWS were normalised against average leg-length for each participant. Leg-length was defined as the distance between the anterior superior iliac spine and the medial malleolus on the same side, and the arithmetic mean of the left and right leg-length formed the average leg-length value used for normalisation. The gait deviation index (GDI) was calculated using the template provided by its authors[28]. For the amputee group, the GDI was calculated for six trials per limb per participants and averaged to obtain the value used in subsequent analyses. A representative trial from the left and right limb was used from each able-bodied participant, and contributed to the normative database required for the calculation of the GDI. In doing so, the GDI distribution for the able-bodied participants has a mean value of 100, with every 10 points below equal to one standard deviation away from the mean. The average of the three TUGTs was used in further statistical analyses. The time taken to stand (t_{stand}) was derived from the TUGT. Both the summary scales and individual questions from the PEQ were utilised.

Normalcy of data was assessed using the Anderson-Darling test. Summary statistics were calculated using measures appropriate to their distribution - mean and standard deviation for normal distributions, and median and interquartile range for non-normal distributions. Analysis of variance was used to compare results between the able-bodied group, transtibial amputee group and transfemoral amputee group for normally distributed data (Table 1). Kruskal-Wallis one-way analysis of variance was used for data that did not conform to a normal distribution. A *P*-value of less than 0.05 was considered significant.

Spearman's rank correlation coefficient, ρ, was used to determine the relationships between the GDI and participant characteristics, performance-based measures and self-report measures. Strict significant criteria for the correlation coefficient were required to minimise the chance of coincidental findings, possible due to the large number of relationships investigated in this study[29]. Significance was set at $P \leqslant 0.001$, or $|\rho| \geqslant 0.70$.

Stepwise regression analyses were used to determine the major predictors of the GDI (dependent variable), with participant characteristics (as listed in Table 1 and including aetiology), performance-based measures and responses from the PEQ used as independent variables in the regression models. The alpha-to-enter and alpha-to-exclude were set to 0.2 to accommodate the small sample size[30]. Predicted R^2 values were calculated using a leave one out cross-validation protocol. Three types of regression analyses were performed for various reasons. The GDI was the dependent variable in all models.

All independent variables: A purely explorative model, including all independent variables to determine the best possible predictors of the GDI.

Omission of SL relationships: Clinical utility requires that reliance on instrumentation be minimised. Of the outcome measures adopted in this study, with the exception of the GDI, instrumentation was required only for the calculation of SL. Other measures needed little more than a stopwatch to obtain. SL relationships were omitted from the second regression analysis to minimise the need for instrumentation and consider applicability.

Forced inclusion of walking speed relationships, omission of SL relationships: Walking speed is often considered a robust measure of functional ability[1] in population groups with movement disorders. This was investigated in the final regression analysis by forcing the inclusion of walking speed relationships as independent variables.

Since frustration is known to affect self-efficacy[31], responses to self-report measures will differ between participants reporting frustration and participants reporting an absence of frustration. The PEQ contains within it questions relating to frustration. To account for differences in self-efficacy, participants were separated based upon the presence (n = 16) and absence of frustration (n = 4) as measured by the frustration

Table 1 Summary of results

Participant characteristics	Summary statistic	Transtibial	Transfemoral	Able-bodied
Number	Count	12	8	28
Number of women	Count	3	3	16
Age (yr)	Mean (SD)	61.7 (12.6)	63.3 (12.0)	60.6 (7.8)
BMI (kg/m^2)	Mean (SD)	27.3 (6.5)	25.4 (4.4)	25.6 (3.1)
Age$_{amp}$ (yr)	Mean (SD)	40.9 (19.2)	38.9 (23.0)	NA
Time (yr)	Median (IQR)	17.0 (27.3)	22.5 (38.5)	NA
Use (h/d)	Median (IQR)	15.5 (1.0)	13.0 (10.0)	NA
Performance-based outcomes				
GDI (-)[a]	Mean (SD)	81.2 (13.6)	68.8 (8.8)	NA
nSL (-)[a,b]	Mean (SD)	0.76 (0.11)	0.65 (0.10)	0.87 (0.06)
nSSWS (/s)[a,b]	Mean (SD)	1.36 (0.27)	1.01 (0.23)	1.72 (0.19)
TUGT (s)[a,b]	Median (IQR)	10.0 (2.0)	12.7 (7.5)	7.9 (1.4)
6MWD (m)[a,b]	Mean (SD)	412 (91)	295 (85)	520.3 (56.2)
Self reported outcomes				
AM (/100)	Mean (SD)	78.4 (18.5)	64.0 (19.9)	NA
AP (/100)	Mean (SD)	72.2 (14.5)	63.0 (14.2)	NA
FR (/100)	Median (IQR)	76.0 (64.4)	67.6 (59.6)	NA
PR (/100)	Median (IQR)	94.7 (15.1)	95.8 (20.9)	NA
RL (/100)	Mean (SD)	63.4 (24.3)	64.7 (25.4)	NA
SB (/100)[a]	Median (IQR)	93.6 (11.3)	80.13 (34.6)	NA
SO (/100)	Median (IQR)	70.5 (46.0)	85.3 (67.1)	NA
UT (/100)	Median (IQR)	77.9 (18.0)	68.3 (44.7)	NA
WB (/100)	Median (IQR)	86.2 (23.4)	53.8 (61.2)	NA

[a]Significant differences between transtibial and transfemoral amputees, $P \leqslant 0.05$; [b]Significant differences between able-bodied and amputee groups. BMI: Body mass index measured with prosthesis on; IQR: Inter-quartile range; nSL: Leg-length normalised average step length; nSSWS: Leg-length normalised self selected walking speed; TUGT: Timed-up-and-go test; 6MWD: Six-minute walk distance; AM: Ambulation; AP: Appearance; FR: Frustration; PR: Perceived response; RL: Residual limb health; SB: Social burden; SO: Sounds; UT: Utility; WB: Well being; NA: Not available; GDI: Gait deviation index.

questions in the PEQ [Larger studies (n = 135) by our group have shown that approximately 75% of LLAs experience some form of frustration as measured by the PEQ]. Regression analyses were performed using only participants reporting frustration. The small sample size prohibited separate analysis of the participants who were not frustrated.

Receiver operating characteristic curve

The utility of a regression equation in diagnosing presence of a gait pathology was assessed by constructing receiver operating characteristic (ROC) curves as follows. Participants were classified as either pathological or non-pathological according to their measured GDI and a chosen cut-off, GDI$_{meas,cut}$. In this study, a range of cut-off values for GDI$_{meas,cut}$ were investigated (65-95 in increments of five) because a definitive threshold for amputee gait is not yet available. They were then classified as pathological or non-pathological according to the GDI predicted by the regression equation and a range of cut-off values, GDI$_{pred,cut}$ (55-105, as determined by the GDI$_{pred}$ of each amputee participant). Finally, sensitivity and specificity were calculated for each value of GDI$_{pred,cut}$ and plotted as sensitivity against 1 - specificity. The area under the curve (AUC) was used as an overall measure of performance (AUC = 1 is perfect, AUC = 0.5 is no better than random[32]). The significance of the two-by-two classification table for a specific value of GDI$_{pred,cut}$ was assessed using Fisher's exact test.

ROC curve analyses were performed using MedCalc for Windows, version 11.4.2.0 (MedCalc Software, Mariakerke, Belgium). All other analyses, unless otherwise stated, were performed at the 0.05 significance level using Minitab Statistical Software (Version 15).

RESULTS

Participant characteristics

The participant characteristics are summarised in Table 1. The sample was predominantly male (70%) with trauma being the most common reason for amputation (65%). Other reasons for amputation included cancer (10%), infection (10%) and vascular insufficiencies (15%). Two participants with transfemoral amputation used a walking stick during testing; all other participants completed testing unaided. The participant characteristics were similar for the able-bodied group, transtibial amputee group and transfemoral amputee group (Table 1).

Outcome measures

Results for the self-report and performance-based measures are summarised in Table 1. Significant differences were present between the transfemoral and transtibial amputee groups for all performance variables. The transtibial amputee group reported values closer to able-bodied than the transfemoral amputee groups,

Table 2 Correlations with the gait deviation index, Spearman's rank correlation coefficient displayed

Parameter	Correlation coefficient, ρ
Participant characteristics	
Age	-0.13
BMI	-0.27
Age at amputation	-0.16
Time since amputation	0.14
Performance-based outcomes	
nSL_{pro}	0.73[b]
nSL_{int}	0.83[b]
nSL_{ave}	0.78[b]
nSSWS	0.7[b]
TUGT	-0.60
6MWD	0.74[b]
Self-report measures	
Ambulation	0.44
Appearance	0.22
Frustration	-0.14
Perceived response	0.02
Residual limb health	-0.22
Social burden	0.37
Sounds	-0.01
Utility	0.33
Well-being	0.20

[b]$P \leqslant 0.001$, indicates significant relationships. BMI: Body mass index measured with prosthesis on; nSL: Leg-length normalised average step length; nSSWS: Leg-length normalised self selected walking speed; TUGT: Timed-up-and-go test; 6MWD: Six-minute walk distance.

but significant differences existed between the amputee groups and able-bodied participants. The transfemoral and transtibial amputees were similar for all scales of the PEQ, except Social Burden, where the transfemoral amputee group reported greater feelings of burden on friends and family as a result of their amputation.

