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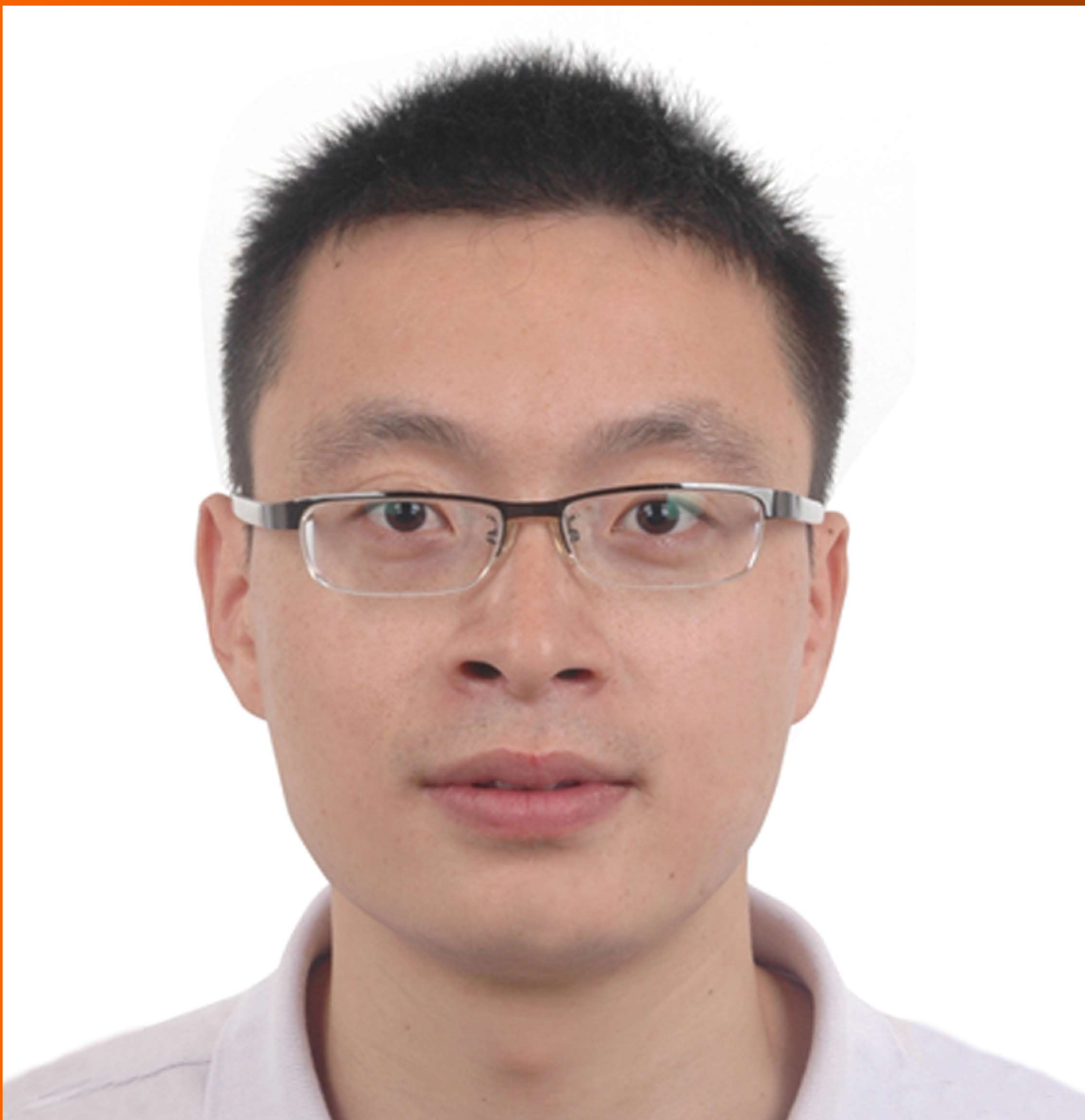

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EDITORIAL

Fractures in sport: Optimising their management and outcome

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Abstract

Fractures in sport are a specialised cohort of fracture injuries, occurring in a high functioning population, in which the goals are rapid restoration of function and return to play with the minimal symptom profile possible. While the general principles of fracture management, namely accurate fracture reduction, appropriate immobilisation and timely rehabilitation, guide the treatment of these injuries, management of fractures in athletic populations can differ significantly from those in the general population, due to the need to facilitate a rapid return to high demand activities. However, despite fractures comprising up to 10% of all of sporting injuries, dedicated research into the management and outcome of sport-related fractures is limited. In order to assess the optimal methods of treating such injuries, and so allow optimisation of their outcome, the evidence for the management of each specific sport-related fracture type requires assessment and analysis. We present and review the current evidence directing management of fractures in athletes with an aim to promote valid innovative methods and optimise the outcome of such injuries. From this, key recommendations are provided for the management of the common fracture types seen in the athlete. Six case reports are also presented to illustrate the management planning and application of sport-focussed fracture management in the clinical setting.

Key words: Fractures; Sport; Management; Optimisation; Outcome

Core tip: This is an editorial article, on the topic of optimising the management and outcome of sport-related fractures, providing an informed commentary on the current management of acute fractures in the athlete with an aim to try optimise their outcome. The article begins with a brief overview of the topic, which is followed by a discussion on the management strategies and associated outcomes of the common fracture

patterns seen in sporting populations. The published evidence relevant to this is also discussed. The authors then present a series of case reports to illustrate the management of such injuries in the clinical setting.

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INTRODUCTION

Sports injuries are a major source of morbidity for the athlete[1]. The time required for treatment and recovery can have substantial financial implications both for the individual and for their team[1]. Given the economic revenues associated with professional sport, there has been a major focus in recent years to minimise the impact of sporting injuries, through optimisation of management, acceleration of rehabilitation and promotion of injury prevention[2-4]. Such initiatives have largely focused on acute soft tissue injuries and overuse injuries, such as ligament ruptures and stress fractures, that are commonly associated with sports medicine[2-4]. Little attention, however, has been placed on the management and outcome of acute fractures[5].

Acute fractures comprise 5% to 10% of all sports injuries and account for one of the longest return times to sport post-injury[3,6-16]. Until recently, much of the previous fracture research had focussed on osteoporotic fractures, overlooking cohorts of sporting individuals[17,18]. While fracture management in both cohorts adheres to the general principles of orthopaedic trauma with accurate fracture reduction, appropriate immobilisation and timely rehabilitation, management of fractures in athletes provides a unique challenge, due to the requirement to return to high impact activities as rapidly as able with the optimal symptom profile possible[1,5,18]. Thus in order to properly to assess the optimal management techniques for these injuries, and so maximise their outcome, dedicated research has to be performed focussing specifically on these individual cohorts[5,19-21].

In this editorial we analyse the evidence available for the management of acute sport-related fractures, and discuss the developing methods suggested to optimise management and outcome of these injuries. We will focus on the common fracture locations and types experienced by the athlete[5,22], and, for each of these, we will discuss the standard management of these injuries as well as review the innovative treatment strategies currently being developed to optimise outcomes in the high level athlete. This will be supplemented by a series of case reports which will illustrate the application of these strategies in clinical practice. The topic of sport-related stress fractures is not covered in this editorial as this has been covered previously in various reviews.

OPTIMISING THE MANAGEMENT AND OUTCOME OF SPORT-RELATED FRACTURES

When planning the management of acute sport-related fractures, the standard principles of orthopaedic trauma management should always form the basis of decision-making[18]. These are to achieve anatomical fracture reduction, to apply adequate fracture immobilisation, and to perform timely rehabilitation to facilitate the return of normal physiological functioning[18]. However, with fractures in the athlete, particularly high level athletes, there is a requirement to achieve rapid return to high demand activities with lowest symptom profile, in order to restore sporting careers[1,5,18]. As such, specific modifications can be made when treating these injuries to achieve this[1,5,18].

However, it is difficult to provide a unifying set of principles to guide the management of sports-related fractures, as fracture management is often unique to fracture location and fracture pattern[18,19]. And so, in order to establish the optimal modality for treating these injuries, each fracture type has to be assessed individually, with the relevant evidence assessed for each. The four major questions that require defining for each fracture type are: (1) Should management be operative or conservative? (2) Which method of surgical fixation is best to use? (3) Which method of immobilisation is best to use? and (4) How quickly can sporting activities be resumed?

In order to achieve this, we will assess the five most common fracture types for both the upper and lower limb[5,22], and discuss the developing management initiatives that aim to optimise outcome of these injuries in the high level athlete.

UPPER LIMB SPORT-RELATED FRACTURES

Upper limb fractures comprise three quarter of all sports-related fractures, with the five most common types being finger phalanx, distal radius, metacarpal, clavicle and scaphoid[5,22]. In general, around ten percent of upper limb sport-related fractures are treated operatively[20,21]. Both return rates and return times are promising, with rates ranging between 85% and 87% and return times averaging around 9 wk[20,21].

Finger phalanx

As a whole, the management of finger phalanx fractures varies little between athletic populations and the general population[18,23-25]. The majority of such fractures are undisplaced or minimally displaced and can be treated satisfactorily with an appropriately designed splint for 2 to 3 wk[18,23-27]. For the high level athlete, the exception to this rule is the undisplaced condylar fracture, which has a high rate of displacement in active individuals[24].

Weiss *et al*[28] noted a displacement rate of 72% with non-operative management of such fractures. As such these often benefit from primary surgical fixation in the athletic population[23,24].

Stable displaced extra-articular fractures are often amendable to conservative management with closed reduction and splinting[18,23-25]. However, displaced intra-articular fractures, displaced proximal base fractures and displaced unstable extra-articular fractures often require surgical stabilisation[18,23-25]. While closed reduction and K-wiring is routinely chosen for stabilisation of such fractures in the general population, there is a developing consensus that internal fixation should be employed in the high level athlete, with interfragmentary screw or plate fixation, as this can facilitate an accelerated return to sporting activity[23-25]. Such decisions can be complex and management is best directed by a specialist hand surgeon with experience in such injuries[23-25].

Methods of immobilisation remain similar to the standard techniques, with Alumafoam, thermoplast, or "finger tip" protectors, regularly employed[23-25]. The challenge with the athlete is designing an orthotic that can allow early return to sport. This is often best achieved in conjunction with a specialist orthotist and should be guided by the rules of the sport, as well as the function of the athlete[23-25].

Regarding the best time to return to sport, guidelines suggest that return within the first week post-injury should be possible with adequate orthotic protection[23-25]. However return to full contact sport should be withheld till there is evidence of radiographic healing, normally around 3 wk, with continued used of protective splinting till 6 wk post fracture[23-25].

Distal radius

Around ninety percent of sport-related distal radius fractures are treated conservatively, being either undisplaced fractures or dorsally displaced extra-articular fractures that can be reduced and splinted into satisfactory anatomical alignment[5,20-22,27,29]. However, for the high level athlete, it is becoming increasingly accepted that such fractures with evidence of radiological instability, such as dorsal comminution, dorsal angulation > 20 degrees, articular radiocarpal fracture, ulnar fracture, and loss of radial length, are best treated with primary surgical intervention, to avoid unsuccessful attempts at conservative management, which delay return to sport[30-32].

Regarding the choice of surgical fixation, the majority of fractures can be adequately managed with locked volar plating[30]. However, clinicians must remain aware of the importance of achieving accurate anatomical reduction in the high level athlete, and occasionally, this is not possible with volar plating alone, particularly with comminuted and intra-articular fractures[30]. Additional plating or bridging external fixation with K-Wire augmentation may be required to provide more accurate reduction[30]. Such decisions should be directed by specialists with experience in the management of sport related distal radial fractures[30].

Immobilisation techniques vary little from standard practice, with a short arm "colles" cast for conservative management and a wrist splint for post-surgical immobilisation[18,30]. Regarding return to sport, it is clear that non-contact, "non-upper-limb" activities can be commenced within 2 to 4 wk of injury with the fracture appropriately immobilised[18,30]. However, both with operative and conservative cases, return to full contact sport should not be performed until there is satisfactory fracture healing, normally around 8 wk post-injury[18,30].

Metacarpal

The majority of sport-related metacarpal fracture are undisplaced or minimally displaced and will not require surgery[5,20-22,26,27,33]. These can be treated satisfactorily with an appropriately designed splint and associated buddy strapping[18,24,25,34,35]. For the high level athlete, the exception to this rule is the undisplaced intra-articular metacarpal head fracture and the undisplaced intra-articular thumb metacarpal base fracture, which are unstable, and require primary surgical fixation[18,24,25,34,35].

Most displaced extra-articular fractures can be managed conservatively, with reduction and splinting into satisfactory alignment[18,24,25,34,35]. However, displaced intra-articular fractures and displaced unstable extra-articular fractures often require surgical stabilisation[18,24,25,34,35]. Internal fixation with either interfragmentary screws or plating is the preferred modality in the high level athlete, facilitating an earlier return to rehabilitation and sport[24,25,34]. Rettig *et al*[33] found that internal fixation of metacarpal fractures resulted in a return time to sport of 14 d while management with closed and K-wiring resulted in a return time of 36 d to sport. When closed reduction and K-wiring is required, K-wires can be cut under the skin and buried to facilitate an accelerated return to sport[35].

A variety of immobilisation methods continue to be used, ranging from short arm "colles" casts to gutter splints, with neither more beneficial than the other[18,24,25,34,35]. The challenge with the athlete, is designing a suitable orthotic that can permit adequate function with appropriate protection on return to sport[24,25,34,35]. This is often best achieved in conjunction with a specialist orthotist and should be guided by the rules of the athlete's sport, as well as the position of the athlete[24,25,34,35].

Guidelines at present advise return to non-contact, "non-upper-limb" sporting activities within 1 wk post-injury and return to full contact sports within 4 wk post-injury[24,25,34-36]. However, recent studies have suggested that an accelerated return to full contact sport can be achieved with one week of injury[36]. While the authors advise against this, due to the possibility of re-injury, if clinicians decide to attempt this, patients should be thoroughly counselled regarding the risk of re-fracture and strongly advised to maintain protective splinting throughout.

Clavicle

Up to 20% of sport-related clavicle fractures undergo primary surgical intervention[20,21], compared to around 5% in the general population[37]. This is due to the differing management of displaced mid-diaphyseal clavicular fractures for the two populations[38-41]. While displaced mid diaphyseal fractures are regularly managed conservatively in the general population, with acceptable union rates and functional results[37,42], recent research has promoted surgical fixation of such injuries in athletes (particularly contact athletes) when there is complete displacement, shortening greater than 2 cm or comminution[38-41,43,44]. This is directed by the research from the Canadian Orthopaedic Trauma Association[43] and McKee *et al*[45] who found that operative management of such fractures provides significantly improved shoulder function, symptom profile and union rates in active individuals. Further studies in high level athletes have found that conservative management of such injuries can result in return times of up to two seasons, with refracture rates of over 50%[40], while surgical management results in return times between 68 d and 83 d with no episodes of refracture[39-41]. Nevertheless, given that conservative management remains an acceptable alternative, avoiding the substantial surgical risks, clinicians should involve all patients in a well-informed discussion regarding both sets of management, before proceeding with surgical intervention[18].

Regarding the optimal method of surgical fixation, several studies have found similar return rates and return times to sport for both plate fixation (rates 98% to 100%; times 45 d to 36 wk)[39-41,46,47] and intramedullary nailing (rates 98% to 100%; times 17 d to 3.2 mo)[40,48-50]. However, clinicians should remain aware that the optimal method of fixation is dependent on the location and the nature of the fracture pattern[18,50]. Simple, transverse and oblique, two part mid-diaphyseal fractures are suitable for either form of fixation[18,50], and in such instances, the authors advise that clinicians should use the technique that they are experienced with and feel comfortable performing[40]. Complex comminuted mid-diaphyseal fractures and distal clavicle fractures, however, are not suitable for intra-medullary nailing, with recorded difficulties in achieving and securing accurate reduction[18,46,50]. In such instances, clinicians should employ open reduction internal fixation[18,46,50].

There is little variation for immobilisation techniques in the athlete compared to those of standard practice[18,51,52]. Use of a sling is appropriate for both conservatively and surgically managed fractures, with no clear advantage being shown between this and figure of eight immobilisation[18,51,52].

Return to sport is an important issue with such fractures, due to the risk of refracture[40]. The authors advise that non-contact, "non-upper-limb" activities be commenced within 1 to 2 wk post-injury, for both operative and non-operative cases[18,51,52]. However commencement of contact and "upper-limb" sports should not be commenced till around 8 wk post-injury, with clear evidence of radiographic and clinical healing[18,51,52]. For, the rare cases of conservatively managed displaced mid-diaphyseal fracture, such times may extend to 16 wk[40].

Scaphoid

Up to 25% of sport-related scaphoid fractures are treated surgically[21], while only around 5% of those in general population undergo primary surgical intervention[53]. This is because evidence-based recommendations advise primary surgical intervention of undisplaced and minimally displaced waist fractures in the athlete, while such injuries are routinely managed conservatively in the general population[18,54]. Level 1 Evidence from McQueen *et al*[55] found that primary surgical management of undisplaced scaphoid waist fractures with a percutaneous headless screw results in return times to sport of 6.4 wk while conservative management of such injuries resulted in return times of 15.5 wk. Nevertheless, as conservative management remains an acceptable alternative, the authors advise that clinicians involve patients in a well-informed discussion regarding both sets of management, before proceeding with surgical intervention[18].

Regarding the optimal surgical modality, the Herbert Headless Compression Screw is the most validated method available[54,56,57]. This can be performed percutaneously for minimally displaced fractures, leaving a minimal scar with limited post-operative symptoms, allowing the athlete to return to unimpaired upper limb activities as quickly as possible[54,55].

One of the major benefits of undergoing primary surgical intervention in the athlete, is that no formal post-operative immobilisation is required, allowing rapid commencement of physiotherapy and return to sports[54,55]. Conservative management requires use of a short arm "colles" cast for 8 to 12 wk, delaying commencement of physiotherapy and subsequent return to sport[54-56]. The addition of thumb extension to "colles" casting appears to offer limit benefit in term of time to union and post-treatment function, and so is no longer recommended[57].

Return to sport is clearly accelerated in those athletes who undergo surgical intervention due to the more rapid commencement of upper limb mobilisation exercises[54-56]. Non contact, "non-upper-limb" activities can be commenced within 1 to 2 wk, followed by a graduated return to contact activities, by around 6 to 8 wk post-surgery[54]. With conservative management, non contact activities can be commenced within 1 to 2 wk of injury, however contact sports should not be commenced until removal of cast with clear evidence of radiographic healing[54].

LOWER LIMB SPORT-RELATED FRACTURES

Lower limb fractures comprise one quarter of all sports-related fractures, with the five most common types being ankle, metatarsal, toe phalanx, tibial shaft and fibula[5,22]. Around forty percent of them are treated operatively[20,21]. Return rates are promising at around 86%, however return times can be prolonged, often averaging around 27 wk[20,21].

Ankle

Until recently, it was recommended that all sport-related ankle fractures be treated surgically, to facilitate an early return to sport[58]. However, emerging evidence shows that surgical intervention is associated with increased rates of persisting symptoms, with similar or prolonged return times to sport compared to conservative management[19]. As such, current recommendations advise that stable undisplaced fractures (*i.e.*, isolated Weber A lateral malleolus, isolated Weber B lateral malleolus and medial malleolus) be treated non-operatively[18,19]. Those that require surgical intervention include displaced unstable fractures (displaced bimalleolar and bimalleolar equivalent fractures), fractures with posterior malleolar fragments greater than a third the articular surface and fractures with sydesmotic disruption[18,19].

The area for debate is the management of undisplaced, radiologically unstable fractures (*i.e.*, undisplaced bimalleolar fractures and undisplaced Weber C fractures), with some advocating primary surgical fixation to facilitate early return to sport and others advocating attempted conservative management to avoid the post-surgical symptom profile[18,19,58]. Robertson *et al*[19] found that conservative management of undisplaced bimalleolar fracture resulted in return times of 27 wk to sport while surgical management of displaced bimalleolar ankles resulted in return times of 43 wk. Seventy-one percent of the surgically managed patients reported persisting symptoms at follow-up compared to 17% of the conservatively managed patients[19]. As such, current recommendations advise attempted conservative management of these fracture types, with close follow-up and surgical intervention if displacement occurs[18,19].

Regarding the optimal surgical method, open reduction internal fixation with lag screw and tubular plate remains the standard modality[58]. Intra-medullary fixation is an evolving concept though the evidence for use in the athletic population is not available at present[59]. The decision to repair associated soft tissue structures remains debatable, particularly for the high level athlete[60]. Strömsöe *et al*[61] found that additional deltoid ligament repair resulted in no improvement to sporting function at a mean of 17 mo post-surgery. It is recommended that associated ligament repair only be performed if these structures block intra-operative fracture reduction[18,19,61]. There remains debate over the optimal method of syndemotic stabilisation, with current evidence suggesting that tightrope fixation provides superior results over screw fixation in terms of ankle function, time to return to activities and need for further intervention[60,62]. While it is recommended for use in the elite athlete, long term follow-up of tightrope fixation is limited[57,59]. As such, use of this specialist technique should be restricted to surgeons who are experienced with this procedure[57,59]. For those that undergo screw fixation, there is no functional benefit in screw removal, so this is only recommended if there are adverse symptoms arising from it[63].

Immobilisation of ankle fractures in the elite athlete is now more commonly performed with a moon boot orthosis as this allows for regular removal and earlier commencement of physiotherapy[18]. With stable fractures, weight bearing should be encouraged as early as possible to reduce muscle wastage and deconditioning[18,19]. Times for immobilisation are as per standard ankle fracture management, and should be adhered to properly, to allow for optimal fracture healing before recommencement of sporting activities, limiting the chance of repeat injury[18,19].

Regarding return to sport, the authors recommend commencement of non-contact sporting activities between 6 to 8 wk post-injury, with progression of exercise intensity under the care of the physiotherapists[18,19]. Return to contact sporting activities can then normally be performed around 12 to 16 wk post-injury, though should be guided by radiological evidence of healing[18,19]. The exception to this are those who undergo syndesmotic fixation: in such cases weightbearing should not be commenced till 8 wk post-surgery, so full return to sporting activities is often delayed up to and beyond 20 wk[18,19].

Metatarsal

The key difference between the management of metatarsal fractures in the athletic population compared to that in the general population is that, in the elite athlete, primary surgical intervention is recommended for the acute undisplaced or minimally displaced 5th metatarsal proximal meta-diaphyseal (Jones) fracture[18,64]. Level 1 evidence from Mologne *et al*[65] has found that primary surgical intervention of these injuries resulted in improved return times to sport (surgical 8 wk *vs* conservative 15 wk), improved rates of union (surgical 95% *vs* conservative 67%) and improved times to union (surgical 7.5 wk *vs* conservative 14.5 wk). This has subsequently been confirmed by a systematic review assessing eighteen studies on this subject[64]. Given that conservative management remains an acceptable alternative, the athlete should be thoroughly counselled on the treatment options, detailing both the risks of non-union with conservative management and the risks of infection and nerve damage with surgical management[18,64]. If conservative management is initially attempted, this can be converted to surgical management if a delayed union becomes apparent, normally within two to four months of the initial injury[64,66-68]. This can improve return times to sport in such circumstances[64,66-68].

The preferred surgical technique for the Jones fracture is the intramedullary screw, having the strongest evidence base of all the available methods[18,64]. Reported return to sport times range between 7.5 wk and 12.4 wk and return rates range between 88% to 100%[65,67,69-75]. While there is no evidence-base to recommend a percutaneous technique over an open technique, a percutaneous technique leaves the athlete with a smaller scar which theoretically should reduce the post-operative symptom profile[64].

Immobilisation is an important factor in achieving healing with the Jones fracture, and appropriate adherence to recommended rehabilitation protocols is key to improve the success of both operative and non-operative management[67]. Post-operative immobilisation can be performed with a moon boot to facilitate early range of motion exercises, though conservative management may best be performed in a below knee cast, at least initially, to limit return to activities and allow for optimal fracture healing[18,67,72-74]. Post-operatively, current recommendations advise return to weightbearing 2 wk post-surgery, with commencement of physiotherapy and graduated return to activities by 6 to 8 wk post-surgery[18,67,72-74]. Athletes must be advised not to over accelerate rehabilitation as this significantly increases the chances of treatment failure[67]. For conservative management, immobilisation is required for up to 12 wk, non weightbearing for 6 wk and partial weightbearing for 6 wk[65,75,76]. Compliance is vital, particularly in the restless athlete, as failure to adhere with this results in a high rate of non-union[18,67].

Regarding return to sport for surgically managed Jones fractures, this can normally be achieved around 8 to 12 wk post-surgery, but again, it is important to avoid an over accelerated return as this can damage fixation, impair healing and result in non-union[18,67,72-74]. As such return should only be performed when there is clear evidence of clinical and radiological healing[67]. For conservatively managed Jones fractures, it is similarly important to avoid an over accelerated return, as this results in a high rate of delayed union and non-union[65,67,75,76]. Athletes can expect to wait till up to 16 wk post-injury till return to full level sport, and this again should not be performed till there is clear evidence of clinical and radiological healing[18,64]. For other metatarsal fractures, whether treated conservatively or surgically, these can normally return to sporting activities between 6 to 8 wk post-injury[18].

Toe phalanx

The majority of sport-related toe phalanx fractures are undisplaced or minimally displaced and so can be treated conservatively, with very satisfactory results[18,21,77]. However, those with gross displacement or significant articular involvement will normally require surgical intervention[18,21,77].

There is little evidence to direct the optimal surgical modality, though, with high level athletes, internal fixation with interfragmentary screw fixation or plate fixation is recommended over closed reduction and K-wiring, as this can facilitate a more rapid return to sporting activities[77].

Immobilisation is best performed with buddy strapping and a forefoot offloading shoe, as this allows the athlete to continue weightbearing during the immobilisation period[18,77]. This is normally for a period of 3 to 4 wk, followed by a graduated return to activities under the care of the physiotherapists[18,77].

Regarding return to sport, while it can tempting for the high level athlete to pursue an accelerated resumption of activities, given the perceived insignificance of such injuries, clinicians must limit return times to a minimum of 4 wk, for both conservative and surgical management, to allow the fracture to heal sufficiently[18,77]. This prevents the risk of re-injury and development of deformity or longstanding pain complications[18,77].

Tibial shaft

The key difference between the management of tibial shaft fractures in the athletic population compared the general population is that, in the elite athlete, primary surgical intervention is recommended for undisplaced and minimally displaced tibial shaft fractures[18,78]. While such injuries have traditionally been treated non-operatively, with an above knee cast followed by a patellar tendon bearing cast, a recent systematic review has found that, in athletic populations, primary surgical fixation results in improved return rates to sport (surgical 92% *vs* conservative 67%). with improved return times to sport (surgical 12 to 54 wk *vs* conservative 28 to 182 wk)[18,78]. Given that conservative management remains an acceptable alternative, avoiding the considerable risks associated with surgery, such decisions require an informed discussion with patient[18]. The risks of surgery should be detailed clearly, including infection, compartment syndrome and neurovascular injury, though patients should also be advised that up to one third of patients managed conservatively require delayed surgical intervention for fracture displacement[18,78-81]. The authors recommend primary surgical intervention for high and middle level athletes with undisplaced or minimally displaced tibial shaft fractures, and attempted conservative management for low level athletes with such injuries. For those managed conservatively, regular follow-up with radiographic review is required to assess for displacement, with appropriate surgical intervention offered accordingly, if this occurs[79-81].

The management of displaced fractures is similar between athletic and non-athletic populations with surgical intervention universally required[18,78]. To note, manipulation and casting of such fractures has been found to result in return times over 2 years, with re-intervention rates over 25%[79]. This is not recommended in the athlete[78].

Intra-medullary nailing remains the preferred technique in the athlete, with the strongest evidence base of all methods[21,82-88]. Return rates range between 70% to 100%[21,82,83,86,87] and return times between 12 to 54 wk[21,82-85,87,88]. Plate fixation often requires a period between 4 to 6 wk non-weightbearing post-operatively,

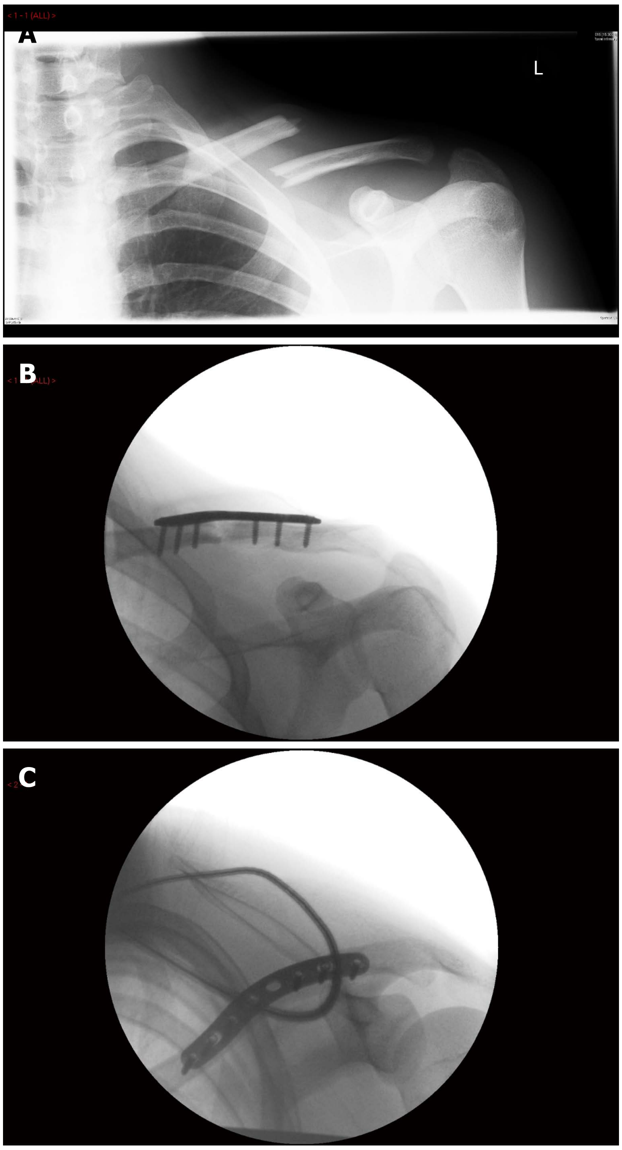

Figure 1 The management of a displaced mid diaphyseal clavicle fracture. A: Pre-operative radiograph demonstrating complete displacement with shortening; B: Intra-operative antero-posterior radiograph; C: Intra-operative skyline radiograph.

and as such, demonstrates prolonged return times compared to IM nailing[79].

Recommended immobilisation techniques following IM Nailing include use of a moon boot orthotic weightbearing as tolerated for 4 to 6 wk, allowing for range of motion exercises throughout[18]. For conservative management, preferred immobilisation is with an above knee cast for 4 to 6 wk followed by a patellar tendon bearing cast for 4 to 6 wk, with weightbearing guided by radiological evidence of healing[18,79,80].

Rapid return to sport is a key issue with these fractures but it is important to perform this in a time-appropriate manner as over-accelerated return can risk failure of fixation and non-union[18]. Following intramedullary nailing, progressive immobilisation under the care of the physiotherapist can begin immediately with return to gentle running activities between 6 to 12 wk[18,21,82-88]. Return to full contact sports can normally be performed by 24 wk[18,21,82-88]. There should be clear evidence of radiological union before this is permitted[18]. For conservative management, mobilisation under the care of the physiotherapist cannot be commenced till removal of cast, and as such return to sporting activities is often delayed due to muscle atrophy and deconditioning[18,79,80,89]. Running activities are usually not commenced till between 16 and 20 wk and return to full contact sport can often does occur till over 40 wk post-injury[18,79,80]. Particularly in these cases, this should not be resumed till there is clear evidence of radiological healing, due to a high risk of re-fracture on return to sports[18].

Fibula

The management of sport-related fibula fractures varies little from that in the general population[18,20,21]. Virtually all these injuries are treated conservatively with favourable return times to sport and limited post-injury symptom profiles[20,21]. The main consideration with the management of these injuries in the high level athlete is to avoid over-accelerated return to full level sport before adequate healing has been achieved, as this may promote development of a non-union[18]. Despite the initial self-limiting nature of such fractures, development of a non-union often requires surgical intervention, which can significantly delay return to sport[18].

Immobilisation of such fractures in the athlete is often best performed with a moon boot weightbearing as tolerated as this allows ongoing physiotherapy exercise to be performed[18].

Regarding return to sport, this should be performed in a graduated fashion between 6 to 8 wk, guided by both radiological and clinical evidence of healing[18]. Clinicians should remain alert for the patient who develops persistent fracture pain on return to sport[18]. Appropriate reduction of activities advised with regular follow-up performed, to exclude the development of a non-union[18].

Case 1: A displaced mid diaphyseal clavicle fracture (Figure 1)

A 20-year-old semi-professional rugby player suffered a fall onto his left shoulder following a tackle during a match. He sustained a mid diaphyseal clavicluar fracture, that was completely displaced on radiographs and clinically shortened greater than 2 cm. It was closed and distally neuro-vascularly intact with no evidence of skin tenting.

Following an informed discussion in clinic, outlining the options of conservative *vs* surgical management, detailing both the associated risks and predicted outcomes of both treatments, with surgical intervention recommended, the patient opted for surgical management, with a view to be able to return to his sporting career as soon as able.

He underwent open reduction and plate fixation

Figure 2 The management of an undisplaced bimalleolar ankle fracture. A, B: Pre-cast antero-posterior and lateral radiographs; C, D: Initial antero-posterior and lateral radiographs in cast; E, F: Two-week follow-up antero-posterior and lateral radiographs in cast.

of his clavicle the two days later. There were no complications. Post-operatively, he was immobilised in a sling for 2 wk, then commenced physiotherapy at this stage.

He returned to non-contact training activities 8 wk post-operatively and returned to full level rugby 10 wk post-operatively. At 2-year follow-up, he is occasionally troubled by scar sensitivity, particularly when wearing a rucksack but otherwise reports no other symptoms.

Key message: Primary surgical fixation of displaced mid shaft clavicle fractures can facilitate early return to contact sports with good recovery of shoulder function.

Case 2: An undisplaced bimalleolar ankle fracture (Figure 2)

A 24-year-old district level soccer player suffered a forced inversion injury to her left ankle during a tackle. She sustained an undisplaced right bimalleolar ankle fracture. This was closed and distally neuro-vascularly intact. She was placed into a below knee backslab on the day of her injury and this was then converted into a below knee cast one day later in fracture clinic. Radiographs confirmed no displacement of the fracture.

In clinic, her consultant detailed the options of conservative *vs* surgical management, describing both the associated risks and the predicted outcomes of both treatment, and recommending conservative management. She opted for conservative management with a preference to avoid surgery. She was kept crutch-assisted partial weightbearing in a below knee cast for 6 wk.

Radiographs at one, 2 and 6 wk demonstrated no displacement of the fracture, and the cast was removed at 6 wk. She commenced physiotherapy at this stage, with a progressive weightbearing programme.

She returned to training activities 14 wk post-injury and returned to full level soccer 20 wk post-injury. At 2-year follow-up, she reports no adverse symptoms.

Key message: Successful conservative management of undisplaced, radiologically unstable, ankle fractures can result in rapid return to sport with the avoidance of the surgical intervention and an improved outcome symptom profile.