Bivariate analysis

The relationship between the GDI and participant characteristics, performance variables and scales of the PEQ are summarised in Table 2. The GDI demonstrated significant relationships with normalised average step-length, normalised self-selected walking speed (nSSWS) and the 6MWD. Significant correlations were not observed between the GDI, participant characteristics and scales from the PEQ.

Table 3 presents the correlation coefficients for the relationships between the performance-based measures used in this study. The strongest correlation was between nSSWS and 6MWD ($\rho = 0.96$), and all correlations were significant.

Multivariate analysis

The results of multivariate analysis are summarised in Table 4. The 6MWD was the strongest individual predictor of GDI [adjusted R^2 (R^2_{adj}) = 68.6, predictive R^2 (R^2_{pred}) = 60.4], despite intact limb step length producing the greatest adjusted R^2 value (R^2_{adj} = 70.9, R^2_{pred} = 56.8). The forced inclusion of SSWS produced regression equations with the lowest adjusted and

Table 3 Correlations between performance-based measures, Spearman's rank correlation coefficient displayed

	nSL_{pro}	nSL_{int}	nSL_{ave}	nSSWS	TUGT
nSL_{int}	0.87				
nSL_{ave}	0.98	0.95			
nSSWS	0.84	0.91	0.88		
TUGT	-0.70	-0.71	-0.71	-0.82	
6MWD	0.86	0.89	0.89	0.96	-0.83

All correlations significant, $P \leqslant 0.001$. nSL: Leg-length normalised average step length; nSSWS: Leg-length normalised self selected walking speed; TUGT: Timed-up-and-go test; 6MWD: Six-minute walk distance.

predicted R^2 values. The time taken to stand from a chair with arms (t_{stand}; derived from the TUGT) and mobility-related questions (particularly AM_C "Over the past four weeks, rate your ability to walk up stair when using your prosthesis", see Table 4) contributed significantly to all regression equations with at least two independent variables.

ROC curve

The equation selected for further analysis predicted GDI using 6MWD, AM_C, t_{stand} and age (R^2_{adj} = 90.2; R^2_{pred} = 86.2; Table 4). It was chosen because of its superior predictive strength and clinical applicability when compared to other regression equations (Table 4). The plot of measured GDI against predicted GDI shown in Figure 1 illustrates the concordance between measured and predicted values for participants in this study.

The resulting ROC curves for a range of measured cut-offs (65-85) are shown in Figure 2. Also in this figure are mean values and 95%CI for AUC for each of the measured cut-offs. The curves and AUC values showed that the diagnostic capability of the regression equation was not sensitive to choice of measured cut-off. Fisher's exact test of the 2 × 2 classification table gave $P < 0.05$ for all ROC curves.

DISCUSSION

This study has shown that it is possible to predict overall gait deviation, as measured by the GDI, using combinations of simple performance-based and self-report outcome measures in a sample of persons with lower-limb amputation. Of the outcome measures investigated in this study, temporospatial data were the strongest correlates of the GDI (Table 2).

The strongest correlation was observed between the intact limb SL and the GDI (Table 2). This parameter provides insight into the extent of gait asymmetry, which is considered an indication of gait pathology[33], and explains its strong correlation with the GDI. Asymmetries in prosthetic gait have been attributed to a number of factors, including lack of plantarflexion and decreased range of motion of the prosthetic ankle joint, absence of proprioception and sensory feedback, pain, and prosthetic alignment[34]. Despite good predictive abilities,

Table 4 Regression analysis; gait deviation index dependent variable

No.	R^2_{adj}	R^2_{pred}	Independent variables 1	2	3	4
All variables						
1	70.9	56.8	nSL_{int}			
2	76.1	59.6	nSL_{int}	AM_C		
3	82.6	66.5	nSL_{int}	AM_C	t_{stand}	
4	89.3	81.4	nSL_{int}	AM_C	t_{stand}	6MWD
No step-length parameters						
1	68.6	60.4	6MWD			
2	79.8	72.0	6MWD	AM_C		
3	86.1	82.7	6MWD	AM_C	t_{stand}	
4	90.2	86.2	6MWD	AM_C	t_{stand}	Age
Forced inclusion of walking speed						
1	57.4	46.4	nSSWS			
2	71.1	53.7	nSSWS	AM_C		
3	79.6	65.2	nSSWS	AM_C	t_{stand}	
4	82.1	70.7	nSSWS	AM_C	t_{stand}	UT_D[1]

[1]Not significant. Note 1: The table is organized such that the predicted gait deviation index is a function of the independent variables listed. The coefficients of the independent variables have been suppressed until the utility of these equations have been proven for use with individual patients; Note 2: Participants reporting an absence of frustration (n = 4) in the four weeks prior to testing were not included in the regression analysis. No.: Number of independent variables; R^2_{adj}: Adjusted R^2; R^2_{pred}: Predictive R^2; nSL_{int}: Leg-length normalised intact limb step-length; t_{stand}: Time to stand; AM_C: Over the past four weeks, rate your ability to walk up stairs when using your prosthesis; 6MWD: Six-minute walk distance; Age: Chronological age; nSSWS: Leg-length normalised self-selected walking speed; UT_D: Over the past four weeks, rate your comfort while standing when using your prosthesis.

these equations are not clinically practical, requiring non-standard technology for the measurement of SL.

Unlike SL, 6MWD and SSWS can be measured with relative ease in clinical contexts. SL and SSWS were mutually exclusive in regression models because of their strong correlation with one another. The 6MWD was more strongly associated with the GDI than walking speed (Table 2) most likely because it is strongly correlated with energy expenditure[35], and energy expenditure is correlated with gait deviation[36]. In this study, energy expenditure would have had only minimal impact on SSWS, because the latter was calculated over a distance of only 15 m. The inclusion of 6MWD (Table 4) in the first regression model provides further evidence that energy expenditure is better correlated than walking speed over short distances with gait deviation.

One goal of this study was to develop a set of simple tests that can be used to identify patients whose gait is sufficiently impaired to warrant intervention. The ability of a regression equation to predict measured GDI is encouraging, but an R^2_{pred} is a measure of agreement, not a measure of the performance of the equation when used as a diagnostic tool. On the other hand, the ROC curve does provide an overall measure of performance. The areas under the curve (all greater than 0.7; Figure 2), implies that this can be an effective diagnostic tool. Fisher's exact test applied to a range of measured cut-off values confirmed that that the selected regression

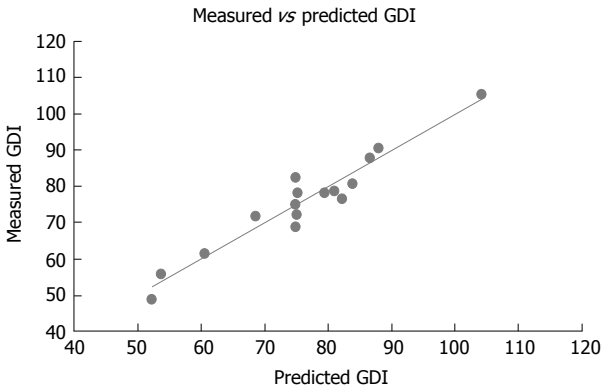


Figure 1 Measured *vs* predicted gait deviation index for selected equation, constructed using a combination of six-minute walk distance, AM_C, t_{stand} and chronological age (adjusted R^2 = 90.2; predictive R^2 = 86.2). AM_C: Over the past four weeks, rate your ability to walk up stairs when using your prosthesis; t_{stand}: Time taken to stand; GDI: Gait deviation index.

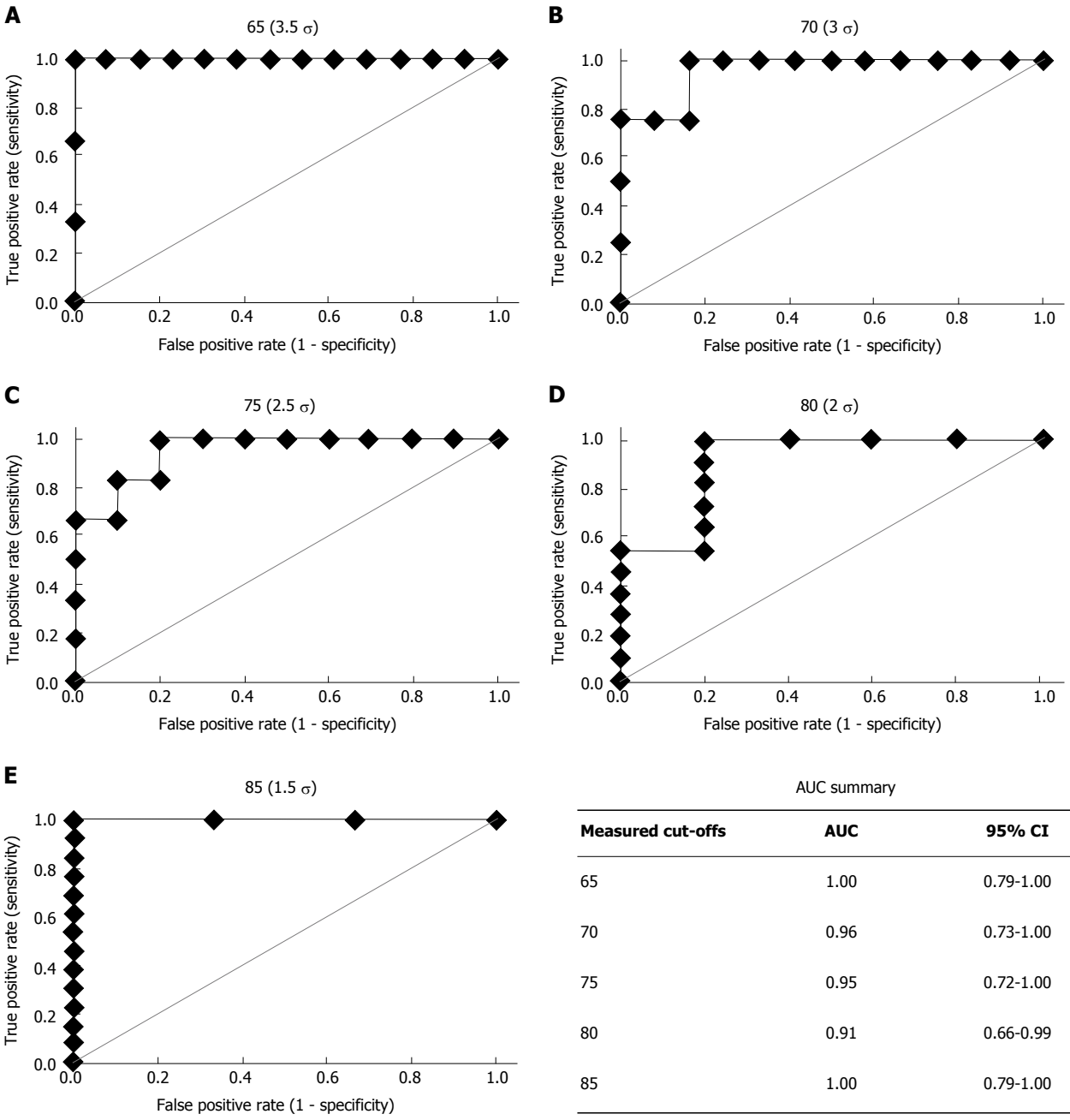
equation was better than chance, $P < 0.05$.

The results from this study indicate that using a battery of outcome measures (excluding 3DGA) in combination provides a better perspective on functional status than using single or only a few measures. This is encouraging, because it implies that low cost and more readily available outcome measures can be highly informative. For example, the effects on function and gait deviation that may arise with changes to componentry would be best assessed using a standardised battery of outcome measures rather than an ad hoc selection of single measures. The statistical analyses demonstrate that characteristics observed across a number of outcome measures may contribute collectively to the quantification of kinematic deviation. In this study, a combination of performance-based and self-report measures provided the best indication of kinematic deviation. The results from this study have shown the ideal outcome measures to assess gait deviation to be: 6MWD, t_{stand}, self-report questions addressing stair climbing and chronological age. Walking speed over longer distances provides a better indication of gait deviation than SSWS over short distances (< 15 m).

Study limitations

The sample size was small and comprised mainly traumatic amputees and experienced prosthetic users. This study did not assess test responsiveness, a necessity for clinical utility. Future work should investigate the responsiveness of the regression models either in response to rehabilitation or componentry modifications, and extend the sample to include more participants with various aetiologies, levels of amputation and prosthetic experience.

The GDI is an overall summary measure of kinematic patterns. It does not, and cannot, substitute for clinical experience and 3DGA. Rather, it provides an efficient method to communicate overall gait pathology. The GDI has demonstrated applicability for use with children with cerebral palsy[28] and adults with unilateral lower



AUC summary

Measured cut-offs	AUC	95% CI
65	1.00	0.79-1.00
70	0.96	0.73-1.00
75	0.95	0.72-1.00
80	0.91	0.66-0.99
85	1.00	0.79-1.00

Figure 2 Receiver operating characteristic curves for a range of measured cut-offs [65-85 (A-E), or 3.5-1.5 (A-E) standard deviations (σ) away from the able-bodied mean] for the predictive equation comprised of six-minute walk distance, AM_C, t_{stand} and age. Also included in the bottom right cell are mean values and 95%CIs for AUC for each of the measured cut-offs. AM_C: Over the past four weeks, rate your ability to walk up stairs when using your prosthesis; t_{stand}: Time taken to stand; AUC: Area under the curve.

limb amputation[37], making it an appropriate outcome measure for use in this study. In addition, kinetic characteristics were excluded, as were data on muscle activation patterns. Both are important measures of gait biomechanics.

Time to stand was derived from the TUGT. In lower functioning individuals there was a clear demarcation between the time to stand and the initiation of walking gait, making the measurement of the time taken to stand relatively straightforward. In contrast, the transition between the standing phased and initiation of walking was sometimes difficult to discern in high functioning individuals. Some of these participants tucked the intact limb under the chair prior to the start of the test to facilitate forward progression during the standing phase of the TUGT. Where this occurred, the time to stand was recorded as the point at which the trailing leg aligned with the stance limb. Future studies should consider using a designated sit-to-stand test, and contemplate using multiple sit-to-stand assessment such as the five-times sit-to-stand test due to their demonstrated correlation with functional status in older people[38].

This study offers a practical alternative to quantifying kinematic deviation without conducting complete 3DGA.

Performance-based measures were strong correlates of the GDI, thus rejecting the null hypothesis. It was possible to predict the GDI using a combination of performance-based measures and self-report items related to mobility and prosthetic utility. Accuracy was reasonably high for a range of designated cut-off points for the GDI. Further work is required to determine appropriate GDI cut-off points for each level of amputation.

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COMMENTS

Background

Successful prosthetic fitting is reliant on the appropriate matching of functional ability to prosthetic componentry. But, functional status is not a straightforward concept and its measurement even less so. There are numerous outcome measures currently available, and selection of appropriate measures for the assessment of functional status following lower-limb amputation is complicated. Identifying the smallest subset of appropriate measures required to encapsulate functional status could encourage the systemic and standardised use of outcomes measures throughout the rehabilitation system.

Research frontiers

In comparing the benefits of using self-report *vs* performance-based measures with older persons, it was shown that neither type of measure is superior, nor are these measures interchangeable. Instead, each assess distinct, although related constructs. Further, self-report and performance-based measures may be complementary. Studies have shown that by complementing performance-based measures with self-report measures it was possible to improve prognostic information in a sample of older person. The challenge remains to determine a suitable combination of self-report and performance-based measures to adequately assess functional status in individuals with lower-limb amputation.

Innovations and breakthroughs

This study has provided a set of simple self-report and performance-based measures to facilitate evaluation of functional status in the physical domain. In this study, functional status was best assessed using a timed walking test, a sit-to-stand assessment and an evaluation of advanced levels of mobility such as stair ambulation. These measures, in combination, enable calculation of overall kinematic deviation in prosthetic users.

Applications

The subset of outcome measures developed in this study that are able to assess kinematic deviation and functional status (in the physical domain) in individuals with lower-limb amputation require no more than a stopwatch and a self-administered questionnaire. All are relatively straightforward to implement in clinical practice. It is hoped that this research will contribute to the development of a standardised set of outcome measures for use within the lower-limb amputation population group, which in turn, will facilitate comparison between rehabilitation facilities and ultimately result in improved outcomes for individuals with lower-limb amputation.

Terminology

GDI: Gait deviation index; a one-dimensional index that summarises kinematic deviation; ROC curve: Receiver operator characteristic curve; illustrates the sensitivity and specificity of a diagnostic test.

Peer-review

This study provides a great foundation for clinicians and researchers looking for simple, low cost objective and subjective measures to approximate more complex gait analysis. Study design and statistical analysis were appropriate.

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Allograft tissue irradiation and failure rate after anterior cruciate ligament reconstruction: A systematic review

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Abstract

AIM: To evaluate whether anterior cruciate ligament (ACL) allograft irradiation is effective for sterility without compromising graft integrity and increasing failure rate.

METHODS: A literature search was conducted using PubMed, Cochrane, and Google. The following search terms were used: "Gamma irradiation AND anterior cruciate ligament AND allograft" with a return of 30 items. Filters used included: English language, years 1990-2015. There were 6 hits that were not reviewed, as there were only abstracts available. Another 5 hits were discarded, as they did not pertain to the topic of interest. There were 9 more articles that were excluded: Three studies were performed on animals and 6 studies were meta-analyses. Therefore, a total of 10 articles were applicable to review.