Case 3: An undisplaced scaphoid waist fracture (Figure 3)

A 26-year-old right hand dominant professional cyclist suffered a fall from his bike during a race onto his right outstretched hand. He sustained an undisplaced scaphoid waist fracture. The injury was closed and distally neuro-vascularly intact.

Following extensive discussion in clinic, outlining the options of conservative *vs* surgical management, detailing the associated risks of treatment and the predicted outcomes, with surgical intervention recommended, the patient opted for surgical fixation, with the aim to be able to return to his sporting career as soon as able. He underwent retrograde percutaneous screw fixation of his scaphoid fracture three days later. There were no complications.

Post-operatively, he required no immobilisation and commenced physiotherapy within 1 wk of his surgery. He returned to non-contact, "non-upper limb" training activities 3 wk post-operatively and returned to cycling 7 wk post-operatively. At 2-year follow-up, he reports occasional pains around his scaphoid region following prolonged cycles, particularly in the cold, though is otherwise functionally well.

Key message: Primary surgical fixation of undisplaced scaphoid waist fractures can facilitate early return to upper limb sports with good recovery of wrist function.

Case 4: A minimally displaced tibial shaft fracture (Figure 4)

A 23-year-old professional soccer player suffered a twisting injury to his right lower leg, as his studs got caught in the turf, during a tackle. He sustained an undisplaced tibial shaft fracture, which was closed and distally neurovascularly intact. In the Emergency Department, he was placed into an above knee cast, and further radiographs demonstrated minimal fracture displacement with acceptable alignment to consider non-operative management. He was admitted as an inpatient to monitor for post-injury compartment syndrome.

On the ward round the following morning, there

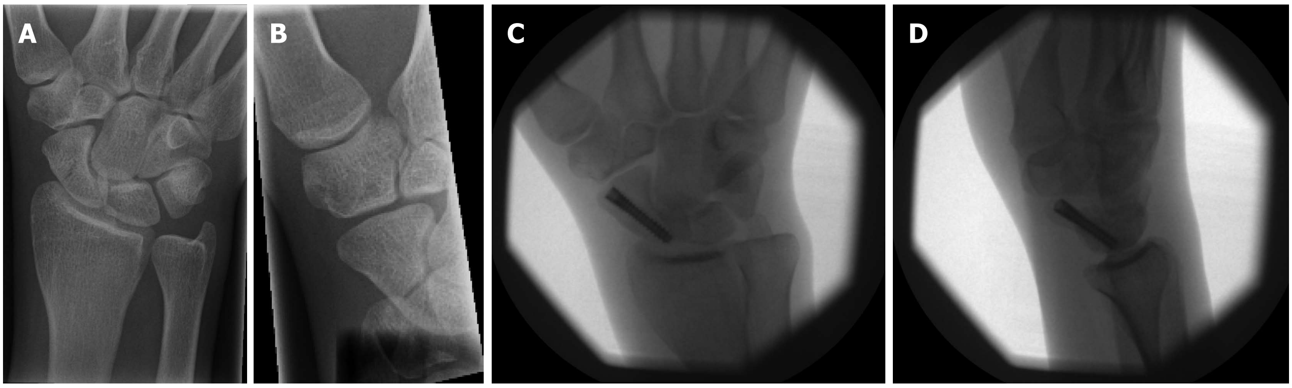

Figure 3 The management of an undisplaced scaphoid waist fracture. A, B: Pre-operative postero-anterior and 45-degree oblique radiographs; C: Intra-operative antero-posterior radiograph; D: Intra-operative lateral radiograph.

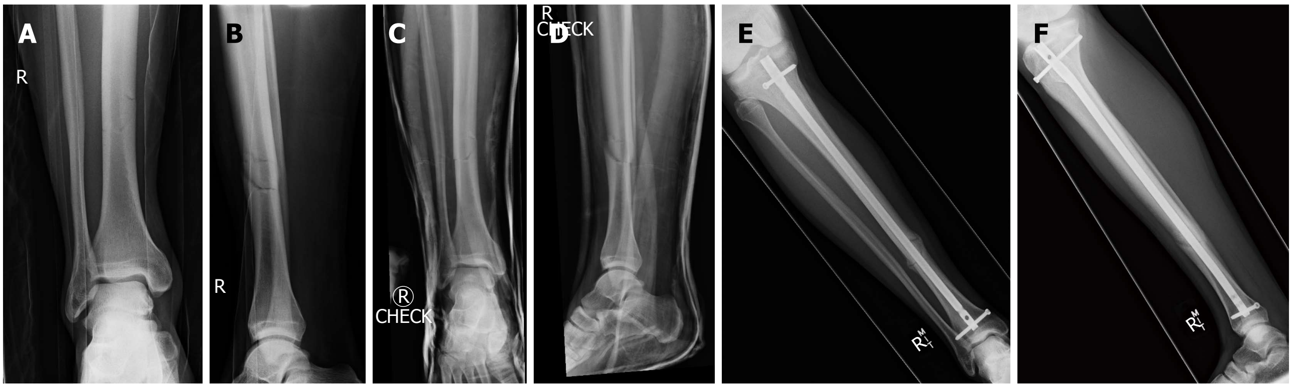

Figure 4 The management of a minimally displaced tibia shaft fracture. A, B: Pre-cast antero-posterior and lateral radiographs; C, D: Initial antero-posterior and lateral radiographs in cast; E, F: Twelve-week post-operative antero-posterior and lateral radiographs.

was an extensive discussion between the patient and his consultant, regarding the options of conservative *vs* surgical management. The risks associated with each form of treatment and the predicted outcomes from both were detailed clearly, with surgical intervention recommended. The patient opted for surgical intervention, with the aim to return to his sporting career as soon as able. He underwent intra-medually nailing of his tibia that day. There were no complications.

Post-operatively, he was weightbearing as tolerated in a moon boot and commenced physiotherapy day 1 post-surgery. He commenced training activities at 16 wk post-surgery and returned to full level soccer at 35 wk post-surgery. At 2-year follow-up, he reports mild anterior knee pain on prolonged kneeling but is otherwise functioning well.

Key message: Primary surgical fixation of undisplaced and minimally displaced tibial shaft fractures can facilitate early return to sport with good recovery of lower limb function.

Case 5: An undisplaced fifth metatarsal jones fracture (Figure 5)

A 27-year-old amateur level soccer player suffered a twisting injury to his left foot after turning rapidly to avoid a tackling opponent. He sustained a left 5th metatarsal Jones fracture, which was undisplaced on radiographs. The injury was closed and distally neurovascularly intact.

He was seen in fracture clinic the next day and following an extensive discussion, regarding the options of conservative *vs* surgical management, detailing the associated risks and predicted outcomes of both, with surgical intervention recommended, the patient chose to persist with conservative management, with an aim to avoid surgery. He was placed into a below knee cast and kept non-weightbearing with crutches for 6 wk. He was then converted to a moon boot orthotic, partial weightbearing with crutches for a further 6 wk.

At his 9 wk follow-up appointment, he reported having returned to gentle running activities and suffering a lot of pain from the fracture site during this. Radiographs at that time showed he was progressing to a delayed union. His consultant then explained the current status of his fracture, detailing the likelihood and timeframe to union with both surgical and conservative management, discussing the associated risks and predicted outcomes of each treatment method, and recommending surgical intervention. The patient then opted for surgical management with an aim to return to sport as soon as able with minimum persisting pain. He

Figure 5 The management of an undisplaced fifth metatarsal jones fracture. A: Initial Antero-posterior and oblique radiographs; B: Nine-week follow-up antero-posterior and oblique radiographs; C: Eight-week post-operative antero-posterior radiograph; D: Eight-week post-operative oblique radiograph.

underwent percutaneous screw fixation of his fracture two days later. There were no complications.

Post-operatively, he was mobilised partial weightbearing with crutches in a moon boot for 2 wk, and then was progressed to full weightbearing over the next 4 wk under the care of the physiotherapists. Repeat radiographs at his 6 wk appointment confirmed progressive union of his fracture. He commenced training activities 8 wk post-surgery and returned to full level soccer 12 wk post-surgery. At his 2-year follow-up, he reports no symptoms from his fracture.

Key message: Primary surgical fixation of undisplaced fifth metatarsal Jones fractures can result in more rapid return to sport and improved union rates than conservative management. If delayed union develops with conservative management, operative intervention still remains a valid option to promote fracture union and facilitate an early return to sport.

Case 6: A radiologically unstable distal radius fracture (Figure 6)

A 26-year-old right hand dominant amateur team cyclist suffered a fall from his bike whilst racing, landing on an outstretched right hand. He sustained a right distal radius fracture that was dorsally displaced and angulated, with associated dorsal comminution. It was a closed injury and was distally neuro-vascularly intact. He underwent closed reduction and below elbow "colles" backslab application under "Bier's Block" Regional Anaesthesia in the Emergency Department. Post-Manipulation radiographs confirmed satisfactory reduction of the fracture.

He was seen in Fracture Clinic the following day, where his consultant had an extensive discussion with him regarding the options of conservative *vs* surgical management, detailing the associated risks and the predicted outcomes for both, and recommending surgical intervention. The patient opted for conservative management with the desire to avoid surgery. He was then reviewed 1 and 2 wk post-injury, with radiographic follow-up and conversion to a below elbow "colles" cast at the 2 wk appointment. Check radiographs at that stage showed the fracture had lost reduction.

His consultant then explained the current status of his fracture, describing the predicted function and outcome with conservative management *vs* surgical management, detailing the associated risks and the predicted outcomes for both, and recommending surgical intervention. He opted for surgical management due to the concerns raised about his resultant hand and wrist function if he developed a malunion of the fracture. The following day he underwent operative fixation of the fracture. Intra-operatively, satisfactory reduction of the fracture was achieved with a volar locking plate alone, although a combined volar and dorsal approach was required, with intra-operative K-wire stabilisation of fracture fragments to achieve this. There were no intra-operative complications.

Post-operatively, he was kept in a futura wrist splint for 3 wk, mobilising as able, and commencing formal physiotherapy within the first post-operative week.

Figure 6 The management of the radiologically unstable distal radius fracture. A, B: Initial postero-anterior and lateral radiographs radiographs; C, D: Post-manipulation postero-anterior and lateral radiographs; E, F: Two-week follow-up postero-anterior and lateral radiographs; G, H: Intra-operative antero-posterior and lateral radiographs.

He was advised to avoid heavy lifting for 6 wk post-surgery. He commenced non-contact "non-upper-limb" training activities at 4 wk post-surgery and returned to cycling at 10 wk post-surgery. At 2-year follow-up, he reports pain in the wrist during prolonged cycles, especially in the cold, though he does not wish to have further procedure to correct this. He reports no other symptoms or functional limitations.

Key message: Primary surgical fixation of radiologically unstable, undisplaced or reduced, distal radius fractures can avoid the likely risk of loss of fracture reduction seen with conservative management, and so facilitate early return to sport.

DISCUSSION

The optimal management of sport-related fractures is key in order to allow athletes to return to sport as quickly as able with the lowest side effect possible. The management principles for these injuries are largely comparable to those the general population; however there remains key examples where management between the athlete and general population differ[19,23-25,30,33-35,39-41,43,45,55,60,64,65,77,78]. It is vital for clinicians to be aware of such examples, and to appropriately inform both the athlete and the sports team of the available management options, as choice of the incorrect treatment can result in reduced return rates to sport and delayed return times to sport[19,23-25,30,33-35,39-41,43,45,55,60,64,65,77,78]. Given the importance of high level sport in modern society, both financially and socially, such decision can have significant consequences.

Ongoing research is required to assess for further optimisation of fracture management within athletic populations, to improve the return rates, return times and symptom profiles following these injuries. Clinicians should keep records of management of these injuries and publish findings accordingly. Similarly, well-organised prospective epidemiological studies should be performed to detect variations in management, and the influence this has on the outcomes following these injuries. Finally, future well-conducted randomised trials assessing the management of these injuries should be actively encouraged and funded, as these will form the key stone to establish the optimal treatment of sport-related fractures.

Despite an ongoing drive to optimise outcomes with these injuries, clinicians treating such athletes should always adhere to robust orthopaedic principles, and should never compromise appropriate periods of immobilisation for accelerated return to sport. Severe consequences can arise from over-accelerated rehabilitation, however the outcome of these injuries shows much promise when managed appropriately. It is recommended that experienced specialists should take charge of the orthopaedic care of high level athletes, as the management of their injuries is a specialised area, with unique treatment strategies and differing goals compared to the standard population.

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EDITORIAL

Role of decision aids in orthopaedic surgery

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Abstract

Medical treatment of patients inherently entails the risk of undesired complication or side effects. It is essential to inform the patient about the expected outcomes, but also the possible undesired outcomes. The patients preference and values regarding the potential outcomes should be involved in the decision making process. Even though many orthopaedic surgeons are positive towards shared decision-making, it is minimally introduced in the orthopaedic daily practice and decision-making is still mostly physician based. Decision aids are designed to support the physician and patient in the shared-decision-making process. By using decision aids, patients can learn more about their condition and treatment options in advance to the decision-making. This will reduce decisional conflict and improve participation and satisfaction.

Key words: Shared decision-making; Decisional conflict; Empowerment; Orthopaedic surgery; Patient decision aid

Core tip: In shared decision-making the caregiver provides expertise and evidence, and the patient and caregiver choose diagnostic and treatment options consistent with their values and preferences. To support patients in discussing their health decisions with their treating physician, patient decision aids have been developed. It is thought that empowering patients to participate in the decision making process with the help of decision aids results in increased satisfaction and physical function and reduced decisional conflict, anxiety, and resource utilization.

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SHARED DECISION MAKING

In shared decision-making (SDM) the caregiver provides expertise and evidence, and the patient and caregiver choose diagnostic and treatment options consistent with their values and preferences. To support patients in discussing their health decisions with their treating physician, patient decision aids have been developed[1]. It is thought that empowering patients to participate in the decision making process with the help of decision aids results in increased satisfaction and physical function and reduced decisional conflict, anxiety, and resource utilization[2].

OUTLINE OF THE PROBLEM

Medical treatment of patients inherently entails the risk of undesired complication or side effects. It is essential to inform the patient about the expected outcomes, but also the possible undesired outcomes. The patients preference and values regarding the potential outcomes should be involved in the decision making process. Even though many orthopaedic surgeons are positive towards SDM, it is minimally introduced in the orthopaedic daily practice and decision-making is still mostly physician based[3-5].

Many surgeons hold the opinion that the inequality between doctor and patient medical knowledge make SDM challenging. Other surgeons say that time constraints, patient characteristics and the clinical situation influence the ability to carry out SDM. Some surgeons claim they already apply SDM in their daily practice as they explain the treatment options and the potential advantages and disadvantages.

On the other hand, there is a high need from patients to be adequately informed and to understand their disease, the available treatment options and their possible outcomes and adverse effects. Poor SDM causes patients to feel insufficiently informed or overwhelmed with the information about their diagnosis and treatment options. As a result, patients experience a high level of decisional conflict, which influences the ability to make a well-considered decision that reflects their personal circumstances, values and preferences as well.

Decision-making can be challenging when evidence-based guidelines are inconclusive or when well-designed, randomized clinical trials show a small and probably non-clinically important difference between two treatments. As surgeons we have an obligation to consider resources, safety, simplicity, efficiency and patient self-management and to share our expertise with patients. Surely, if available evidence is inconclusive, the surgeon should take into account the patient's preferences, rather than to decide for the patient.

The Ottawa Decision Support Framework asserts that participants' decision needs will affect decision quality, which in turn affects behaviour, health outcomes, emotions, and appropriate use and costs of services. Unresolved needs adversely affecting decision quality include: Conflict in making a decision, inadequate knowledge, and unrealistic expectations[6]. To facilitate SDM patients should be actively informed and should be a partner in the decision making process instead of a subject for who is decided.

POSSIBLE SOLUTION

Elwyn *et al*[7] proposed a model regarding how SDM can be practiced in the consulting room when a treatment decision is to be made. They defined three phases in the conversation: (1) choice talk; (2) option talk; and (3) decision talk. The choice talk is comprised of awareness that a choice is to be made. The option talk is to inform patients about treatment options and their pros and cons, often by integrating the use of decision support tools. During the decision talk patient and physician add value to the potential outcome and make a final decision.

Decision aids are designed to support patient is the decision making, their goal of is threefold: (1) It provides facts about the condition, options, outcomes, and probabilities; (2) should help clarify patients' evaluations of the outcomes that matter most to them; and (3) guide patients in the steps of deliberation and communication so that a choice can be made that matches their informed values. By using the decision aids, patients can learn more about their condition and treatment options in advance to the decision-making. They could bridge the (information) gap between doctor and patient[8]. Optimal preparation before consultation will make patients better capable of conversing with their physician and make better use of their time at the outpatient clinic[9]. This will reduce decisional conflict and improve participation and satisfaction[10]. Similar results have been found in studies to other disciplines[11,12]. Increased satisfaction will also have a positive effect on the relationship between patients and their care-providers. Having more realistic expectations is also likely to cause a decrease in the overuse of surgical treatments[13].

Decision aids are especially designed for preference-sensitive treatment options. This involves making value trade-offs between benefits and harms that should depend on informed patient choice. When there is insufficient evidence about the outcomes, there cannot be a single "best" choice defined. The decision is therefore highly depending on the preferences of the patient, how the patient values the benefits and harms of a treatment.

Instead of simply offering generic advice, lectures, laboratory tests or prescriptions, patient are encouraged to participate in care with the help of a decision aid. The decision aid is designed to support, rather than replace, the counseling provided by health care practitioners. Also, the intent is not to burden the individual with the decision, but to help patients and providers work together to make decisions about treatment.

The designing process of a decision aids is carried out by experts about the specific diagnoses and treatment options. The content is based on the most recent evidence from national and international guidelines and publications and should be reviewed by patients on comprehensibility. The design of decision aids should be conform the International Patient Decision Aid Standards, an international collaboration that developed quality criteria for content, development and evaluation. All information should be in accordance with current protocol, which makes the decision aid applicable in every orthopaedic practice. The content should be thorough, but succinct enough that patient can view it in the limited time they have at the outpatient clinic.

A decision aid can be offered by several media but our preference goes out to an online module, having the advantage that it can be adjusted easily to the most recent evidence and that it is available at all times.

PEARLS AND PITFALLS

Although results of the use of decision aids seem promising, research also states that several conditions may be necessary for successful implementation: (1) good quality decision aids to meet the needs of the population; (2) practitioners willing to use decision aid in their practice; (3) effective systems for delivering decision support; and (4) practitioners and healthcare consumers who are skilled in shared decision making[14].

Some strides have been made in achieving these conditions, but the use of patient decision aids will not occur properly without adequate attention to these barriers to implementation[15,16]. The right logistic implementation in the clinical practice is the key for a good use of the decision. It seems the most challenging in adopting the patient informed choice as standard care. Using decision aids should not be experienced as a burden, but as a time saving mechanism. Since it can provide information about treatment options, physicians can devote their consult purely to decision making and patients that have more realistic expectations result in less overuse of treatment options.

Decision aids can be very helpful in the decision-making process, but do not serve as a replacement of the conversation with the patient, it is a useful tool in improving SDM. Some patients may not want to be involved and leave the treatment decision solely up to their physician, arguing that he or she is the expert on the subject. We should respect the autonomy of the patient, even if this means that the decision is attributed to the caregiver. Furthermore, it is our task to make the decision aid applicable and available for all patients and accelerate adoption of SDM as the standard for practice, with resulting benefits to all patients, physicians, and the health care community.

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EDITORIAL

Coronal shear fractures of distal humerus: Diagnostic and treatment protocols

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Abstract

Coronal shear fractures of distal humerus involving the capitellum and the trochlea are rare injuries with articular complexity, and are technically challenging for management. With better understanding of the anatomy and imaging advancements, the complex nature of these fractures is well appreciated now. These fractures involve metaphysealcomminution of lateral column and associated intraarticular injuries are common. Previously, closed reduction and excision were the accepted treatment but now preference is for open reduction and internal fixation with an aim to provide stable and congruent joint with early range of motion of joint. Various approaches including extensile lateral, anterolateral and posterior approaches have been described depending on the fracture pattern and complexity. Good to excellent outcome have been reported with internal fixations and poor results are noted in articular comminution with associated articular injuries. Various implants including headleass compression screws, minifragment screws, bioabsorbable implants and column plating are advocated for reconstruction of these complex fractures. Inspite of articular fragments being free of soft tissue attachments the rate of osteonecrosis and osteoarthritis is reported very less after internal fixation. This article summarizes the diagnostic and treatment strategies for these rare fractures and recommendations for management.

Key words: Capitellum; Trochlea; Elbow; Fracture; Distal humerus; Treatment

Core tip: Coronal shear fractures of the distal humerus are rare, complex fractures. The radiographic evaluation and better understanding by computed tomography helps in the management of these technically challenging

fractures. Open reduction and internal fixation by various approaches and implants is advocated. We aim to review the existing diagnostic and treatment protocols with our recommendations for management.

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INTRODUCTION

Coronal shear fractures of the distal humerus involving capitellum and trochlea account for less than 1% of elbow fractures[1,2]. These injuries result from axial loading of the capitello-trochlear area by the forces transmitted through the radial head and could be associated with more complex distal humeral fractures and dislocation with concomitant ligamentous injuries[1,3]. The complexity of these fractures in recent times has been better appreciated by digital imaging and computed tomographic scans[3-6]. Open reduction and internal fixation provides anatomical reduction, stability and early mobilisationand has become preferred treatment. Closed reduction, immobilisation and fragment excision are known to be associated with poor outcomes[7,8]. Failure of fixation or non-anatomic reduction leads to articular incongruity, posttraumatic arthrosis, stiffness and potential ulnohumeral instability[8-10]. The intraarticular and complex nature of these fractures makes optimal surgical exposure and implants debatable. The surgical approach and reconstruction of articular surfaces is technically challenging and several extensile approaches and fixation devices for reconstruction of articular surfaces are propagated in recent case series[3-5,8]. For articular surface reconstruction various implants including headless screws, miniscrews can be used. Despite several case series the management protocol is still not defined. In this article we review the existing literature regarding diagnostic advancements and treatment protocols for these complex fractures.

RELEVANT ANATOMY

The capitellum is described as portion of spherical surface of distal humerus projecting anterior and inferior as a smooth, round hemispherical structure. Its articular surface does not extends posterior to the coronal plane of humerus[6]. The axis of flexion and extension of the elbow joint passes through the capitellum and range of flexion that develops from this centre is 0-140 degrees[11]. Intact radiocapitellar articulation is necessary for valgus and longitudinal stability of the elbow and forearm. Capitellar excision leads to coronal plane instability when medial structures are injured along with. Moreover ulnotrochlear disruption will lead to instability and arthritis over years. Valgus instability and painful distal radioulnar junction have been reported following excision[3].

The mechanism of injury in these fractures is fall on outstreched arm with complexity of fracture propotional to acting force. Often direct axial compression of radial head with capitellum is responsible for fracture pattern. Spontaneous reduction after elbow instability will also lead to injury pattern. The incidence is higher among women because of high rate of osteoporosis and carrying angle difference than men[5-7]. Usually the associated injuries are of lateral collateral ligament, trochlea, epicondyle, condylar and elbow dislocation[3-8]. Lateral collateral ligament injury is seen in 40% and radial head fracture is reported in 30% of the patients[2,8,9].

CLASSIFICATION

The most commonly used classification system is that of Bryan and Morrey with type Ⅳ fractures described by McKee *et al*[10] and Bryan *et al*[12]. In this system, type Ⅰ fractures are complete capitellar fractures with little or no extension into the lateral trochlea, type Ⅱ fractures are anterior osteochondral fractures with minimal subchondral bone; and type Ⅲ fractures are comminuted or compression fractures of the capitellum. McKee *et al*[10] described type Ⅳ fractures in six patients with coronal shear fractures of capitellum that extended medially including most of the trochlea identified by the presence of the pathognomonic "double arc sign" on lateral radiographs.

As per Trauma Association (OTA)/AO classification system, capitellarfracturesare denoted 13B3-distal humerus, partial articular, and frontal plane- and are further subclassified as B3.1, indicating isolated capitellum fractures; B3.2, trochlea fractures; or B3.3, capitellum and trochlea fractures with a secondary fracture line in the sagittal plane. Capitellum and trochlea fractures may also be components of more complex, multifragmentaryintercondylar fractures (*i.e.*, 13C3.3)[13].

Dubberley *et al*[8] recently proposed a treatment - and outcome-oriented classification of capitellum and trochlea fractures. Type Ⅰ fractures involved the capitellum with or without the lateral trochlear ridge; type Ⅱ injuries involved the capitellum and trochlea as a single piece and type Ⅲ injuries consisted of fractures of both the capitellum and the trochlea as separate fragments. Each fracture type was additionally subclassified as A or B based on the presence of posterior condylar comminution, which was found to influence surgeon choice of fixation method and outcome.

Based on radiographs and intraoperative findings Ring *et al*[7] identified five articular segment injury patterns (types Ⅰ to Ⅴ) distal to the base of the olecranon fossa, representing progression of the severity of the articular injury beyond an isolated capitellum fracture. Most of the fractures required an extensile lateral approach to the elbow to reduce and reconstruct the articular surface with buried implants. An olecranon osteotomy was required when the articular fracture extended to the medial epicondyle (type Ⅴ).

CLINICAL EVALUATION

Careful history of injury mechanism should be done followed by evaluation of the elbow to identify open fractures and movement block. Elbow instability is best assessed under anaesthesia and is difficult in emergency due to pain and spasm. A thorough neurovascular and bony examination should be done. Clinically crepitus with elbow movements and painful limited range of motion or impingement is often present. Pain is mostly localized along lateral aspect of the elbow but can be diffuse due to ligamentous and associated injuries. Examination is often difficult due to pain and swelling. Associated injuries, wrist and shoulder joints, forearm compartments and secondary musculoskeletal survey are a must in these patients.

IMAGING

The anteroposterior view radiograph in most cases cannot show the fracture fragment and a lateral view is essential[1-3]. The oblique view also details more of the injury hence standard AP, lateral and radiocapitellar views should be done in every case.

On lateral view isolated capitellar fracture appears as half-moon shaped fragment lying free[12]. The capitello-trochlear fracture or type Ⅳ McKee[10] is typically described as double arc sign on lateral view but this sign is not pathognomonic of this type as it may not be present in all cases. A simple capitellar fracture on radiographs turns out to be a complex fracture intraoperatively with most of them having part of trochlea involved[1-4]. This sign thus may be misleading as isolated trochlea also present as half-moon or double arc sign[14]. In our previous series none of the six patients with type Ⅳ fractures show this sign. Three patients were associated with lateral condyle and in other three the fragment was internally rotated[15]. Imaging of the joints above and below the level of injuries will reveal bony injuries and soft tissues should be judged by clinical evaluation and magnetic resonance imaging. Plain radiographs have a 66% sensitivity and a negative predictive value of 63%-67% for fractures extending to trochlear region[1,2].

The inability to determine the extent, thickness and size of the fragment in standard radiographs has necessitated some authors to propose a two and three dimensional computed tomography (CT) scan in order to establish a better preoperative description of the injury and thorough analysis of anatomical features of the fracture[1-7]. This approach has a profound effect on implant choice and therapeutic strategy (Figure 1). Three-dimensional (3-D) scans are also useful when evaluating for concomitant injuries like transcondylar or intercondylar distal humerus fractures. On the CT scan, if the fracture extends into the medial epicondyle or if posterior involvement of the trochlea is indicated, the preferred surgical approach might be through an olecranon osteotomy[3,7]. Concomitant capitellar fractures and radial head fractures may be missed on plain radiographs, but diagnosed on CT scan[6]. Fractures of radial head, olecranon, lateral or medial epicondyle, lateral and medial columns, lateral collateral disruption and dislocation elbow are known concomitant injuries and should be taken into consideration.

CLOSED REDUCTION/EXCISION

Closed management has been reported in some series and is a reasonable option only if strict anatomic alignment can be obtained. Moreover reduction techniques are difficult in swollen elbows and later risk of displacement is there leading to complications[6]. Prolonged immobilization often leads to elbow stiffness. If comminution has occurred, the fracture fragments may act as loose bodies, and mechanically block elbow motion[2,3]. Intact radiocapitellar articulation is essential to both valgus and longitudinal stability of elbow and forearm. Capitellar excision creates instability in coronal plane when medial structures are disrupted. Poor clinical outcome were reported in more than 50% of patients at follow up after capitellar excision in various series[2,4]. Other complications are valgus instability and painful distal radioulnar joint. The non-operative treatment is reserved only for medically unfit patients.

OPEN REDUCTION AND INTERNAL FIXATION

In various series good to excellent outcomes have been reported with ORIF in majority of patients with these fractures. The superior results are attributed to anatomic reduction and stable fixation with early range of motion excercises[1,3,5-8,11,14,15].

APPROACHES

Extensile lateral approach

This is most commonly used approach for isolated capitellar and Type Ⅳ capitellum farctures[1,3,6,9,15,16]. Under regional/general anaesthesia the injured elbow is assessed clinically for ligamentous stability. It is done under tourniquet control. A skin incision is made centered over the lateral epicondyle extending from the anterior aspect of the lateral column of the distal end of the humerus to approximately 2 cm distal to the radial head (Figure 2). A continuous flap is raised by elevating the common extensor origin along with the anterior capsule and connected to the Kocher interval distally with forearm pronated. In patients with a lateral epicondylar fracture fragment, the epicondylar fragment with the lateral collateral ligamentous complex origin is reflected distally to enhance exposure. Fracture

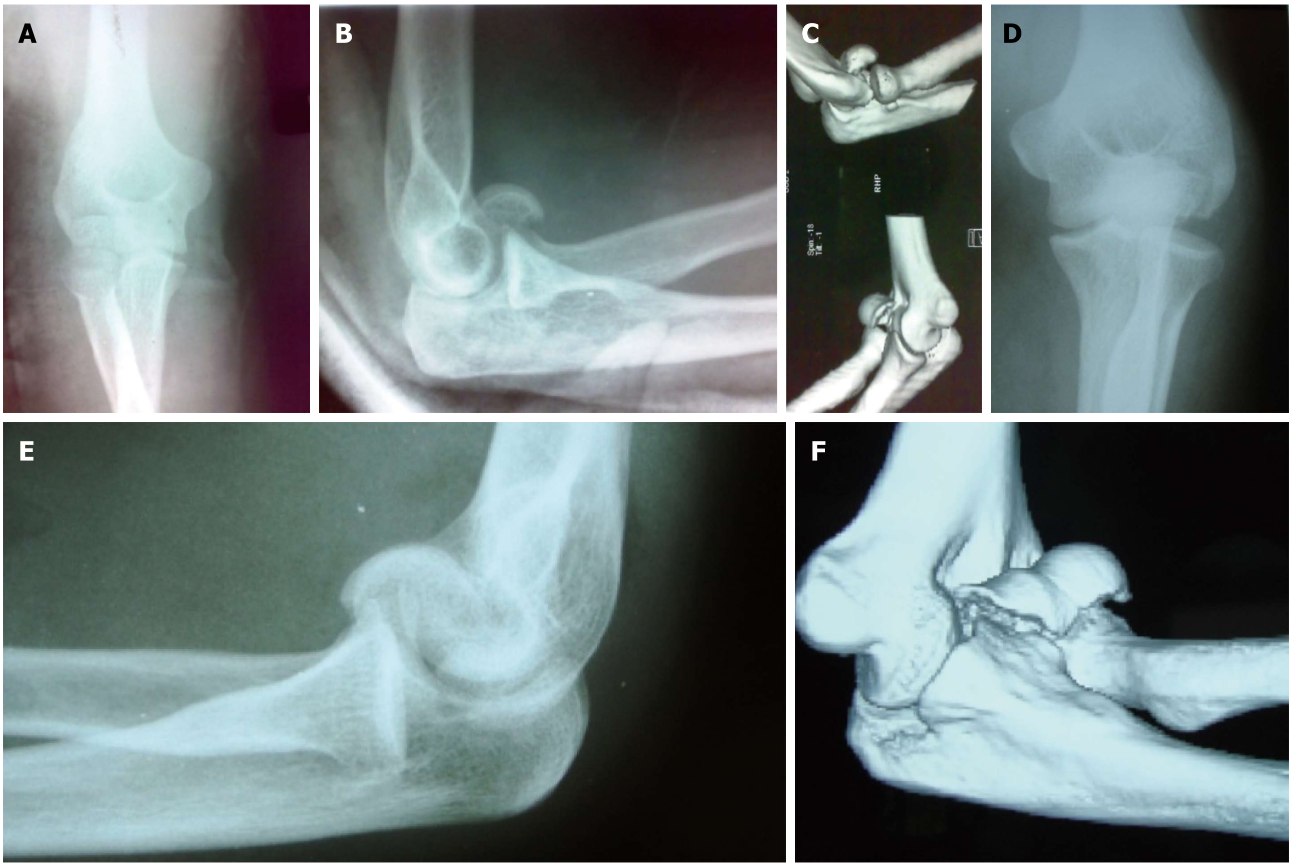

Figure 1 Radiographic and three dimensional tomograhic images of type 1 and type 4 capitellum fractures. A: Thirty-year-old female with history of fall presented with pain in the elbow region. On anteroposterior view no fracture is seen; B: On lateral view capitellum fracture is seen; C: Her computed tomogram confirms type 1 fracture; D: Thirty-four-year-old male presented with elbow pain after road side accident. Anteroposterior view shows noobvious fracture; E: Lateral view shows a capitellar fracture; F: His computed tomogram shows type 4 capitellotrochlear fragment. The choice of implant and approach is decided preoperatively if detailed imaging is done.

fragments are reduced and provisionally fixed with K-wires. The large articular fragments can be fixed by miniscrews on table. The proper position of the debrided fragment on the fracture bed should be located precisely by using K-wires as joy stick. The guide to correct positioning is the medial remaining trochlear fragment and trochlear ridge rather than lateral articular congruence. Two screws are used to fix the fracture and provide rotational control. Supplemental fixation with mini-fragment screws or Kirschner wires can be used to reconstruct complex fracture patterns. The radial wrist extensors are repaired to the soft-tissue cuff on the lateral supracondylar ridge, and the Kocher interval is closed in continuity with the proximal exposure. The remainder of the wound is closed in layers.

Anterolateral approach

This approach has advantage that it approaches the capitellum and trochlea without disruption of LCL or an olecranon osteotomy[17,18]. The incision begins proximally overlying the lateral aspect of the biceps muscle. It is directed medially to cross the elbow joint obliquely and then directed back laterally over the proximal forearm (Figure 3). The surgical dissection continues between the biceps and brachioradialis origin. The lateral antebrachial nerve is protected. The radial nerve is identified on the deep surface of the brachioradialis and retracted laterally. The dissection continues distally to the biceps tendon. Brachialis is reflected medially off the distal humerus metaphysis and elevated distally to expose the capsule. The capsule is opened longitudinally directly over the displaced fracture fragment. The fragment is reduced under direct visualisation and provisionally K wire is fixed from anterior to posterior. Then wire can be exchanged for headless screws or bioabsorbable pin. The skin and subcutaneous tissue is closed with absorbable sutures and elbow is immobilized in back splint. We have found this approach suitable for capitellum fractures with excellent results.