RESULTS: There is a delicate dosing crossover where gamma irradiation is both effective for sterility without catastrophically compromising the structural integrity of the graft. Of note, low dose irradiation is considered less than 2.0 Mrad, moderate dose is between 2.1-2.4 Mrad, and high dose is greater than or equal to 2.5 Mrad. Based upon the results of the literature search, the optimal threshold for sterilization was found to be sterilization at less than 2.2 Mrad of gamma irradiation with the important caveat of being performed at low temperatures. The graft selection process also must include thorough donor screening and testing as well as harvesting the tissue in a sterile fashion. Utilization of higher dose ($\geqslant$ 2.5 Mrad) of irradiation causes greater allograft tissue laxity that results in greater graft failure rate clinically in patients after ACL reconstruction.

CONCLUSION: Allograft ACL graft gamma irradiated

with less than 2.2 Mrad appears to be a reasonable alternative to autograft for patients above 25 years of age.

Key words: Anterior cruciate ligament reconstruction; Graft choice; Allograft; Gamma irradiation; Anterior cruciate ligament graft failure rate

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Core tip: The dose of gamma irradiation is directly correlated with increased failure rate of allograft in both *in vitro* and *in vivo* studies. Optimal gamma irradiation dose is less than 2.2 Mrad and should be performed in the setting of a low temperature.

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INTRODUCTION

Rupture of the anterior cruciate ligament (ACL) has been reported to have an incidence of 100000 to 200000 in the United States with about 400000 ACL reconstructions performed worldwide annually[1,2]. ACL reconstruction is a common procedure in an orthopaedic sports medicine practice and has been shown to have favorable return to play outcomes and preservation of knee function. Both autograft (from the patient) and allograft (cadaver) can be used for the ACL reconstruction procedure[3]. Advantages of autograft include lower graft failure rate in the young (< 25 years old) and active patient population, lower infection rate, and no risk of disease transmission or immune reaction[4-7]. Alternatively, advantages of allograft include no donor site morbidity with decreased operative time, earlier return to sports and lower postoperative pain. In the older population, allograft has comparable outcomes compared to autograft reconstruction with a decrease in patient morbidity, surgical time, and smaller incision[8]. Since using allograft tissue for ACL reconstruction (Figure 1) has proven to be successful in older patients with less physical demands, determining the most favorable processing method of the allograft tissue while minimizing catastrophic failure rates is of paramount importance.

For allograft tissue currently used, it must first undergo a detailed sequence of procedures that include medically and serologically screening donors to rule out viral contamination *via* nucleic acid testing. The Food and Drug Administration and the American Association of Tissue Banks have set industry standards for donor eligibility and tissue preparation. The donor is subjected to a rigorous physical and medical examination and an array of serological tests to detect antibodies for human immunodeficiency virus 1 and 2, hepatitis C virus, hepatitis B antigen, and syphilis[9,10]. The rigorous donor selection process serves to eliminate specific contaminants by evaluating the allograft tissue's physical composition, including uniformity in shape and density as well as its biological properties to assess the level of microbial burden and risk for disease transmission[9,11,12].

After appropriate graft donor selection has occurred, the next step is to sterilize the graft to a sterility assurance level (SAL) of 10^{-6} organism[9,11,12]. There have been numerous preparations tested to determine the optimal sterilization method including peracetic acid and ethylene oxide, but many of the methods were abandoned after they were found to have detrimental effects on the mechanical properties of the graft and/or cause an inflammatory response in recipients[13,14]. Other methods of sterilization, such as gamma irradiation, have proven to be more promising. This process uses a source emitting high-frequency electromagnetic radiation to disrupt the DNA (nucleic acids) of living organisms on the tissue to eliminate microbes and inactivating viruses[15]. The International Atomic Energy Agency has developed a set of standards that govern the proper radiation sterilization of tissue allografts. Their protocol incorporates the principles that were put in place by the International Organization for Standardization to guide the radiation sterilization process of industrially produced health care products[16].

Some authors cite that anywhere from 0.92-2.5 Mrads is needed to eliminate bacterial bioburden and fungal spores to achieve SAL of 10^{-6} on musculoskeletal allografts[2,9,12,17,18]. However, the effect of gamma irradiation on viruses is controversial. It has been reported that, in order to inactivate human immunodeficiency virus (HIV) and hepatitis, doses as high as 4.0-5.0 Mrad are required[17,18].

Unfortunately, gamma irradiation can have destructive effects on allografts by disrupting the polypeptide chain sequence and inducing minor crosslinking without interfering with collagen's normal banding pattern[19]. There have been reports of gamma irradiation of 3 Mrad causing a reduction on the mechanical properties of the allograft tissue[20]. Additionally, the temperature at which the gamma irradiation is performed is also important to consider. The mechanical destruction has been reported to be lessened when grafts were irradiated at low temperatures (*i.e.*, on dry ice) when compared to the same process performed at room temperature[17,21]. However the production of free radicals has also been cited to be a benefit of performing irradiation at higher temperature as the free radicals have anti-microbial effects[17].

The balance between sterilization of the allograft tissue without compromising the biomechanical properties, strength and functional outcomes is a topic of debate. The purpose of this systematic review article is to further explore the effect of gamma irradiation on

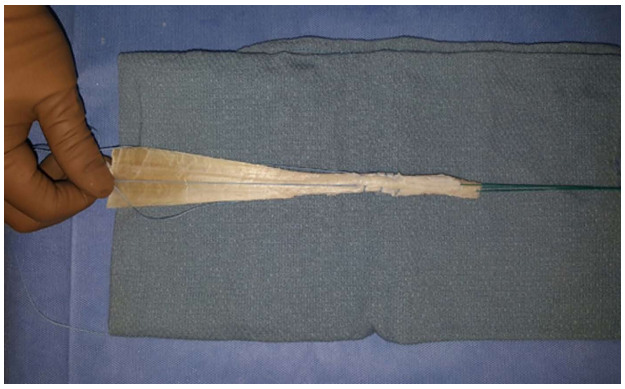

Figure 1 Non-irradiated Achilles allograft tissue. A non-irradiated Achilles tendon allograft used in an anterior cruciate ligament reconstruction procedure.

the catastrophic failure rate and functional outcomes in patients after ACL reconstruction with allograft tissue.

MATERIALS AND METHODS

Systematic review of clinical studies

A literature search was performed using PubMed, Cochrane, and Google with the following search terms with a return of 30 items: "Gamma irradiation AND anterior cruciate ligament AND allograft". Filters used included: English language, years 1990-2015. There were 6 items that were not reviewed, as there were only abstracts available. Another 5 articles were discarded, as they did not pertain to the topic of interest. There were 9 more articles that were excluded: Three studies were performed on animals and 6 studies were meta-analyses. Therefore, a total of 10 clinical articles were applicable to review (Figure 2).

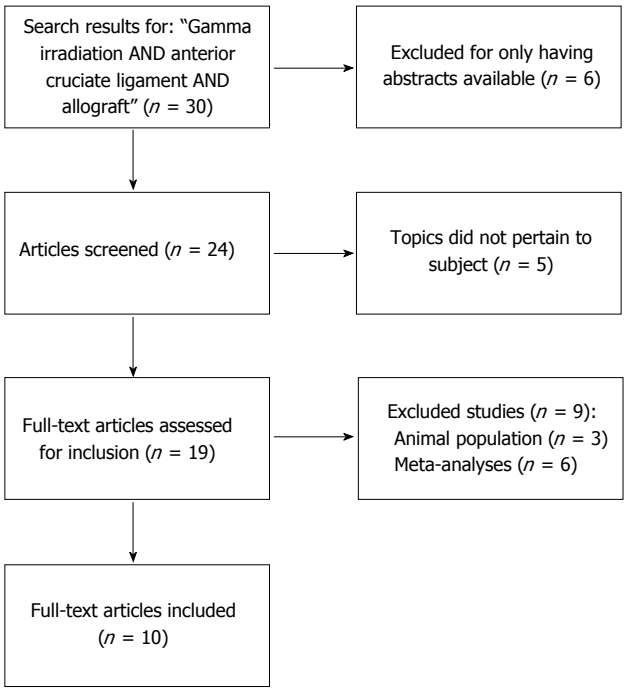

Figure 2 Systematic review of the literature with exclusion and inclusion criteria.

RESULTS

With regards to the effects from gamma irradiation, there are several articles that have extensively studied the effects of irradiation on ACL grafts (Tables 1 and 2). There were four prospective, randomized trials by the same author who attempted to answer this question. The results of these studies all demonstrated that patients who had allografts exposed to > 2.5 Mrad of irradiation had a significantly greater laxity than autograft or non-irradiated allografts; however there were no significant differences in any of these studies on the International Knee Documentation Committee (IKDC) outcome scores or range of motion[22-25]. Unfortunately, none of these studies report graft temperature during irradiation and therefore should be interpreted with caution. As stated earlier, it is important that the grafts be irradiated at low temperatures to decrease the free radical formation as to not weaken the allograft biomechanical properties[17,21].