Olecranon osteotomy

When the medial extension of the fracture fragments is significant and there is significant posterior comminution the olecranon osteotomy approach provides better visualisation and fixation ease[7,8,19,20]. A posterior skin incision is used. Full thickness skin flaps are created medially and laterally. The ulnar nerve is mobilized and isolated. An apex distal chevron osteotomy is created at the midlevel of olecranon. The olecranon fragment and triceps are then reflected proximally. The fixation

Figure 2 Type 4 capitellum fracture with fracture lateral condyle in adult male-radiological and clinical outcome. A: Anteroposterior view of left elbow showing type 4 capitello trochlear fragment with lateral condyle fracture in a 34-year-old male after road traffic accident; B: Lateral view showing the fracture fragment. The internally rotated fragment is not giving double arc appearance; C: Lateral extensile approach was done. Intraoperative picture; D: The fragment was free of soft tissue attachments. It was debrided on table and repositioned; E: It was fixed with two cannulatedcancellous screws from posterior to anterior direction and lateral condyle was fixed with K-wire; F: Follow-up anteroposterior view; G: Lateral view. Follow-up shows good consolidation; H: Excellent supination; I: Excellent pronation; J: Flexion; K: Extension. Patient is having excellent MEPS score.

Figure 3 Type 1 capitellum fracture in young female showing anterior approach detail and clinico-radiological follow-up. A: Twenty-two-year-old nursing student had a fall on left elbow and had type 1 capitellum fracture; B: Anterior approach incision; C: Radial nerve exposed; D: Capitellum fracture surface visible; E: Provisional fixation with K-wire; F: After reduction and fixation with K-wire; G: Lateral radiograph showing fixation with headless screws; H: Excellent extension at follow-up; I: Flexion.

by this approach may utilise headless, cannulated screws in combination with reconstruction plates. The osteotomy may be repaired with tension band construct or cannulated screw system. In studies published till now the differences between the outcomes between extended lateral and the posterior midline approach are negligible[3,9,19,20].

Arthroscopic assisted reduction

There are very few reports on reduction and fixation by arthroscopic assisted methods and this is useful for excsion in very small fragments[21-23]. Moreover indications of fixation of complex fractures by this method are unclear and further studies are required to doucument any advantage over previous techniques.

Isolated trochlea fracture

Standard medial approach with medial epicondylectomy is performed[14]. The ulnarnerve is identified and secured. The trochlear fractureis exposed. The fragment is debrided of tissues and the fracture bed is prepared. Apposition is achieved and secured with a smooth K-wire. Two Headless screws can be used from anterior to posterior direction for definitive fixation. Articular congruency is restored and range of motion of the elbow is checked. Medial epicondyle is secured with mini screws and the wound is closed in layers.

IMPLANTS AND RECONSTRUCTION

Supplemental bone graft may be required in impacted fragments after their elevation[24-26]. Small articular fragments not amenable to fixation by 3.5 mm screws should be fixed by 2.7 mm miniscrews and buried in subchondral bone[3,15,23] (Figure 4). The terminally threaded Herbert screws and fully threaded acutrack provide


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Figure 4 Type 4 capitello-trochlear fracture with medial epicondyle and olecranon chip fracture in adolescnt. It was managed by articular reconstruction by lateral approach. A: Fourteen-year-old male presented with left elbow type 4 capitellum fracture after road traffic accident. Associated injuries are medial epicondyle and chip fracture olecranon. Anteroposterior view; B: Lateral view showing double arc sign; C: Extensile lateral approach was done. Intraoperative picture showing fractured fragment; D: Major capitellar fragment debrided on table; E: On table reconstruction of the articular fragment was done by 2.7 mm screw; F: Final fixation was done by two headless screws; G: Follow-up AP view; H: Lateral view; I and J: Rotations at follow-up; K: Flexion at follow-up. The patient is having excellent Mayo Elbow Performance Score; L: Extension. The lag is attributed to type of fracture and the approach.

fracture site compression through variable thread pitch designs. Biomechanical data have demonstrated that acutrak screw fixation of capitellum fractures is superior to posteroanterior 4.0-mm cancellous lag screws and Herbert screws but in clinical series this has not been demonstrated[27,28]. Divergent fashion placement screws is recommended to ensure rotational control with sufficient spread of screws to avoid iatrogenic fracture of the capitellum[29,30]. Supplemental fixation is often required to reconstruct more complex fracture patterns with posteroinferior/lateral metaphyseal comminution and/or trochlear extension. Supplemental fixation options include minifragment screws, threaded K-wires, and bioabsorbable pins. When extensive posterolateral comminution is present, plating of the lateral column with pelvic reconstruction, precontoured, or locking plates may be required to buttress the lateral column[31]. Lateral collateral ligament may be repaired primarily to its origin using transosseous sutures passed through drill holes or suture anchors or using figure-of-8 tension-band wire technique in cases of avulsion or fractured parts[3]. Medial collateral ligament disruption may require primary repair or a hinge orthosis. Incomplex fractures with comminution authors had similar results in terms of complications, the need for removal of hardware, and poorer results occurred in the type 3 fractures[8,11]. This probably reflects difficulty in reconstructing small fragments using the devices available at present. The on table reconstruction of radial head fractures and capitellar fractures had been reported with excellent results[15,32]. Further development of devices that allow reconstruction of this specifically shaped articulation may improve the outcome further in the future.

POSTOPERATIVE PROTOCOL AND FOLLOW UP

The splint is removed in approximately 1 wk, and the patient is encouraged to do gentle active range of motion exercises. When extensive intra-articular comminution has occurred, the elbow may need to be immobilized for a longer period of time. Passive range of motion and strengthening is not started until bony healing is evident, at about 6 to 8 wk postoperatively. We advocate use of oral indomethacin (25 mg, three times daily), for 4 wk to minimize the possibility of heterotopic ossification in cases with elbow dislocation. With medial collateral ligament/associated injuries, the limb is placed into a functional brace. In the presence of concomitant ligamentous or functionally equivalent osseous injuries, a ligament-specific protocol is instituted, with mobilization in pronation (lateral-sided injury) or supination (medial-sided injury). Strengthening exercises are initiated on clinical and radiographic evidence of fracture union.

A number of series have reported on patient outcomes following ORIF of capitellum and trochlea fratures[2,8,9,11,15]. Only a few have attempted to co-rrelate clinical and functional outcome with fracture subtype[3,8,11,15]. A functional arc of ulnohumeral motion is achieved in most of these patients despite a mean postoperative flexion contracture of 14.5° to 17.5°. In a cohort of 28 patients, Dubberley *et al*[8] reported significantly inferior functional elbow evaluation scores when there was medial trochlear extension and/or capitellum-trochlea comminution. Fracture subtypes differed significantly with respect to grip strength and flexion-extension power, but not with respect to elbow or forearm motion. In other series patients with type Ⅳ fractures patients had significantly reduced terminal flexion and net ulnohumeral arc and greater loss of terminal extension compared with patients with type Ⅰ fractures[3]. Ashwood *et al*[11] validated the concept of posterior comminution and articular fragmentation as an important determinant of outcome after capitellar and trochlear fractures. The poorer results occurred in patients with severe injuries associated with posterior comminution of the humerus and who required more extensive reconstructive procedures[11]. The complications following surgical treatment include fixation failures, pain, instability, stiffness and neurologic complications. Hardware complications include impingement and subcutaneous positioning. Total elbow arthroplasty represent a salvage treatment for severe arthrosis, osteonecrosis, nonunion/malunion[33].

CONCLUSION

Coronal shear fractures involving the capitellum and trochlea are significant articular injuries and the changing trends in their management reflects better understanding of complex articular fracture pattern. The recommendations include use of CT, open reduction and internal fixation of all displaced fractures and selection of approach depending on fracture pattern. We recommend use of anterolateral approach for these fractures to prevent postoperative flexion contracture. With posterior comminution, olecranon osteotomy is the preferred approach. Early range of motion should be initiated following stable fixation. The implants of choice are headless cannulated screws and supplementation should be done by minifragment screws/pins/column plates. The counseling about postoperative flexion contracture and sequelae should be done in complex fracture patterns. The increased flexion contracture in these patients may be due to the increased severity of the injury and to the extended surgical dissection needed to facilitate exposure of the anterior articular segments. The severity of articular communition significantly reduces the functional outcome scores of elbow. Although earlier reports indicated no cases of osteonecrosis or collapse in the region of the fracture, these have been documented with longer follow-up. The on table reconstructions have been reported with success in these fractures and reconstruction should take precedence over excision to restore articular surfaces.

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REVIEW

Use of antibiotic-loaded cement in total knee arthroplasty

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Abstract

Bone cement has the capacity to release antibiotic molecules if any antibiotic is included in it, and these elution properties are improved as cement porosity is increased. *In vitro* studies have shown high local antibiotic concentration for many hours or few days after its use. Antibiotic loaded bone cement (ALBC) is helpful when treating an infection in total knee arthroplasty (TKA) revision surgery. The purpose of this paper was to review the evidence for the routine use of ALBC in TKA in the literature, its pros and cons. Many authors have recommended the use of ALBC also in primary TKA for infection prophylaxis, but the evidence based on data from National Registries, randomized clinical trials and meta-analysis suggest a protective effect of ALBC against infection when used in hips, but not (or only mild) in knees. A possible explanation to this finding is that the duration and quantity of locally elevated antibiotic levels after surgery are smaller in TKA, due to the smaller amount of cement used for fixation in TKA-only a layer in the bone surface. There are some concerns about the routine use of ALBC in primary TKA as prophylaxis against infection: Firstly, there is a risk of hypersensivity or toxicity even when the chance is highly improbable. Secondly, there is a reduction in the mechanical properties of the cement, but this can be probably neglected if the antibiotic is used in low doses, not more than 1 g per 40 g cement package. Another significant concern is the increased economic cost, which could be overlooked if there were enough savings in treating fewer prosthetic infections. Finally, there is also a risk of selection of antibiotic-resistant strains of bacteria and this could be the main concern. If used, the choice of the antibiotic mixed in ALBC should consider microbiological aspects (broad antimicrobial spectrum and low rate of resistant bacteria), physical and chemical aspects (thermal stability, high water solubility), pharmacological characteristics (low risk to allergic reactions or toxicity) and economic aspects (not too expensive). The most commonly used antibiotics in ALBC are gentamicin, tobramycin and vancomycin. In conclusion, there is a paucity of randomized clinical trials in the use of ALBC in primary TKAs and the actual evidence of the effect of ALBC in reducing the risk of infection is insufficient. This, in addition to concerns about patient safety, risks of increase in the antibiotic resistance of microorganisms and the increase in costs in the procedure, lead us to recommend a cautious use of ALBC, perhaps only in high-risk patients (immunocompromised, morbidly obese, diabetic and patients with previous history of fracture or infection around the knee) unless the benefits of ALBC use were fully proven. Meanwhile, the rigorous use of peri-operative prophylactic systemic antibiotics and adoption of efficient antiseptic procedures and improved surgical techniques must be considered the gold standard in infection prevention in TKA surgery.

Key words: Antibiotic loaded cement; Antibiotic toxicity; Total knee arthroplasty; Infection; Prophylaxis; Economic cost; Antimicrobial resistance

Core tip: The bone cement capacity to release antibiotic molecules has been helpful in the treatment of prosthetic infections. Many authors have recommended the use of antibiotic loaded bone cement (ALBC) in total knee arthroplasty (TKA) for infection prophylaxis, but the actual evidence suggests a minimal, if any, protective effect against infection in TKA. There are some concerns against its routine use in primary TKA: The risk of toxicity, possible mechanical properties reduction, a significant increase in the cost of the cement, and the risk of selection of antibiotic-resistant bacteria. We recommend a cautious use of ALBC, perhaps only in high-risk patients, unless its benefits were better proven.

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INTRODUCTION

The development of an infection after a total knee arthroplasty (TKA) is a serious complication, which is difficult to cure with antibiotics because the biofilm mode of growth protects the infectious bacteria against the systemic antibiotics effects and the host immune system[1-3].

TKA infection usually requires revision surgery, causes significant limitation and less satisfaction in the patient[4], long hospitalization and very expensive procedures to treat it[5]. The usual rate of infection after TKA is 1%-2%[3,5,6], but the rates tended to decrease in the last decade probably because of an improved patient selection and patient optimization, increased awareness of correct systemic antibiotics and chlorhexidine decolonization protocols[7]. In the last years some authors in large retrospective series have reported deep infection rates lesser than 1%, using antibiotic-loaded bone cement (ALBC)[8,9] or without ALBC use[10].

Since the use of ALBC was introduced by Buchholz and Engelbrecht[11] in 1970 by adding gentamicin to the Palacos bone cement, demonstrating the helpfulness of polymethylmethacrylate (PMMA) as a carrier for topical delivery of antibiotics, the use of antibiotics in the cement has been widely used in the revision surgery of infected arthroplasties because its use seems to be helpful in the treatment of infection, and in non-infected revisions, where a higher risk of infection is well-known[12-14].

There is a consensus in using systemic antibiotics perioperatively to prevent TKA infection. An experimental study suggested that the use of ALBC with vancomycin might lengthen the duration of antibacterial activity in the joint from 28 to 40 h[15].

The use of ALBC in primary TKA to prevent infection varies in different countries. The percentage of orthopaedic surgeons routinely using ALBC in primary TKA is higher than 90% in countries such as the United Kingdom[16], Norway[17,18] or Sweden[4], although the scientific background for its use is uncertain[13,14], while its use is much lesser in other countries like the United States[19-22] and other European countries such as Spain, Poland or Russia[23]. Moreover, in many countries, such as Australia, the use of ALBC is increasing year after year even when the yearly report of the Australian National Joint Replacement Registry reports that the risk of revision for infection or the risk of revision for any cause are the same if an ALBC or a plain cement is used[24].

The use of ALBC to reduce the incidence of infection in primary TKA has been encouraged based on the Nordic National Registries of Arthroplasties results that showed a reduction in the rate of infection using ALBC, mainly in total hip arthroplasties (THA)[17,18,25]. Nevertheless, the evidence in TKA is lower than in THA: there is a small number of prospective studies that have evaluated the rate of infection in groups with plain cement or ALBC, and the results of them seem to be controversial[21,26].

The objectives of this article are: (1) To review the antibiotic elution properties of PMMA; (2) To update the available evidence supporting the routine use of ALBC in TKA based on its effect in reduction of deep infection and on risk of revision surgery for infection or for any cause; and (3) To highlight the main concerns about the routine use of ALBC in primary TKA: A possible reduction in the mechanical properties of the cement, risks of allergic reactions or toxicity because of the antibiotics, the risk of development of antimicrobial resistances, and the economic cost.

ANTIBIOTIC ELUTION PROPERTIES OF PMMA

During the polymerization reaction of bone cement

Table 1 Ideal properties of antibiotics to be used in antibiotic loaded bone cement

Broad antibacterial spectrum
Low percentage of resistant bacteria
Low protein binding
Low risk for allergic reactions
Low toxicity risk
High water solubility
Thermal stability
Chemical stability

there is an increase in temperature that causes the formation of air bubbles. Some of these bubbles escape from cement, but some other do not escape, causing some porosity in it. The final porosity of bone cement depends not only on the composition and method of manipulation, but also on the viscosity of the cement[2]. An increased cement porosity causes a decrease in the mechanical properties, but an increase in the capacity of the cement to release antibiotic molecules if any antibiotic is included in it.

The composition of different bone cements differs and so the potential for release antibiotics is not the same: Palacos cement seems to release higher gentamicin concentrations than other cements because of its high viscosity[27]. But the elution can be different with different antibiotics: CMW1 was better than Palacos and Simplex in the release of vancomycin[28].

The initial release after exposure of ALBC to a fluid is mainly a surface phenomenon, while sustained release over the next days is a bulk diffusion phenomenon[2]. The elution of antibiotics from ALBC has been advocated to be effective for many days[29], but some other authors sustain that the process is sufficient for only few hours[30,31]. Nevertheless, the hydrophobicity of the cement limits the antibiotic release at less than 10%, and most of this antibiotic is released during the first hours after surgery[2,32,33]. Three days after its use there is no effect of antibiotic in the ALBC in *in vitro* studies[33].

The elution can be improved by using liquid antibiotics instead of powder ones in the cement, but this choice creates a reduction in the compressive strength of the cement[34]. The use of vacuum-mixing of the cement causes a reduction in the cement porosity[2] and different effects on the elution properties of antibiotics in different commercially available cements[35]. However, the vacuum-mixing technique has been related to lesser quantity and size of bubbles in the cement, and the lesser porosity has been related to a worse elution of the antibiotic in the surrounding tissues[36].

The ideal properties of antibiotics to be used in ALBC are related in Table 1. The most commonly used antibiotics for its use in ALBC are aminoglycosides (mainly gentamicin and tobramycin)[36]. These antibiotics maintained their antibacterial properties after being mixed with PMMA, keeping a greater duration of the activity against most of the pathogen bacteria when *in vitro* analysed[37,38]. Another frequently used antibiotic in ALBC is vancomycin because of its activity against Gram-positive pathogens (the most frequent causes of TKA infection), but it lacks of any effect on Gram-negative[38].

The association of two or more antibiotics in the cement has been used for the treatment of prosthetic infection. The systemic use of more than one antibiotic is justified because of possible synergistic combination of antibiotics. Vancomycin and aminoglycosides (gentamicin or tobramycin) is a usual combination of antibiotics used in bone cement, and combining tobramycin and vancomycin in bone cement improves elution of both antibiotics *in vitro* and may translate into enhanced elution *in vivo*[39]. Nevertheless, there is no sufficient clinical experience in the use of more than one antibiotic in cement in the prevention of infection of TKA.

EFFECTS OF ALBC ON INFECTION PROPHYLAXIS IN TKA

Data from studies based on National Registries

In THA there are some studies from the Norwegian Arthroplasty Registry that have proven that the rate of revision because of infection and the rate of revision for any cause was lower if an ALBC was used, but all these data refer to hip surgery[18,25,40]. As far as we know, there is only one randomized study that has proved that gentamicin loaded cement was more effective in reducing the infection rate in THA than systemic antibiotics[41]. However, this reduction showed no statistical significance in a later revision of the same group with a longer follow-up[42].

In TKA, there is some evidence from the Finnish Registry[14] of a lower infection incidence if an ALBC was used in primary TKA, but the relative risk (RR) (1.35, 95%CI: 1.01-1.81) is much lower than the previously reported in THA. Moreover, data from other Registries do not support the Finnish data: in the Australian Registry in the short, mid or long-term follow-ups, when data from more than 100000 TKA were analysed there was no difference between ALBC and plain cement in the rate of revision because of infection (0.4%-0.5% at 1 year, 1.0% at 5 years, 1.3% at 13 years) or in the rate of revision for any cause (5.4% *vs* 5.3%, RR 1.07)[24]. In another recent analysis of two-year revision rates in the Canadian Joint Replacement Registry analysing more than 20000 TKA inserted with ALBC and more than 16000 with plain cement there were no significant differences between groups in total revision rates, even when age, sex, comorbidities and diabetes were standardized (1.40% *vs* 1.51%). The revision rates for infection were also similar in both types of cement[43].

Data from randomized trials and large comparative series

There is even more confusion when we analyse the results of prospective studies. A randomized controlled trial (RCT) that compared cefuroxime loaded cement with plain cement in 340 TKA found a decrease in the deep infection incidence in the antibiotic group, but the deep infection incidence was higher in this study[26]. Two more papers from the same researchers recommended the use of ALBC in patients with a higher risk of infection: diabetic patients[44] and rheumatic patients[45].

On the other hand, some other studies have not found a decreased infection incidence if ALBC was used: in a large retrospective study including more than 22000 TKA Namba *et al*[46] did not find that the use of tobramycin or gentamicin loaded cement prevented infection after TKA in the general population (in fact the infection rate was higher in the group of patients treated with ALBC, even after a multivariate stepwise logistic regression analysis was done), or in the subgroup of diabetic patients[46]. In another prospective non-randomized study including 1625 TKA, Gandhi *et al*[21] was not able to find that the use of cement with tobramycin was associated with a decrease in the infection rate[21]. More recently, Hinarejos *et al*[47] in the larger randomized clinical trial about ALBC in TKA, analysing almost 3000 patients, found that ALBC with erythromycin and colistin does not decrease the incidence of global infection or deep infection, which is 1.4%, considered to be in the standards of infection incidence, not as the high incidence reported in the randomized study by Chiu *et al*[26].

Data from meta-analysis

A meta-analysis studied the efficacy of ALBC in THA and considered that the rate of deep infection could be reduced from 2.3% to 1.2% with its use. The RR of revision was also significantly reduced (0.72) when using ALBC in THA[48]. However, this effect has not been found in the knee in none meta-analysis.

Recently, a meta-analysis has studied the protective effect of ALBC in TKA and THA[49]. They found that the superficial infection rate was similar with ALBC and with plain cement. A reduced rate of deep infection could be found when analysing only the trials on THA, but there was no effect in the trials on TKA or in those including both hips and knees. The possible effect of antibiotics in the cement in hips is not necessarily the same as in knees. A second recent meta-analysis about the use of ALBC only in TKA has also failed to find differences in the deep infection rate including only RCTs or including also comparative trials with enough quality[50].

In summary, the evidence based on data from some Registries, RCTs and meta-analysis suggests a protective effect of ALBC against infection when used in hips, but not in knees. A possible explanation to this finding is that the duration and quantity of locally elevated antibiotic levels after surgery are smaller in TKA, due to the smaller amount of cement used for fixation in TKA (usually only a thin layer on the surface)[43].

MECHANICAL PROPERTIES OF ALBC

In vitro studies suggest that the addition of antibiotic to PMMA causes a decrease in the compressive and tensile strengths of bone cement by small quantities of antibiotic powder, and continues to decrease as doses of antibiotic increase[51]. It is widely accepted that high-dose ALBC (more than 2 g per 40 g of cement) should only be used in cement spacers or beads, which are used temporarily (usually some weeks) in the treatment of prosthetic infections because of the worsening of mechanical properties of the cement. For the prophylactic use of ALBC the antibiotic should be used at low doses, less than 2 g per 40 g of cement, because the main objective of the cement is the implant fixation[31,52]. Other authors are more restrictive and based on *in vitro* studies suggest not to add more than 1 g of antibiotic per 40 g of cement because of the decrease in the mechanical properties, which can be perceived with only 1 g of antibiotic[33].

The negative effect of antibiotics on the mechanical properties of the cement could appear even in the low-dose antibiotics when using some antibiotics such as imipenem[38], or if liquid antibiotic instead of powder is used[34,53].

The use of vacuum-mixing of the cement causes less porosity[35] and less reduction of the tensile fatigue strength of ALBC than hand-mixing[22,54]. Nevertheless, as it has been said before, the reduction in the cement porosity is desirable in terms of mechanical strength of the cement, but not in the antibiotic elution properties.

When the aseptic loosening has been analysed comparing ALBC and plain cement, trying to refuse a negative effect of adding low doses of antibiotics on the mechanical properties of PMMA, there was not a significant difference in the incidence of aseptic loosening when using one or the other type of cement[26]. In radiostereometric analysis studies there were no significant differences in prosthetic subsidence between both types of cement in hips[55] or between different ALBC in TKA[56]. Finally, the results from the Norwegian Arthroplasty Register found that the use of ALBC does not decrease the survival rate of hip replacements compared to plain cement[18], suggesting a good mechanical performance in a wide clinical setting.

RISK OF TOXICITY OF ALBC

Bone cellular toxicity of ALBC

Some experimental studies have evaluated the negative effects of some antibiotics on the osteoblasts derived from trabecular bone and have found decreased levels of alkaline phosphates suggesting cellular toxicity, mainly by gentamicin[57,58]. Nevertheless, probably the concentrations necessary for this cellular toxicity are not achieved when ALBC is used *in vivo* in low doses with prophylactic purposes[52].

Renal toxicity of ALBC

A study found that almost half of the studied patients after using ALBC had detectable aminoglycoside serum concentrations, mostly in high-doses antibiotics cement spacers, but also in some primary surgery cases after low-doses antibiotics ALBC. Many of these patients had an elevation in serum creatinine, so the authors recommended measuring aminoglycoside serum concentrations in the early postoperative period and further monitoring of some patients[59]. On the other hand, Springer *et al*[60] studied the risk of using high doses of antibiotics (gentamicin and vancomycin) in cement spacers for treatment of infected TKA and they concluded that both antibiotics seem to be clinically safe when used locally in ALBC spacers[60].

Patrick *et al*[61] described two cases of acute renal failure after the use of ALBC incorporated in THA. Both patients received antibiotic-laden spacers and subsequently developed acute renal failure in conjunction with elevated serum tobramycin concentrations, suggesting antibiotic toxicity. Several other case reports of acute renal failure associated with the use of ALBC have been reported[62-64]. As ALBC with vancomycin and/or aminoglycosides has the potential for systemic toxicity, it should be used according to guidelines and with monitoring in patients at increased risk for nephrotoxicity[61].

In any case, the risk of nephrotoxicity related to local delivery of antibiotics in the bone cement is much lower than with systemic antibiotics[65] and has been neglected when used in low doses[66,67]. All the reported confirmed cases of acute renal failure happened in cases of infected arthroplasties when an ALBC spacer was used. The risk is much lower in prophylactic use of ALBC for primary fixation of TKA, because the dose of antibiotic in the cement and the amount of cement used are usually lower.

RISK OF ALLERGIC REACTIONS

Antibiotics contained in ALBC, though at low levels, are systemically absorbed and can potentially cause allergic reactions. Particular attention should be paid to an individual's antibiotic allergy history prior to implantation of any ALBC.

The most frequently used antibiotics in ALBC are aminoglycosides (gentamicin and tobramycin), which very rarely cause allergic reactions. The possibility of an allergic reaction may become greater if other antibiotics such as cephalosporins are used[68].

Recently, a case of systemic hypersensitivity reaction to vancomycin-loaded bone cement causing a diffuse painful desquamating rash has been reported in a patient with a prior history of Stevens-Johnson reaction to vancomycin[69]. Antibiotics to which a patient has had a potentially life-threatening reaction should not be used in ALBC.

DEVELOPMENT OF ANTIMICROBIAL RESISTANCE

There is an increasing concern in the emergence of drug-resistant organisms. No direct evidence links the development of bacterial resistance to the routine use of ALBC in primary arthroplasties and some authors do not believe that this risk is increased[67].

On the other hand, there is some evidence supporting the concern about antimicrobial resistance and the risk of selecting resistant mutans bacteria: *in vitro* studies show up to 8% of the antibiotic in ALBC is quickly released after surgery, and thereafter there is a low-dose release, that may not be effective at fighting infection, but can cause antibiotic microbial resistance. Some experimental studies have shown the capacity of many usual TKA pathogens to grow on different ALBC. Prolonged exposure to antibiotic at a dose concentration below the inhibitory one allows the development of mutational resistance in bacteria[2,30]. The use of cement with gentamicin for first implants was associated with the development of coagulase-negative staphylococci resistant to gentamicin[70]. Josefsson *et al*[42] found that 88% of the infected patients who had received gentamicin-loaded cement in primary arthroplasty harboured at least one gentamicin-resistant isolate. Aminoglycoside (gentamicin and tobramycin) resistance rate is higher if an antibiotic spacer is used in 2-stages revision arthroplasty[71], suggesting that the risk of selecting resistant mutans when using ALBC is real.

In a large series of patients Hansen *et al*[7] found that the introduction of routine ALBC in TKA in a hospital did not cause any significant change in the infecting pathogen profile or any alarming increase in antibiotic resistance, but they recognized that the sample size of the infected cohort might not be big enough[7].

CLINICAL DECISION MAKING

Another problem with the use of ALBC relates to clinical decision making. It has been proved that the antibiotic contained in old cement mantles may influence the reliability of cultures taken from the joint fluid[72] as well as from tissues during revision surgery[32]. It is important to consider the presence of antibiotics in the cement mantle of patients with TKA when evaluating aspirate and tissue cultures to decide if a TKA failure is aseptic or septic.

ECONOMIC COST OF ALBC

The additional cost of using commercially available ALBC with tobramycin has been considered 210 USD if one 40-g packet of PMMA is used and 420 USD in case of using two packs[73]. The increase in the cost per package was even greater than 300 USD in another study[21], so the resulting extra-cost of using 2 packages is considered to be 600 USD[68]. The economic cost of routinely using ALBC in all primaries TKA could be reduced in a very significant way by hand-mixing the antibiotic with the PMMA[9,73], but the elution characteristics and mechanical properties of this hand-made ALBC could be affected.

The additional cost in the cement used for prophylaxis of infection could be compensated if it was really useful in decreasing the risk of infected TKA[67], as the costs for revision of a TKA for infection has been considered to be about 50000 USD[22], and even higher than 100000 USD in some countries[74].

A cost-effectiveness analysis considering revisions due to infection in THA according to the Norwegian Arthroplasty Register data[75] concluded that using ALBC in all primary hips is not cost-effective unless the RR for infection using plain bone cement was > 2.4 than using ALBC, but this is not the case[68]. Another cost-effectiveness analysis stated that a decrease of 1.2% in the rate of TKA infection is necessary to recover the extra costs of the routine use of ALBC[23]. Considering that the protective effect of ALBC in TKA is, according to the available prospective studies and Register studies much less (if any), the routine use of ALBC in economic terms is not justified.

From a merely economic point of view, the use of ALBC might only be justified in high risk groups of patients such as those having rheumatoid arthritis[45], immunodepression, morbid obesity[76-78], and diabetes[78-80], or patients with previous history of infection or fracture in the knee, and those having long surgeries[6,14,81,82], groups where a much higher infection rate than the average could be expected. Moreover, a recent study stated that the use of ALBC in primary TKA might not be justified even in the group of patients considered as high risk[10].

CONCLUSION

Bone cement has the capacity to release antibiotic molecules if any antibiotic is included in it. *In vitro* studies have shown high antibiotic concentrations for many hours or few days after its use. The use of ALBC is helpful in the treatment of infection in revision TKA. If used for infection prophylaxis, the choice of the antibiotic should consider microbiological, physical, pharmacological and economical aspects. The most commonly used antibiotics for prophylaxis in ALBC are gentamicin and tobramycin.

Many authors have recommended the use of ALBC in TKA for infection prophylaxis, but the evidence based on data from National Registries, randomized clinical trials and meta-analysis suggests a protective effect of ALBC against infection when used in hips, but not (or only mild) in knees. A possible explanation is that the quantity of locally delivered antibiotics after TKA is small.

There are some concerns about the routine use of ALBC in primary TKA: the risk of toxicity or hypersensivity, the possible reduction in the mechanical properties (that can be neglected if used in low doses), a significant increase in the cost of the cement, and the risk of selection of antibiotic-resistant bacteria.

There is a paucity of randomized clinical trials in the use of ALBC in primary TKAs and the actual evidence of the effect of ALBC in reducing the risk of infection is insufficient. This, in addition to concerns about patient safety, risks of increase in the antibiotic resistance of microorganisms and the increase in costs in the procedure lead us to recommend a cautious use of ALBC, perhaps only in high-risk patients (immunocompromised, morbidly obese, diabetic and patients with previous history of fracture or infection around the knee) unless the benefits of ALBC were better proven. Meanwhile, the rigorous use of peri-operative prophylactic systemic antibiotics and the adoption of efficient antiseptic procedures and improved surgical techniques must be considered the gold standard in infection prevention in TKA surgery.

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REVIEW

Developmental dysplasia of the hip: What has changed in the last 20 years?

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Abstract

Developmental dysplasia of the hip (DDH) describes the spectrum of structural abnormalities that involve the growing hip. Early diagnosis and treatment is critical to provide the best possible functional outcome. Persistence of hip dysplasia into adolescence and adulthood may result in abnormal gait, decreased strength and increased rate of degenerative hip and knee joint disease. Despite efforts to recognize and treat all cases of DDH soon after birth, diagnosis is delayed in some children, and outcomes deteriorate with increasing delay of presentation. Different screening programs for DDH were implicated. The suspicion is raised based on a physical examination soon after birth. Radiography and ultrasonography are used to confirm the diagnosis. The role of other imaging modalities, such as magnetic resonance imaging, is still undetermined; however, extensive research is underway on this subject. Treatment depends on the age of the patient and the reducibility of the hip joint. At an early age and up to 6 mo, the main treatment is an abduction brace like the Pavlik harness. If this fails, closed reduction and spica casting is usually done. After the age of 18 mo, treatment usually consists of open reduction and hip reconstruction surgery. Various treatment protocols have been proposed. We summarize the current practice for detection and treatment of DDH, emphasizing updates in screening and treatment during the last two decades.

Key words: Developmental dysplasia; Newborn; Infant; Children; Hip; Developmental dysplasia of the hip

Core tip: Developmental dysplasia of the hip (DDH) is a common and important topic in pediatric orthopedics. Early diagnosis and treatment are critical. Screening for this condition is of utmost importance. The treatment depends on the age at presentation and the amount of dysplasia of the hip. We summarize the current practice for detection and treatment of DDH, emphasizing updates in screening and treatment during the last two decades.

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INTRODUCTION

The term developmental dysplasia of the hip (DDH) describes the whole range of deformities involving the growing hip including frank dislocation, subluxation and instability, and dysplasia of the femoral head and acetabulum. This term replaced the previously accepted "congenital dysplasia of the hip", which did not describe the developmental aspect of the disorder[1-3].

In a dislocated hip there is no articular contact between the femoral head and the acetabulum. A dislocated hip may be irreducible or reducible. In a subluxated hip, the femoral head is partially displaced from its normal position, but some degree of contact with the acetabulum still remains. The hip is called dislocatable, when application of posteriorly directed force on the hip positioned in adduction, leads to complete displacement of the femoral head from the margins of the acetabulum. Similarly, the hip is called subluxable, if just gliding of the femoral head is noticed. Acetabular dysplasia describes the abnormality in the development of the acetabulum, including an alteration in size, shape and organization[1,4].

Dislocations are divided into two subtypes: Dislocation that occurs in an otherwise healthy infant is called typical and it may occur pre- or post-natally. Dislocation that is associated with neuromuscular disorders is called teratologic and it occurs prenatally[1,3,5].

The normal development of the child's hip relies on congruent stability of the femoral head within the acetabulum. The hip joint will not develop properly if it stays unstable and anatomically abnormal by walking age[1,6].

Early diagnosis and treatment is critical to provide the best possible functional outcome. Different screening programs have been devised to recognize DDH as soon as possible. Despite efforts to recognize and treat all cases of DDH soon after birth, the diagnosis is delayed in some children. Treatment of DDH changes with the age at presentation. At a later age, treatment involves more extensive surgery with more complications with a worse functional outcome.

INCIDENCE AND RISK FACTORS

The incidence of a dislocated hip at birth is 1:1000-5:1000, the incidence of subluxation and dysplasia is 10:1000; when implementing universal ultrasonographic screening, the reported incidence is 25:1000-50:1000[1,5,7]. The incidence is higher in cultures that still practice swaddling with the lower extremities fully extended and wrapped together. Studies in Native Americans showed, following a change from traditional swaddling to "safe swaddling", a decrease in the prevalence of dysplasia from 6 times the United States average to the same prevalence as the rest of United States population[6]. Similar experience was documented in Japan and Turkey[8,9]. It has been shown that keeping the legs in a naturally flexed and abducted position without restricting hip motion lessens the risk of DDH[6,10-15]. In "safe swaddling" the infant hips should be positioned in slight flexion; additional free movement in the direction of hip flexion and abduction may have some benefit[13].

Risk factors include female sex (80% of the affected children) probably due to increased ligamentous laxity as a result of the circulating maternal hormone relaxin. The left side is involved in 60% of the children, the right side in 20% and 20% have bilateral involvement. The left side is more commonly involved, perhaps due to the left occiput anterior positioning of most non-breech newborns where the hip is adducted against the mother's spine with limited space for abduction[1,5].