Rappé *et al*[18] conducted a cohort study comparing non-irradiated Achilles allografts to irradiated Achilles allografts (2.5 Mrad) with the primary outcome of clinical failure (positive Lachman exam, magnetic resonance imaging, and/or side-to-side difference of 5 mm or greater on KT-1000 exam). They found that there was a significant difference in clinical failures between the irradiated (33.3%) and non-irradiated groups (2.4%; $P < 0.01$)[18]. However, there are weaknesses to their study, including a large loss of follow-up in the irradiated group (27%) compared to the non-irradiated group (7%); additionally there was no mention of the temperature at which the irradiation process was performed.

Rihn *et al*[26] compared the outcomes of bone-patella-tendon-bone (BTB) autograft to BTB allograft that underwent 2.5 Mrad of irradiation. They found no differences in the rate of return to sports or the IKDC scores; however, objectively, the allograft group had significantly more laxity on KT-1000, Lachman exam, and pivot shift clunk. However, similar to Rappé *et al*[18], this study made no mention of temperature of the graft preparation and had significant differences in the mean age of the two study groups with the allograft group having an older mean age.

The increase in laxity and failure rates was also noted in the studies by Sun *et al*[22-25] with 34% failure seen in the irradiated allograft group (2.5 Mrad), 6.4% in the autograft group and 8.8% in the nonirradiated allograft group. Sun *et al*[23] compared hamstring autograft to irradiated allograft with over 2.5 years of follow-up and reported the rate of laxity was 32% higher in the irradiated *vs* autograft group (8.3%). In addition, anterior and rotational stability also decreased significantly in the irradiated allograft group; however, the IKDC functional scores were very similar between the two groups. In a subsequent follow-up randomized controlled trial comparing irradiated to nonirradiated hamstring allograft for ACL reconstruction, Sun *et al*[24] found that allograft irradiation is responsible for increased anterior and

Table 1 ***In vivo*** **studies of non-irradiated and irradiated allograft tissue for anterior cruciate ligament reconstruction**

Ref.	Year	Type of study	Graft type	Irradiation dose	No. of patients (at final follow-up/enrolled)	Male	Female	Average age (yr)	Follow-up length	Findings	Weaknesses
Rihn *et al*[26]	2006	Retrospective	BPTB - allograft	2.5 Mrad	39	27	12	44 ± 8.4	4.2 yr	Significant difference between irradiated allograft and allograft with laxity, Lachman, and pivot shift clunk	Age difference in populations
			BPTB - autograft	None	63	43	20	25.3 ± 9.3	4.6 yr	No significant difference on range of motion, effusion, IKDC, KT-1000 when adjusted for age, IKDC physical exam rating, and return to sport	No mention of temperature when irradiation performed
Rappé *et al*[18]	2007	Cohort	Achilles - allograft	2.0-2.5 Mrad	33/45	N/A	N/A	26 (ranage 14-59)	6 mo	Significantly more clincal failures in irradiated allograft *vs* non-irradiated allograft groups with failures occuring about 9 mo earlier in irradiated group (failure of graft = 5 mm or greater on KT-1000 compared to contralateral side, positive Lachman, or magnetic resonance imaging)	Large loss of follow-up in irradiated group
			Achilles - allograft	None	42/45			27 (range 14-57)			No mention of temperature when irradiation performed
Sun *et al*[22]	2009	Prospective, randomized	BPTB - allograft	2.5 Mrad	32/33	24	8	30.1 ± 6.1	31 mo (2% lost to follow-up)	Significant difference between irradiated allograft and autograft with greater laxity on KT-2000, side to side difference on KT-2000, pivot shift grade Ⅱ or Ⅲ, anterior drawer test grade Ⅱ or Ⅲ, and Lachman test grade Ⅱ or Ⅲ	No mention of temperature when irradiation performed
			BPTB - autograft	None	33/33	24	9	29.7 ± 7.2		No significant difference on overall IKDC, range of motion, Harner's vertical jump test, Daniel's one-leg hip test, subjective IKDC, Cincinnati knee score, Lysholm score, and Tegner score	
Sun *et al*[23]	2009	Prospective, randomized	BPTB - allograft	2.5 Mrad	32	24	8	30.1 ± 6.1	31 mo (1% lost to follow-up - treatment group not mentioned)	Significant difference between irradiated allograft, non-irradiated allograft, and autograft with greater laxity on KT-2000, side to side difference on KT-2000, pivot shift grade Ⅱ or Ⅲ, anterior drawer test grade Ⅱ or Ⅲ, and Lachman test grade Ⅱ or Ⅲ	No mention of temperature when irradiation performed
			BPTB - allograft	None	34	22	12	31.8 ± 6.9			
			BPTB - autograft	None	33	24	9	29.7 ± 7.2		No significant difference on overall IKDC, range of motion, Harner's vertical jump test, Daniel's one-leg hip test, subjective IKDC, Cincinnati knee score, Lysholm score, and Tegner score	
Sun *et al*[24]	2011	Prospective, randomized	Hamstring - allograft	2.5 Mrad	31/37	24	7	30.3 ± 7.9	42.2 mo (11% lost to follow-up)	Significant difference between irradiated allograft and autograft with greater laxity on KT-2000, side to side difference on KT-2000, pivot shift grade Ⅱ or Ⅲ, anterior drawer test grade Ⅱ or Ⅲ, and Lachman test grade Ⅱ or Ⅲ	No mention of temperature when irradiation performed
			Hamstring - autograft	None	36/38	28	8	30.9 ± 8.7		No significant difference on overall IKDC, range of motion, Harner's vertical jump test, Daniel's one-leg hip test, subjective IKDC, Cincinnati knee score, Lysholm score, and Tegner score	

Sun *et al*[25]	2012	Prospective, randomized	Hamstring - allograft	2.5 Mrad	31/38	24	7	30.3 ± 7.9	42.5 mo (9.1% lost to follow-up)	Significant difference between irradiated allograft and non-irradiated allograft with greater laxity on KT-2000, side to side difference on KT-2000, pivot shift grade Ⅱ or Ⅲ, anterior drawer test grade Ⅱ or Ⅲ, and Lachman test grade Ⅱ or Ⅲ	No mention of temperature when irradiation performed
			Hamstring - allograft	None	38/39	31	7	31.7 ± 7.8		No significant difference on overall IKDC, range of motion, Harner's vertical jump test, Daniel's one-leg hip test, subjective IKDC, Cincinnati knee score, Lysholm score, and Tegner score	

IKDC: International Knee Documentation Committee; BPTB: Bone patella tendon bone.

rotational instability. Furthermore, the knees that had an ACL reconstruction done with the irradiated graft has significantly more osteoarthritis compared to the nonirradiated group.

In biomechanical testing, Roche *et al*[27] evaluated the effect on gamma irradiation (1.55 Mrad on dry ice or low temperature) with BTB and fascia lata allografts. The authors found no significant difference between the irradiated group and the non-irradiated groups when testing the grafts' tensile strength. Balsly *et al*[9] also reported on the effect of low (1.8-2.2 Mrad) *vs* high dose (2.4-2.8 Mrad) irradiation on the biomechanical properties of allograft tissue (BTB, anterior tibialis, semitendinosus, and fascia lata allografts). All irradiation processing was performed at low temperatures. For the low dose irradiation groups for all types of allografts mentioned, there were no significant difference found between the control groups and the low dose irradiation groups when the tensile strength or modulus of elasticity of the grafts was tested. For the moderate irradiation group, there was either a significant difference or a trend towards having a significant difference when compared to the controls in these same measures.

Fideler *et al*[28] also demonstrated that the initial biomechanical strength of allografts was reduced 15% when compared to controls after 2 Mrad of irradiation. He also showed a dose dependent effect on the integrity of the allograft tissue with increasing gamma irradiation at 3 and 4 Mrads. Curran *et al*[29] reported the average load to failure of irradiated patellar tendon grafts *vs* nonirradiated grafts was 1965 ± 512 N *vs* 2457 ± 647 N, respectively. Furthermore, with cyclic loading, the irradiated grafts elongated 27% more than the nonirradiated grafts ($P < 0.05$).

DISCUSSION

The choice of graft for ACL reconstruction is contingent upon many factors including the age, baseline level of activity, and planned level of future activities[2,3,30]. Much of the debate about whether to use allograft or autograft for ACL reconstruction is related to the morbidity and complications related to each option. Autograft procedures have the disadvantage of increased surgical time due to graft harvesting, which can translate into higher procedural costs (*i.e.*, operating room time). Additional autograft harvesting risks include quadriceps or hamstring weakness from quadriceps/hamstring grafts and anterior knee pain from the BTB procedures. The benefits of using autograft include minimal risk of infection/disease transmission from donated tissue, no possibility of immune reaction to the graft, no cost of the graft (other than increased OR time), and an overall decreased rerupture rate in younger patients under the age of 25 years[2,3,11,22,31].

Reconstruction using allograft has its own unique risks. There are risks of immunogenic reaction, bacterial infection, and disease transmission from the graft donor. However, it has been reported that HIV or hepatitis transmission is 1 in 1.6 million[2,9,17,18,21,26,31,32]. The possibility of an immune reaction stems from the body's response to foreign tissues *via* interactions to human leukocyte antigens (HLAs) on donor cells. Fortunately, recent studies have found that an immune response to allograft tissue has not been a common issue, since the allograft tissue processing (*i.e.*, the freezing process) essentially eliminates active HLA markers[2,31]. Another cited disadvantage of allograft use is increased laxity over time, which can result in knee laxity and failure to return to previous level of activities despite an "intact" graft[31]. Some of the cited advantages of using allograft include smaller incisions, reduced postoperative pain/less donor site morbidity (since no graft harvesting is required), larger graft availability, earlier postoperative knee range of

Table 2 ***In vitro*** **studies of non-irradiated and irradiated allograft tissue for anterior cruciate ligament reconstruction**

Ref.	Year	Type of study	Graft type	Irradiation dose	Temperautre when irradiated	No. of samples	Age (yr)	Findings
Balsly *et al*[9]	2008	Laboratory	BPTB - low dose	1.83-2.18 Mrad	- 20 ℃ to -50 ℃	9	18-55	There was a significant difference for: (1) BPTB - tensile strength in the moderate dose irradiation *vs* control groups (2) Fascia lata - modulus of elasticity in the moderate dose irradiation *vs* control groups
			BPTB - moderate dose	2.4-2.85 Mrad		9		
			BPTB - control	None	N/A	9 controls for low dose 9 controls moderate dose		
			Anterior Tibialis - low dose	1.83-2.18 Mrad	- 20 ℃ to -50 ℃	10	23-64	No significant difference between the tensile strength and modulus of elasticity for all other groups for low dose irradiation *vs* control and moderate dose irradiation *vs* control (other than stated above)
			Anterior Tibialis - moderate dose	2.4-2.85 Mrad		10		
			Anterior Tibialis - control	None	N/A	10 controls for low dose 10 controls for moderate dose		
			Semitendinosus - low dose	1.83-2.18 Mrad	- 20 ℃ to -50 ℃	8	16-54	
			Semitendinosus - moderate dose	2.4-2.85 Mrad		10		
			Semitendinosus - control	None	N/A	10 controls for low dose 10 controls for moderate dose		
			Fascia Lata - low dose	1.83-2.18 Mrad	- 20 ℃ to -50 ℃	10	19-48	
			Fascia Lata - moderate dose	2.4-2.85 Mrad		10		
			Fascia Lata - control	None	N/A	10 controls for low dose 10 controls for moderate dose		
Greaves *et al*[17]	2008	Laboratory	Tibialis - single strand irradiated (age < 45)	1.46-1.8 Mrad	Dry ice temperatures	10 irradiated	< 45	No significant difference in failure loads for irradiated *vs* non-irradiated for each of the three age groups (midsubstance failure = any rupture within graft substance, grip failure = slip from 1 of tendon grips exposing serrated portion of tendon)
			Tibialis - single strand non-irradiated (age < 45)			10 non-irradiated		
			Tibialis - double strand irradiated (age < 45)			10 irradiated		
			Tibialis - double strand non-irradiated (age < 45)			10 non-irradiated		
			Tibialis - single strand irradiated (age 46-55)			13 irradiated	46-55	
			Tibialis - single strand non-irradiated (age 46-55)			13 non-irradiated		
			Tibialis - double strand irradiated (age 46-55)			10 irradiated		
			Tibialis - double strand non-irradiated (age 46-55)			10 non-irradiated		
			Tibialis - single strand irradiated (age 56-65)			10 irradiated	56-65	
			Tibialis - single strand non-irradiated (age 56-65)			10 non-irradiated		
			Tibialis - double strand irradiated (age 56-65)			10 irradiated		
			Tibialis - double strand non-irradiated (age 56-65)			10 non-irradiated		
Baldini *et al*[34]	2012	Laboratory	Tibialis	2.0-2.8 Mrad	Not reported	15	41.8	There were no significant difference in stiffness, failure to load, and failure stress between the irradiated *vs* non-irradiated groups
				None		12	47.4	

Yanke *et al*[35]	2013	Laboratory	BPTB	1.0-1.2 Mrad None	Not reported	10 10	52 ± 11	There was a significant difference in stiffness between the irradiated *vs* non-irradiated groups but none found in strain and elongation

BPTB: Bone patella tendon bone.

motion, and decreased surgical time[2,11].

A discussion with patients about graft integrity is important when allograft is being used for ACL reconstruction. There have been reports about having decreased allograft strength after gamma irradiation, which clinically manifests as laxity and/or catastrophic graft failure. This has been a controversial topic with conflicting studies attributed to the lack of details about how grafts were processed including the irradiation dose and the graft temperature during irradiation[9,17,18,21,26,32]. Our review of the literature found that utilizing the higher dose (≥ 2.5 Mrad) of irradiation causes greater allograft tissue laxity and subsequently increased graft failure rate. However, in the subset of patients that did not have catastrophic failures from the irradiated graft, overall functional outcome as measured by the IKDC scores were similar to the nonirradiated allograft or autograft groups. Ghodadra *et al*[33], compared BTB autograft and Patellar tendon allograft (nonirradiated and low dose irradiation - 1.0 to 1.3 Mrad) using a retrospective cohort and found no differences in postoperative laxity (KT-1000) or failure rates at 6 wk and 1 year. Additionally, the authors found no difference in the laxity between the patellar tendon groups that had the low dose irradiation *vs* no irradiation.

The choice to use an irradiated graft is contingent upon many factors. The important details to know when choosing an irradiated graft are: How the graft was prepared, the dose range of irradiation used, and the temperature of the graft when the irradiation was performed. The results from our systematic review suggest that grafts that are irradiated at low temperatures with 1.8 to 2.2 Mrad of irradiation do not appear to have deleterious effects on the allograft tissue tensile strength or elasticity modulus. However, moderate to high doses of gamma radiation (≥ 2.5 Mrad) will have a major impact on the allograft tissue biomechanical properties which may result in increased laxity that may compromise clinical outcomes and increase rates of functional failure. These above studies suggest that grafts irradiated at low temperatures with less than 2.2 Mrad of irradiation are an acceptable choice to optimize the benefits of sterility and without affecting rate of functional or catastrophic structural failure.

There have been large advancements in allograft tissue processing for ACL reconstruction over the past several decades. There are many advantages of using allograft for ACL reconstruction in the older and less active population when compared to autograft with similar functional outcomes. The concerns of infection with allografts have been mitigated by the changes in the tissue bank facility practices with improved donor tissue screening and use of gamma irradiation. Irradiation has proven to be successful at reducing the bioburden found on allografts (and possibly viral contamination) and appears to not have an effect on the rate of functional failure if it is performed with low dose irradiation (< 2.2 Mrad) at low temperatures. Grafts prepared with higher dose irradiation (≥ 2.5 Mrad) may be weakened and the additional irradiation may compromise the graft's biomechanical properties and clinical outcomes resulting in unacceptable failure rates.

COMMENTS

Background

Anterior cruciate ligament (ACL) reconstruction is a common procedure in the orthopaedic sports medicine practice. The surgery involves using tissue either from the patient (autograft) and/or from cadaver (allograft). It has been shown that the failure rates when comparing allograft to autograft tissue decreases with increased age.

Research frontiers

One of the main concerns with the use of allograft is the balance between the process of graft sterilization and its potential impact on graft integrity. It has been suggested that there is an association between increased gamma irradiation dosage and an adverse impact on the biomechanical properties of the allograft tissue, although controversy remains with regards to dosing thresholds that will compromise the strength of the allograft tissue.

Innovations and breakthroughs

There has been a trend toward increased allograft use in older and lower demand patients in recent years in an effort to decrease the morbidity associated with autograft harvest. With increased allograft use, appropriate graft irradiation exposure has been investigated. Four prospective, randomized trials demonstrated that patients who had allografts exposed to greater than or equal to 2.5 Mrad of irradiation had a significantly greater laxity and clinical failure rates than autograft or non-irradiated (< 2.2 Mrad) allografts (all different studies), but temperature at time of irradiation was not recorded. It is also important that the grafts be irradiated at low temperatures to decrease the free radical formation as to not weaken the allograft.

Applications

The authors used a systematic review of the currently available literature to determine that there is a delicate dosing crossover where gamma irradiation is both effective for sterility without catastrophically compromising the graft structural integrity.

Terminology

Gamma irradiation is a means of allograft sterilization, which uses a source emitting high-frequency electromagnetic radiation to disrupt the DNA (nucleic acids) of living organisms on the tissue.