The breech position is probably the most important single risk factor, whether delivered vaginally or by cesarean section[6,16,17]. Other risk factors include first born children, postural deformities, oligohydramnios and a positive family history[1,18]. Latest evidence suggests that prematurity is not a risk factor for DDH[19].

NATURAL HISTORY

Neonates with mild dysplasia and mild instability noted in the first few weeks of life may have a benign course, with up to 88% resolving by 8 wk of age[6,20]. Those with instability and frank dislocation often have progressive dysplasia. Spontaneous resolution without intervention is unlikely in children over the age of 6 mo[4].

The modifications in the hip joint reflect contracture of the soft tissue and changes in normal growth of the femoral head and acetabulum. Persistent subluxation or dislocation leads to progressive dysplasia of the femoral head and the acetabulum. The labrum may be inverted and serve as mechanical block for concentric reduction of the hip. Other structures that may block reduction are the limbus, which is formed as a pathologic response of the acetabulum to abnormal pressure around the hip; the ligamentum teres, which lengthens and hypertrophies; the pulvinar, a fibro-fatty tissue found in the depth of the acetabulum; the transverse acetabular ligament which contracts; and the capsule that becomes constricted by contracted iliopsoas tendon[1].

Although acetabular changes in DDH are well recognized, little is known about the morphologic changes of the femoral head. A recent study showed that the femoral head in walking children with DDH is often "less round", although the degree of asphericity is extremely variable and not related to the age of the patient. These differences in femoral head sphericity may explain differences in outcome following the same surgical procedure. Further studies are warranted on this matter[21]. It was also shown that hips with different acetabular coverage have distinct proximal femoral shapes[22].

Persistence of hip dysplasia into adolescence and adulthood may result in abnormal gait, decreased strength, limb-length discrepancy with a flexion/adduction deformity of the hip, increased rate of degenerative hip joint disease, postural scoliosis, back pain and ipsilateral genu valgum with consequent arthritis of the knee[23-26]. Patients with unilateral dislocations have a worse prognosis than those with bilateral dislocations because they have problems of limb-length discrepancy, asymmetrical motion and strength, gait disturbance and knee disorders. Patients with chronic subluxation experience symptoms earlier than those with true dislocation[4].

Outcomes after intervention for DDH deteriorate with increasing delay of presentation. A tipping point is reached, probably around the age of eight years, after which complications from treatment may lead to an outcome no better than the untreated clinical course[23,27,28]. The clinical outcome of bilateral DDH treated surgically is worse compared to unilateral cases mainly due to asymmetrical outcome[29].

Avascular necrosis (AVN) of the femoral head is the most feared complication in children with DDH. AVN is iatrogenic and not part of the natural history of the condition. It is potentially devastating and often untreatable[23]. It is commonly accepted that consequences of AVN are more devastating when it occurs at a younger age. The proposed explanation is that the cartilaginous femoral head without an ossific nucleus is more susceptible to ischemia than a more developed femoral head where an ossific nucleus is already present[1,30,31]. However a systematic review of the medical literature did not show any conclusive evidence to support this. The authors conclude that they did not find that the presence of the ossific nucleus had a significant effect on the development of osteonecrosis of any grade after hip reduction in infants with DDH[32].

Surprisingly, a recent study that examined functional outcomes in children with AVN secondary to treatment of DDH at a mean age of 14 years showed that, although there was some limitation in hip function, it was not associated with marked physical disability[33].

SCREENING FOR DDH

Screening is important because the condition is easily treated when caught early, but difficult to treat when detected late and can lead to long-term disability. The physical examination is still the most important means of detection[7,34,35]. In a decision analysis model, the lowest probability of developing degenerative disease of the hip by age 60 was by doing a thorough physical examination of the hip in all newborns[36]. Radiography and sonography are used to confirm the suspicion of DDH. Periodic physical examination should be performed on all children until walking age[5,6]. Despite our better understanding of the pathology and all current methods of screening, many young adults with dysplasia who require hip arthroplasty are not detected at birth[37]. In the future, genetic profiling may improve matters[38].

Physical examination[1,5]

DDH is an evolving process, therefore the physical examination changes as the child grows older. Normal physical examination findings during the immediate postnatal period do not preclude a subsequent diagnosis of DDH[4,39].

All newborn infants should be examined by a physician in the nursery. A general examination should be done to look for associated conditions with an increased prevalence of DDH. Assessment of the hip joint starts with observation for asymmetry - asymmetrical gluteal or thigh skin folds, limb length discrepancy (evaluated by placing the child in a supine position with the hips and knees flexed - unequal knee heights might be noticed - Galeazzi sign), and restricted hip abduction. The Ortolani test in which the dislocated femoral head is reduced into the acetabulum is the most important clinical test to detect dysplasia[40]. The Barlow test in which the examiner dislocates an unstable hip from the acetabulum is also commonly used. Each hip should be examined independently with the other side held in maximum abduction in order to lock the pelvis. Occasionally, soft tissue clicks might be felt during the movement of the hip. In the absence of any other abnormal findings they are considered benign[41].

By the age of 3 mo, the Barlow and Ortolani tests become negative and the limitation of abduction (and asymmetry of abduction) becomes the most reliable sign associated with DDH. A recent study demonstrated that unilateral limitation of hip abduction after eight weeks of age is strongly associated with DDH. The authors recommended that this sign should be actively sought, and if present, should be further evaluated by a formal ultrasound or radiographs. The presence of bilateral limitation of hip adduction was not an accurate sign for DDH[42].

An ambulating child might have a Trendelenburg gait. In children with bilateral dislocation, the diagnosis is more challenging; however, the Trendelenburg sign, waddling gait, and symmetrical but decreased hip abduction might be noticed[4]. Although commonly accepted that DDH can be a cause of walking delay in children, a recent controlled study suggested that even though the median time to the age of independent walking was 1 mo less in healthy controls compared with that of children with late presentation of DDH, this was clinically insignificant as they all walked within the expected time[43].

Imaging

Radiographs of the hips and pelvis have traditionally been used in all children with suspected DDH. However, instability and displacement may be unnoticeable on a simple radiograph during the first few months of life. The ossification center of the femoral head appears by

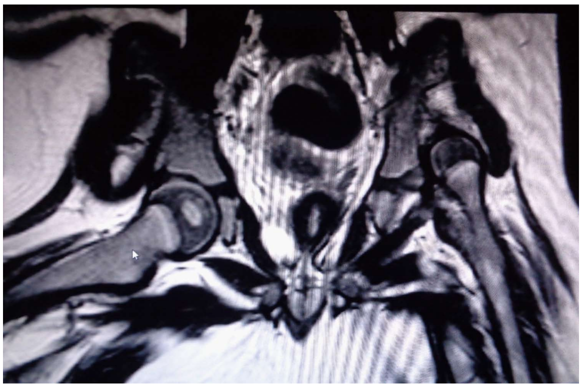

Figure 1 Magnetic resonance imaging of a two-year-old girl with developmental dysplasia of the hip.

the age of 4-6 mo. At this stage radiographs become more reliable[5]. Real-time ultrasonography has been established as an accurate method for imaging of the hip during the first few months of life[44-50]. In patients treated for DDH, a delay in appearance of the femoral head ossification center is commonly seen, even up to 1 year after hip reduction. This allows continued utilization of ultrasonographic imaging for follow-up[1].

Computed tomography (CT) is useful for assessment of quality of reduction after closed or open reduction and fixation in a spica cast[51]. It is also useful in the treatment of adolescents and young adults, defining the dysplasia and allowing for better selection of the appropriate procedures, including pelvic and/or femoral osteotomies[52]. Although ionizing radiation exposure from a limited CT is low, magnetic resonance imaging (MRI) has been effectively used completely avoiding radiation exposure (Figure 1). However, the use of MRI has been challenging as there is an extensive diversity of sequences described in the literature and the time needed to perform the study may be as long as 30 min, requiring sedation. A recent retrospective study assessed different MRI imaging protocols. The authors found that axial and coronal T2 FSE provided excellent contrast between the femoral ossification center, surrounding cartilage, and the acetabulum in less than 3 min per sequence and provided the potential for a total examination time of less than 15 min[53]. Another group performed a retrospective analysis of contrast-enhanced MRI as a possible predictor of AVN after closed reduction in DDH. They found that a global decreased enhancement was associated with a significantly higher risk of developing AVN[54]. Another recent publication supported these findings[55]. MRI is also useful in the assessment of labral abnormalities. Isolated labral tears are best treated with arthroscopic techniques[52].

Arthrography displays the cartilaginous anatomy of the femoral head and the acetabulum. Therefore it is commonly used as an intraoperative dynamic test to assess the quality of reduction and the stability of the hip joint. It has a central role in the decision making between closed and open reduction[1].

Ultrasonography

Ultrasonographic techniques pioneered by Graf include static and dynamic evaluation of the hip joint. This allows assessment of the static anatomy of the hip and the stability of the femoral head in the acetabular socket[56]. However, ultrasound screening should not be performed before 3-4 wk of age in infants with clinical signs or risk factors for DDH because of the normal physiologic laxity that resolves spontaneously by 6 wk of age[56-58].

Screening of all newborns with ultrasonography led to a high rate of reexaminations and resulted in a large number of hips needlessly treated[59,60]. However, it was reported that the majority of patients in the United States with symptomatic dysplasia of the acetabulum at skeletal maturity do not meet the criteria for selective ultrasound screening[61]. Recently, a large randomized controlled study comparing universal or selective ultrasound screening with well performed physical examination showed higher treatment rates, a slight reduction in late diagnosis of dysplasia which was not significant, and increased treatment rates which were not associated with AVN[62]. A Cochrane review of screening programs for DDH in newborns found that studies that compared the addition of ultrasonography to clinical examination reported that, when ultrasonography was performed on all infants, the rate of treatment increased with no significant change in the rate of late detected dysplasia or surgery. Targeted ultrasonography to infants at high risk of hip dysplasia did not significantly increase the rate of treatment but also did not significantly decrease the rate of late detected dysplasia or surgery[63].

Consequently, ultrasonography is the preferred technique for clarifying physical findings, evaluating a high-risk infant, and monitoring DDH as it is followed and treated. Universal ultrasonography screening of newborn infants is not recommended[5,64-67]. It was shown that mildly dysplastic but stable hips recognized by ultrasonography soon after birth, usually resolve without treatment. Therefore, an active sonographic surveillance strategy is sufficient[68].

Several ultrasonography techniques have been developed to evaluate the relationship between the acetabulum and the femoral head of an infant. The most common ones are the Graf, Harcke, Terjesen and Suzuki methods. The Graf method is composed of a quantitative classification system, while the Harcke and Suzuki methods have qualitative definitions, and the Terjesen method contains both quantitative and qualitative descriptions[69]. Studies that compared the reliability and sensitivity of the Terjesen and Graf methods, reached different conclusions[70,71]. A study that compared the Graf, Suzuki and Harcke methods, a correlation was found between the three methods in normal and dislocated hips; however, Graf type IIa and IIb hips were frequently regarded as normal when evaluated by the other two methods[72]. There is no conclusive evidence to prefer one method over the other. However an effective ultrasonographic method should include simple, precise,

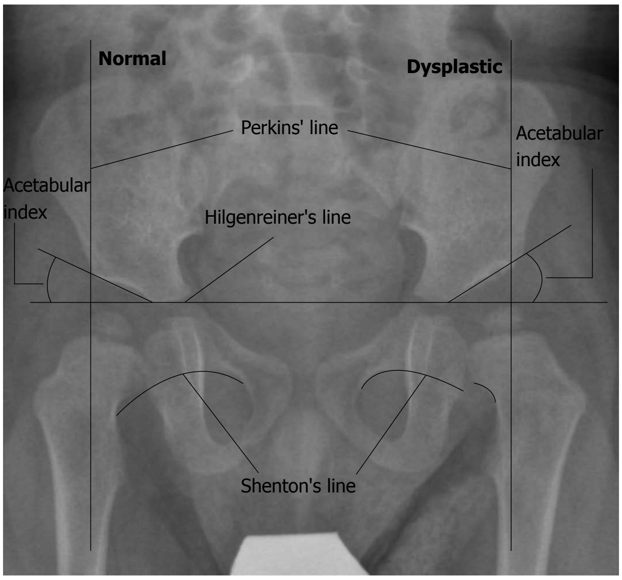

Figure 2 One-year-old girl with developmental dysplasia of the hip on the left side.

quantitative and consistent definitions for a proper examination and diagnosis, and Graf's method meets all these requirements[69].

Radiography

An AP radiograph of the pelvis is obtained in newborns and infants when other conditions, such as congenital short femur, are suspected. Plain radiography becomes useful for DDH when the femoral head ossification center appears at the age of 4-6 mo. A single AP pelvic view is usually sufficient. If subluxation or dislocation is noted, a frog view should be done to assess reducibility. There is still a debate whether minor radiographic variability in young infants constitutes actual disease[6,73].

Some orientation lines and angles are useful in the assessment of the AP pelvic radiograph of the infant. The femoral head is supposed to be in the lower medial quadrant created by the Hilgenreiner's and Perkins' lines. Shenton's line should be continuous without breaks. The acetabular index becomes lower with age and, if too high, may be a sign of dysplasia[74,75]. The center-edge angle may be calculated when the femoral ossification center appears, which reflects both acetabular coverage and femoral head displacement. In children younger than 3 years, the femoral head ossification center is irregular or incomplete, and thus difficult to measure. For that reason, it should be used in children older than 3-5 years[1] (Figure 2).

TREATMENT

The goal of treatment is to acquire and sustain a stable, concentrically reduced hip joint at an earliest possible age with minimal complications[4,30]. There is well-established correlation between residual dysplasia and age of reduction. Ideally, patients should be identified and treated in infancy. Failing this, treatment should be instituted as soon as possible, preferably before 4 years of age[4,74,76]. The goals of treatment in older children with persistent acetabular dysplasia are to delay or prevent the development of osteoarthritis and to obviate the need for arthroplasty at a relatively young age[74].

Subluxation of the hip joint noted near birth can be observed for 3 wk without any treatment, as it is commonly corrects spontaneously. The use of triple diapers is not recommended, as it has not shown better results compared to no treatment. After 3 wk, if there is still evidence of subluxation on physical and ultrasonographic examinations, initiation of treatment is recommended. When complete displacement of the hip joint is noted at birth, initiation of treatment without an observation period is recommended[1,5]. A recent Cochrane review showed that in infants who were identified clinically to have unstable but not dislocated hips, or were identified on ultrasounography to have mild hip dysplasia, postponing treatment by 2 to 8 wk reduces the need for treatment without a significant increase in late diagnosed dysplasia or surgery[63].

The Pavlik harness

This is the most commonly used device today to treat hip instability in infants[77]. Alternatives include the Craig splint and the Von Rosen splint. Although there are few comparative studies, all the three braces are superior to no treatment. The Craig and the Von Rosen splints might be slightly superior to the Pavlik harness[78], but the Pavlik harness remains the standard treatment for the majority of children younger than 6 mo as it is the most thoroughly examined, and found to be safe and highly effective, with success rates greater than 90%[79-83]. The function of the frontal leg straps is to flex the hips, and the rear leg straps to prevent adduction of the hips (extreme abduction of the hips should be avoided as this is related to AVN). The indication for its use is a reducible hip in an infant who is not yet trying to stand. Close follow-up is required, usually at weekly intervals. If the reduction of the hip joint is unsuccessful after 3 wk, other treatment modalities should be considered[1]. Continuation of the harness with the dislocated hip may potentiate acetabular dysplasia, which may increase the difficulty of subsequent closed reduction ("Pavlik harness disease")[84,85]. Higher rates of AVN have also been reported[86-91].

A recent study examined the influence of different risk factors (age, gender, side, family history, breech presentation, first-born girl, oligohydramnios, swaddling, and the severity of hip dysplasia defined by ultrasonography) on the success rate of treatment with the Pavlik harness. Age was the only patient-related variable influencing the success rate of treatment. The authors concluded that Pavlik harness treatment is less effective in children at and over the age of 4 mo at the time the harness is first applied, as well as in hips with complete dislocations and hips with severely deficient acetabular bony roofs[92]. Another study examined the relationship between ultrasonographic findings and failure of treatment with Pavlik harness. Two static ultrasonographic findings linked with treatment outcome were described. A femoral head positioned below the labrum was strongly associated with success, whereas a femoral head located substantially superior and lateral to the labrum was associated with failure[93,94]. Bilateral DDH was not found to be a risk factor for Pavlik harness failure[95].

Femoral nerve palsy is a rare but clinically significant complication of Pavlik harness treatment. It usually appears on the involved side, around the end of first week of treatment, and resolves between several days and 2 wk. This complication was shown to be strongly predictive of failure of treatment, with correlation between the number of days until return of femoral nerve function and the probability of successful treatment with the Pavlik harness (prompt resolution was predictive of treatment success)[96].

A recent study from Switzerland reported results of treatment of infants 0-6 mo of age with an abduction brace instead of a Pavlik harness with results that are comparable to the reported results of treatment with a Pavlik harness. The use of an abduction brace is easier for the patients and the physician. However, this was a retrospective study with a small number of patients, and more research is needed to draw any firm conclusions[97].

The use of the Pavlik harness after the age of 6 mo is not recommended by most authors[92]. However, a recent retrospective study of the outcome of late-diagnosed DDH in infants who were treated with Pavlik harness beginning treatment at the age of 6-24 mo, showed encouraging results in the treatment of hip dislocation type Graf 3. Neither of the Graf 4 hips were successfully reduced[98]. Another study reported a successful treatment with Pavlik harness, in children aged 5 to 13 mo of age. The rate of successful reduction was higher with less severe dislocations[99]. Both of these studies used periods of treatment that were longer than the commonly accepted 3 wk. It is expected that the management of an older child with the Pavlik harness might be complicated because of parental compliance[100]. Additional study examined the results of modified Hoffmann-Daimler method of treatment, for children aged 6 to 44 mo of age with good results[101].