Peer-review

This is a useful systematic review on the use of allograft for ACL reconstruction particularly focusing on the effect of the sterilization process on its biomechanical properties and clinical outcomes. The authors introduce the reader to the ACL reconstruction graft options, sterilization process and associated clinical and laboratory results. This review gives readers the opportunity to implement to their

practice a better use and understanding of gamma irradiation of allograft tissues for ACL reconstruction.

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CASE REPORT

Posterolateral dislocation of the knee: Recognizing an uncommon entity

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Abstract

Posterolateral dislocations of the knee are rare injuries. Early recognition and emergent open reduction is crucial. A 48-year-old Caucasian male presented with right knee pain and limb swelling 3 d after sustaining a twisting injury in the bathroom. Examination revealed the pathognomonic anteromedial "pucker" sign. Ankle-brachial indices were greater than 1.0 and symmetrical. Radiographs showed a posterolateral dislocation of the right knee. He underwent emergency open reduction without an attempt at closed reduction. Attempts at closed reduction of posterolateral dislocations of the knee are usually impossible because of incarceration of medial soft tissue in the intercondylar notch and may only to delay surgical management and increase the risk of skin necrosis. Magnetic resonance imaging is not crucial in the preoperative period and can lead to delays of up to 24 h. Instead, open reduction should be performed once vascular compromise is excluded.

Key words: Knee dislocation; Irreducible dislocation; Medial patellofemoral ligament; Vastus medialis; Medial collateral ligament

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Core tip: Posterolateral knee dislocations are uncommon injuries that are often missed or misdiagnosed. We believe that attempts at closed reduction and preoperative magnetic resonance imaging are unnecessary delays to open reduction. We advocate emergent open reduction once vascular integrity is confirmed on ankle-brachial index testing.

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INTRODUCTION

Posterolateral dislocation of the knee is an uncommon injury. Closed reduction is not possible because of incarceration of medial soft tissue[1,2] and should not be attempted. Open reduction is indicated once this condition is diagnosed and vascular integrity is confirmed. We present a case with posterolateral knee dislocation that presented 3 d after the original injury and discuss the successful management of this injury.

We have obtained the patient's written informed consent for print and electronic publication of the report. There are no conflicts of interest.

CASE REPORT

A 48-year-old male slipped and fell in the bathroom, striking his knee on the bathtub and sustaining a twisting injury to his right knee. He was only able to bear minimal weight on the extremity, and lay on his bed for 3 d prior to presentation. His roommates finally called for an ambulance because of unrelenting pain and increasing swelling of the entire lower extremity. His history was otherwise unremarkable except for smoking (a few cigarettes a day) and alcohol use (1 can of beer every few days).

On presentation in the emergency room, the limb was grossly swollen from the mid-thigh to the ankle, with blistering over the distal anteromedial thigh. The knee was held in slight flexion. There was ecchymotic discoloration and transverse "puckering" over the distal anteromedial thigh, and a smooth, bony prominence was palpable subcutaneously proximal to the "pucker" (Figure 1). There was diffuse tenderness around the knee. Leg swelling was soft and not suggestive of compartment syndrome. Dorsalis pedis and posterior tibial pulses were strong and the foot was warm and pink. The ankle-brachial index (ABI) exceeded 1.0 for both lower extremities. Toe plantar- and dorsiflexion strength was Medical Research Council Grade 5 and sensation was preserved. Radiographs revealed a posterolateral dislocation of the knee (Figure 2). He was taken to the operating room emergently that evening.

Under general anesthesia, the knee was inspected and brought through its range of motion (Figure 3). Under tourniquet control, and incision was made over the anteromedial leg and thigh, directly over the "pucker". There was a large rent in the medial soft tissue, and the medial femoral condyle was found lying in the subcutaneous plane. The medial patellar retinaculum, capsule, medial patellofemoral ligament (MPFL), vastus medialis, meniscotibal and meniscofemoral ligaments were found incarcerated within the intercondylar notch of the femur. These tissues were freed and reduced back to their original subcutaneous position, allowing the femur to be easily translated and reduced laterally over the tibial plateau. The medial collateral ligament (MCL) was torn at its femoral attachment, and the anterior cruciate ligament were ruptured but the posterior cruciate ligament was intact. The MPFL and vastus medialis rent was reapproximated with Ethibond 5. The medial retinaculum was imbricated over the repair with Vicryl 1 to reinforce the repair. The incision was then closed in layers in the usual fashion. Postoperative pulses were strong on the operated limb and postoperative ABI was 1.34 and 1.28 for the posterior tibial and dorsalis pedis pulses on the operated side, respectively, and 1.3 and 1.25 for the contralateral, non-operated side, respectively.

His knee pain resolved completely after surgery and compartments remained soft. He was allowed to bear weight as tolerated in a hinged knee brace locked in extension for 6 wk postoperatively. At 6-wk follow-up, he was ambulating independently in the knee brace and the surgical incision had healed completely.

DISCUSSION

Posterolateral dislocations of the knee are uncommon entities. They can arise from very low energy trauma comprising a valgus moment to a slightly flexed knee, with the tibia rotating relative to the femur. The exact direction of rotation of the tibia relative to the femur is subject to debate[1,3]. An axial load is then necessary to allow the medial femoral condyle to buttonhole through the adjacent soft tissue[1]. The key to managing these injuries is to recognize that closed reduction may not be possible, and the patient should be brought to the operating room as soon as is reasonably possible for an open reduction.

The pathognomonic sign of a posterolateral knee dislocation is the anteromedial distal thigh transverse "pucker" or "dimple sign". While this is immediately obvious with the knee in extension, the anteromedial "pucker" is accentuated by flexion. This is because the medial retinaculum, vastus medialis and MPFL tissue normally translate proximally with knee flexion. With the tissue trapped in the intercondylar notch, proximal translation is not possible and soft tissue attachments invaginate the skin inwards towards the intercondylar notch during flexion, making the "pucker" more prominent (Figure 3). To avoid discomfort, we recommend that knee flexion only be attempted under anesthesia. Another pathognomonic sign is the presence of the medial femoral condyle in the immediate subcutaneous location as a smooth, bony prominence proximal to the "pucker", almost "tenting" the skin. This is because all adjacent soft tissue (capsule, MPFL, vastus medialis, medial retinaculum) has receded around the condyle, allowing it to buttonhole through the tissue and come into prominence. Again, this is accentuated by knee flexion. Similar to other types of knee dislocation, determining the range of motion of an unreduced knee

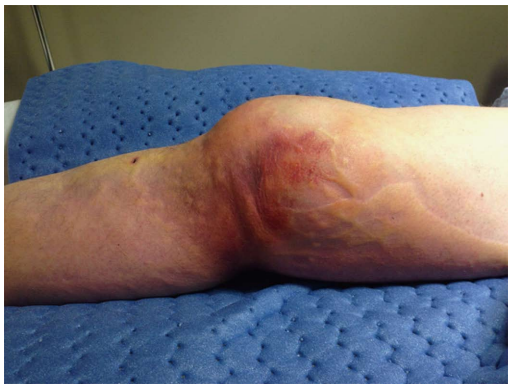

Figure 1 Clinical photograph showing the "pucker" sign with the knee in extension.

at presentation is unnecessary.

Radiographs are also pathognomonic of a posterolateral knee dislocation. Much like rotatory dislocations of the proximal phalangeal joint of the finger, radiographs of a posterolateral knee dislocation will not reveal a true anteroposterior (AP) or lateral view of both the tibia and the femur in any single radiograph. An additional telltale sign is the view of the patella. This is because the patella maintains its in-line attachments to the tibial tuberosity (patellar tendon and quadriceps tendon) and will appear reduced with respect to the proximal tibia, but dislocated with respect to the distal femur. Thus, an AP radiograph of the knee will likely demonstrate an AP of the proximal tibia and an oblique of the distal femur (Figure 2A). Because the AP radiograph is shot directly over the patella with the patella facing the ceiling, the patella will appear in an AP projection also. In addition, medial opening of the tibiofemoral joint is noted, suggestive of medial soft tissue interposition[1]. Similarly, a lateral radiograph of the knee will show a lateral of the proximal tibia and patella, but an oblique of the femur (Figure 2B). An effusion is usually appreciated on the lateral projection as well[4], however in our patient, this was replaced by diffuse soft tissue swelling of the entire limb because of the interval to presentation. An oblique projection will appear to show apparent patella dislocation relative to the femur (Figure 2C).

Similar to other types of knee dislocations, ensuring distal limb viability and preservation of vascularity is of utmost importance. Evaluation of preoperative ABI will allow stratification for further vascular evaluation, and possible skeletal immobilization and vascular exploration, if necessary. It also provides a valuable baseline reading for comparison postoperatively. In a prospective study of 38 knee dislocations, Mills *et al*[5] found that ABIs < 0.9 had sensitivity, specificity, positive predictive value of 100% and ABI > 0.9 had negative predictive value of 100% for arterial injury necessitating surgical intervention. While some authors perform computed tomography angiograms routinely for posterolateral knee dislocation (Table 1)[2,4], we believe that in the presence of palpable pulses, a warm foot and normal ABIs, further vascular imaging is but an unnecessary delay. In a review of reports of posterolateral knee dislocations, only 1 author reported loss of pulses (Table 1). This was because of a high-energy dislocation.

Some authors advocate magnetic resonance imaging (MRI) (Table 1)[2,4] to demonstrate torn structures interposed in the intercondylar notch, evaluate the integrity of the cruciate and collateral ligaments, and demonstrate the pathognomonic MR "dimple sign"[6]. We feel that these findings are equally easily discerned following the skin incision. An urgent MRI does not alter surgical management acutely, and urgent surgical reduction should take priority. Further, the distorted anatomy of an unreduced knee may also impair the diagnostic accuracy of MRI. While cruciate ligament ruptures may be picked up on MRI, these need not be addressed in the emergent setting[2]. Should the patient present with late symptoms or persistent instability in the postoperative period after a period of soft tissue healing, the cruciate ligaments can be easily evaluated with an MRI at that time.

Unlike other permutations of knee dislocation, closed reduction of posterolateral knee dislocation is rarely possible. While some authors advocate attempting a closed reduction (Table 1)[1,7-9], we feel that these attempts are both uncomfortable and unnecessary and serve only to increase the prominence of soft tissue puckering and jeopardize the viability of the already tenuous soft tissue envelope[1], and delay surgical management. Similar to other dislocations involving buttonholing of bony prominences through soft tissue, the classic reduction maneuver of in-line traction functions only to tighten torn tissue around the condylar expansion.

Some authors attempt arthroscopic- or arthroscopic-assisted reduction prior to open reduction, both in an attempt to spare the patient a disfiguring incision, and to allow for closer intra-articular inspection[1]. There are some limitations to this approach. Normal bony anatomy is distorted, making localization of the usual arthroscopic portals difficult. Because of capsular rupture, containment of insufflation fluid is not possible, leading to progressive extravasation, aggravating existing soft tissue edema and swelling, potentially increasing intracompartmental pressures. Entrapped tissue in the intercondylar notch is often on tension, and cannot be extricated by an arthroscopic probe alone[1]. Further, it is not possible to reapproximate torn medial structures arthroscopically, and a final extensile medial incision is inevitable.

Surgical reduction should be performed emergently to reduce the risk of skin necrosis at the point of maximal invagination and tethering[1,2]. The surgical technique for open reduction is not difficult. The surgical approach is extensile and direct, and targeted at achieving maximal exposure of torn structures and the buttonholed medial femoral condyle. Following division or reduction of the interposed tissue, reduction is achieved almost instantaneously by translating the femur laterally with minimal effort. These soft tissues can include medial capsule, retinaculum, MCL, MPFL, vastus medialis and medial meniscus. Division of interposed tissue may be necessary

Table 1 Characteristics of reported cases of posterolateral dislocation of the knee

Ref.	Patient age and gender	Torn structures (besides medial capsule, retinaculum, vastus medialis, MPFL)	MRI	Doppler	Angiogram/ CT angiogram	Attempted closed reduction	Arthroscopic surgery	Interval to open reduction	Open surgery
Current study	48 M	MCL, ACL	No	Yes	No	No	No	4 h	Yes
Nystrom *et al*[8]	24 M and 31 F	MCL, ACL, PCL	No	No	No	Yes	No	Not mentioned	Yes
Huang *et al*[1]	61 M	ACL, PCL, MCL (also degenerative arthrosis)	No	No	No	Yes	Yes	> 8 h	Yes
Jeevannavar *et al*[2]	32 M	MCL, medial retinaculum, partial ACL tear	Yes	Yes	Yes	Yes	No	Not mentioned	Yes
Paulin *et al*[4]	54 M	ACL, PCL, MCL, LCL	Yes	No	Yes	Yes	No	< 24 h	Yes
Quinlan *et al*[3]	38 M, 40 F, 49 M, 20 M, 41 F	ACL, PCL, MCL in all patients, additional medial meniscus tear in 1 patient	No	No	No	3 of 5 cases	No	24 h in 4 cases, few days later in 1 case	Yes
Ashkan *et al*[7]	37 M	ACL, PCL, MCL, LCL, PLC	No	No	No	Yes	No	Following thoracoabdominal surgery	Yes
Urgüden *et al*[9]	51 M and 53 F	Medial retinaculum, MCL, ACL, PCL	No	Yes in 1 patient	No	Yes	No	4 h in both	Yes

ACL: Anterior cruciate ligament; PCL: Posterior cruciate ligament; MCL: Medial collateral ligament; LCL: Lateral collateral ligament; PLC: Posterolateral corner; MPFL: Medial patellofemoral ligament; M: Male; F: Female; MRI: Magnetic resonance imaging; CT: Computed tomography.

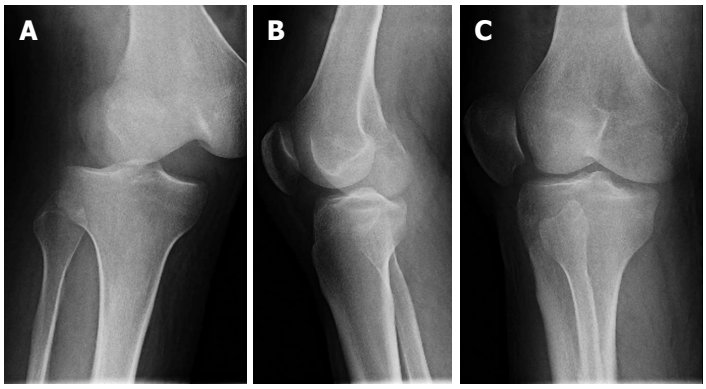

Figure 2 Supine radiographs showing posterolateral dislocation of the knee. A: AP; B: Lateral; C: Oblique. Note similar projections (AP or lateral) of both the tibia and femur are not seen in any single view. AP: Anteroposterior.

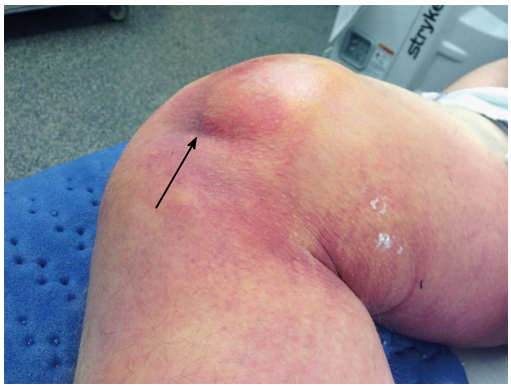

Figure 3 Clinical photograph under anesthesia showing accentuation of the "pucker" sign (black arrow) with flexion of the knee.

if there is tight contracture, especially in late-presenting cases.

Postoperatively, the knee is protected in a hinged knee brace during mobilization. Besides torn medial structures and cruciate ligaments, some authors have found avulsion of lateral structures including the lateral collateral ligament from its femoral attachment[4]. Protected weight-bearing will allow for healing of torn, repaired and reapproximated structures. Long term follow-up is necessary to detect the onset of post-traumatic arthritis.

Posterolateral dislocations of the knee are uncommon entities. Early recognition is key. Pathognomonic findings include the anteromedial "pucker" sign that is accentuated by knee flexion, and characteristic radiographs that do not show the same projections of the long bones in any single view. Attempting closed reduction will not be a rewarding endeavor. Instead, open reduction should be performed as soon as vascular compromise is excluded. MRI is not crucial in the preoperative period and can lead to delays of up to 24 h and can compromise the overlying soft tissue envelope[4]. MRI can be obtained postoperatively following a period of soft tissue healing in patients with persistent symptoms.

COMMENTS

Case characteristics

A 48-year-old man presented with right knee pain and swelling 3 d after twisting his right knee during a fall.

Clinical diagnosis

Gross swelling of the right thigh to ankle with distal thigh blistering. "Pucker" sign was visible over the distal anteromedial thigh. Subcutaneous bony prominence (medial femoral condyle) was palpable proximal to the pucker. Pulses were strong and ankle-brachial index was > 1.0 bilaterally.

Differential diagnosis

Knee septic arthritis, knee effusion, deep vein thrombosis, compartment syndrome, anterior knee dislocation, posterior knee dislocation, cruciate or collateral ligament injury, tumor.

Laboratory diagnosis

All labs within normal limits.

Imaging diagnosis

Radiographs revealed posterolateral dislocation of the knee.

Pathological diagnosis

Posterolateral dislocation of the knee.

Treatment

Operative open reduction and repair of medial retinaculum, medial patellofemoral ligament and vastus medialis.

Related reports

Posterolateral knee dislocations are uncommon and can be missed. Magnetic resonance imaging (MRI) will only delay treatment. Closed reduction may not be possible. Urgent open reduction is necessary to preserve the tenuous soft tissue envelope.

Experiences and lessons

This condition is uncommon. Urgent open reduction is often necessary as closed reduction is usually impossible. MRI in the acute setting will only serve to delay open reduction and will not guide immediate management.

Peer-review

The authors reported a rare case of posterolateral dislocations of the knee. It is a well written case report.

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