If the dysplastic hip treated by Pavlik harness is successfully reduced and free of contracture but still unstable, it should be treated with a fixed abduction orthosis[80,102,103]. Different abduction braces were reported to be successful, including Plastazote and Ilfeld abduction orthoses[104-106]. A part-time use of an abduction brace orthosis between the age of 6 to 12 mo is an effective intervention to improve residual acetabular dysplasia. The optimal duration of abduction bracing is still unclear[107].

Closed reduction and fixation with spica cast

Closed reduction of the hip joint performed under general anesthesia is indicated in patients who failed to achieve stable reduction with the Pavlik harness. It may also be considered as primary treatment for patients with poor social situation or an unreliable family. Better results were achieved when reduction was performed before the age of 6 mo[1,30]. The use of traction before attempted closed reduction is controversial. Although once very popular[108], there is now a trend toward decreasing the use of traction. Dynamic arthrography with fluoroscopy is useful to assess the quality of reduction, the extent of coverage of the femoral head and the optimal position for immobilization[4].

The "safe zone" is the range between maximal passive abduction of the hip and the angle of abduction where the femoral head becomes unstable. Adductor tenotomy (performed either open or percutaneously) can widen the safe zone by decreasing adduction contracture, thereby increasing abduction. Immobilization should not be done in a position of extreme hip abduction, as this is associated with AVN. After closed reduction, a spica cast is applied with the use of a greater trochanter mold, maintenance of 90-100 degrees of hip flexion and controlled abduction. Reduction is confirmed using a limited CT or MRI study[109,110]. A spica cast is utilized for 3 mo without changing, and then an abduction orthosis is used. Assessment of hip maturation is accomplished with serial radiographs. The majority of patients who had successful closed reduction after the age of 18 mo required an additional open procedure[4,111].

Gradual reduction using long-term traction techniques has been described as a mean of closed reduction. The reported reduction rates were high, with a low rate of AVN; however, many of these patients had residual acetabular dysplasia and required future acetabular osteotomy as a secondary procedure. These techniques require long traction periods and prolonged hospitalization, which may be difficult both for the children and the family[112-116].

Open reduction and hip reconstruction

Typically, open reduction is considered for children older than 18 mo. However, open reduction is indicated for all children who failed to achieve a stable concentric reduction of the hip joint by closed techniques.

Open reduction can be performed through different approaches. The inability to perform a pelvic osteotomy or capsulorrhaphy *via* the medial approach limits its use to patients less than 18 mo. Several modifications to this approach have been proposed. These medial approaches require minimal dissection, avoid splitting of the iliac apophysis, and allow direct access to the medial structures. However, they potentially endanger the blood supply to the femoral head and some authors noted an association between the medial approach and osteonecrosis[117-119]. Although not substantiated[120,121], this decreased the popularity of this approach. Newer, medial minimally invasive approaches for open reduction, such as the use of arthroscopy to release the psoas and to remove the ligamentum teres and the pulvinar are under development[122,123]. A modified posteromedial approach to the hip joint has been described as a limited surgical technique for patients up to 18 mo of age. The adductor longus and iliopsoas tendons are sectioned through the posteromedial incision. If concentric reduction is not achieved, hip arthrotomy is performed. Good results were reported with this new technique[124-126].

The modified Smith-Petersen anterolateral approach is very useful because it allows for a concomitant pelvic osteotomy, capsulorrhaphy and usually a shorter period in a spica. Therefore, it is usually the procedure of choice in children older than 18 mo[4,23,127].

Redislocation following open reduction is an important problem with a variable incidence. Frequently, the failure of a primary open reduction is due to errors in surgical technique, like insufficient release of the anteromedial capsule and the inferior articular structures. A common finding in a re-dislocated hip following open reduction is an intact transverse acetabular ligament which was not fully released at the initial procedure. The presence of a stump of the ligamentum teres causing redislocation has also been found. This stresses the importance of complete removal of all obstacles to reduction including the need for complete release of the transverse acetabular ligament[4,128-130]. Risk factors for failed open reduction were not thoroughly evaluated. A recent retrospective match-controlled study examined those risk factors which were: right side (or bilateral) involvement, greater pubic width, and decreased abduction in the spica cast. In several cases, dysplasia of the femoral head or an insufficiently corrected femoral version were thought to be the reason for the failure of the primary surgery[131].

Procedures are being developed in the effort to reduce the rate of redislocation. The transfer and tenodesis of the ligamentum teres has been described with good results. This procedure is done through a medial approach[132,133]. Another technique is the use of a percutaneous Kirschner wire (K-wire) to stabilize the hip after successful reduction. The result of this technique that can be performed with the common anterolateral approach is very encouraging. A reduced rate of redislocation was reported without an increase in complications such as AVN, premature closure of triradiate cartilage and septic arthritis[134,135].

Following open reduction a spica cast is used for 6 wk with immobilization in 30 degrees of abduction, flexion and internal rotation. After cast removal, physiotherapy is recommended[4].

Femoral osteotomy can facilitate reduction and decrease the rate of osteonecrosis by relieving tension in the hip joint. It allows the surgeon to perform shortening and to correct excessive femoral anteversion. Femoral shortening should be used whenever excessive force is needed for hip reduction. The amount of shortening is determined by the amount of overlap between the femoral segments after osteotomy with the hip reduced[4]. In a recent study open reduction without simultaneous femoral osteotomy strongly predicted the need for a secondary procedure, and the authors concluded there should be a low threshold to performing femoral osteotomy during a primary open reduction[136]. Although generally accepted that DDH is associated with increased femoral anteversion, some studies did not show a difference in anteversion compared with normal hips[137,138] while others did[139]. Therefore, the indications for femoral derotational osteotomy remain unclear. Earlier studies reported a common use of derotational osteotomy[140,141]; however, recent literature does not support this practice[142,143]. It should be noted that all these studies utilized a different system to measure femoral anteversion. A recent study showed that femoral anteversion is inconsistent in children with DDH and should be evaluated on a case-by-case basis to establish the necessity of derotational femoral osteotomy[144].

Pelvic osteotomy is indicated for persistence of acetabular dysplasia, when there is insufficiency in acetabular coverage. The need for an acetabular procedure at the time of open reduction in a 1.5-3-year-old child with acetabular dysplasia is controversial. One approach is to delay the acetabular procedure until the remodeling response of the acetabulum following open reduction is assessed. However, in recent years, there has been a tendency to include an acetabular procedure (single innominate osteotomy - Salter[145,146]) at the time of primary treatment to maximize the potential for the development of a normal acetabulum[74,147,148]. A recent study compared acetabular development after femoral varus derotational osteotomy and an innominate osteotomy, in patients 15 mo to 4 years of age. The authors concluded that acetabular remodeling after open hip reduction and innominate osteotomy was more effective for reversing acetabular dysplasia and maintaining hip stability than open reduction combined with a femoral varus derotation osteotomy[149]. A long term follow-up after patients who had been treated with innominate osteotomy showed a 54% rate of survival of the hip at 45 years[150].

In the child older than 3 years, acetabular osteotomy is performed routinely because of the unpredictable remodeling potential of the acetabulum beyond this age. Femoral derotational osteotomy is also usually needed. For an acetabular procedure, either a Salter or Pemberton osteotomy may be performed (Figure 3). The primary indication for Salter osteotomy is a deficiency in anterolateral femoral head coverage in a concentrically reduced hip, while a shallow acetabulum is a relative contraindication. Placement of bone graft and internal fixation is needed. Best results were reported in patients aged 1.5-4 years. Pemberton osteotomy is an incomplete osteotomy that hinges through the triradiate cartilage (Figure 4). As this is an incomplete osteotomy, it is inherently stable and no internal fixation is required. A spica cast is used for 8 wk. This procedure is appropriate for patients older than 1.5 years and until skeletal maturity[74].

A combination of Salter and Pemberton osteotomies, called the Pembersal procedure, was also reported.

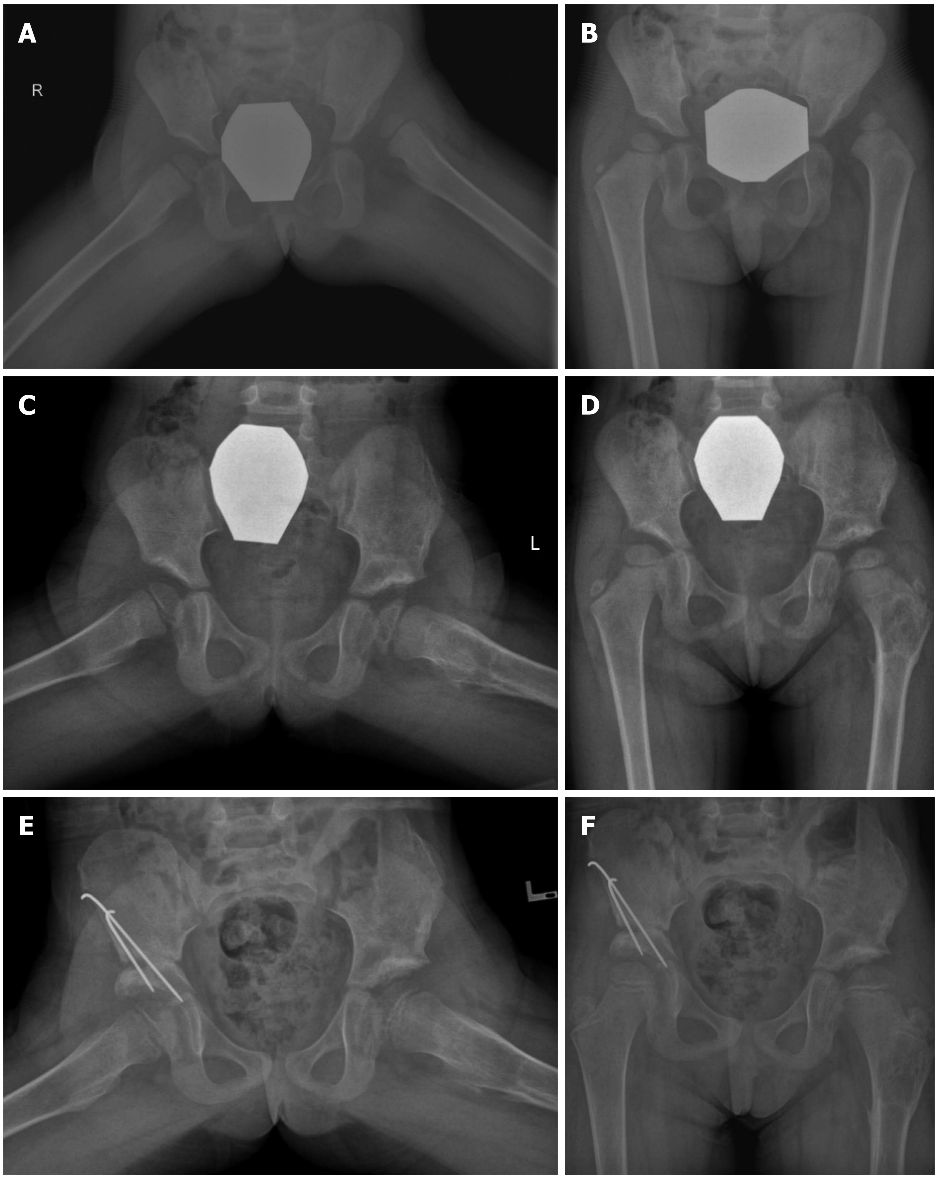

Figure 3 Hip reconstruction. A, B: Female patient, diagnosed with bilateral developmental dysplasia of the hip at the age of 2.5 years; C, D: On presentation left hip reconstruction, that included open reduction, Salter osteotomy and femoral derotational osteotomy with shortening, was performed. Post-operative X-rays after removal of the internal fixation devices are shown; E, F: Due to persistent mild hip dysplasia on the right side, a Salter osteotomy was performed at the age of 4 years.

The main complication of this procedure is iatrogenic damage to the triradiate cartilage. The reported results of this operation are satisfactory; however, whether this procedure provides any advantages remains unclear[151,152].

In the older child or adolescent, if the triradiate cartilage remains open, the triple innominate osteotomy is the procedure of choice. After triradiate cartilage closure, Ganz periacetabular osteotomy, triple innominate osteotomy or a salvage osteotomy (such as Chiari or shelf procedure) should be considered. In triple innominate osteotomy described by Steel[153], concentric hip reduction is a prerequisite. It allows significant mobility of the acetabular fragment and its displacement medially, moving the hip center medially and improving gait mechanics. Placement of a bone graft and internal fixation are required[154]. A modified triple osteotomy was proposed with better preliminary results[155,156]. An endoscopic method of performing triple innominate osteotomy has also been developed; although technically demanding, preliminary studies demonstrate good results with reduced surgical morbidity[157]. Ganz periacetabular osteotomy is indicated only after skeletal maturity as it crosses the triradiate cartilage (Figure 5). This procedure is very stable and immediate crutch weight-bearing is allowed. However the procedure is difficult to learn[74]. Long-term results of the correction of acetabular dysplasia with periacetabular osteotomies have been published. The end point of these studies was conversion to arthroplasty. The preoperative grade of arthritis was a consistent risk factor for failure. There are now consistent data demonstrating the efficacy of pelvic osteotomy for the treatment of symptomatic acetabular

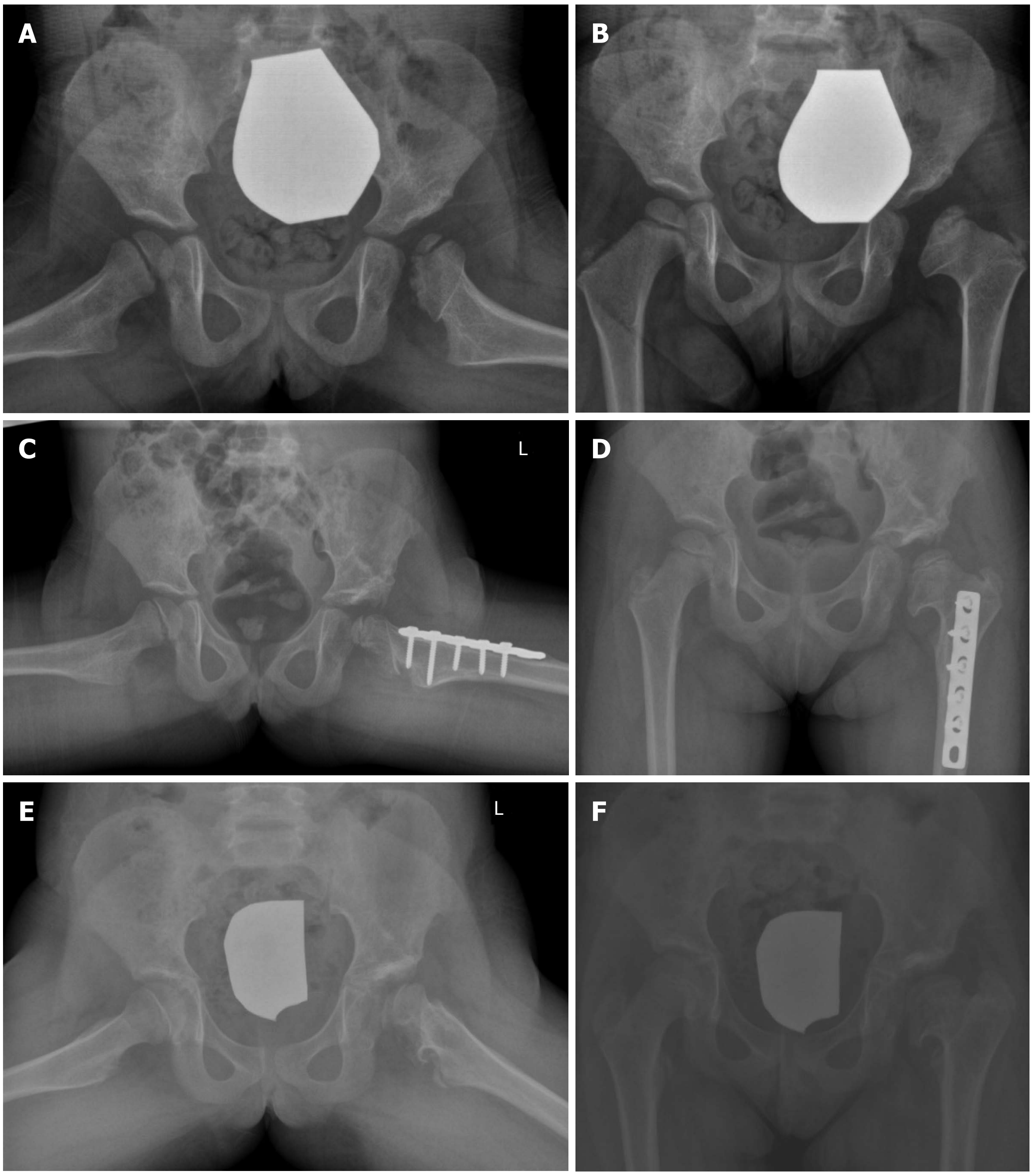

Figure 4 Acetabuloplasty. A female patient was diagnosed with DDH of the left hip at the age of 6 mo using sonography. She was treated with a spica cast. AVN of the left femoral head was seen on follow-up radiographs at the age of 3 years (A,B); C, D: Acetabuloplasty of the left hip with femoral derotational osteotomy was performed at the age of 5 years; E, F: Follow-up X-rays at the age of 8 years. DDH: Developmental dysplasia of the hip; AVN: Avascular necrosis.

dysplasia[158-161].

Salvage procedures are indicated when congruent reduction between the femoral head and the acetabulum cannot be obtained. These procedures increase the weight bearing surface and rely on capsular metaplasia to provide an articulating surface. Usually concomitant femoral varus or valgus osteotomy is performed. A Chiari procedure can be performed on a patient older than 8 years if there is satisfactory range of motion, maintenance of cartilage space and minimal osteoarthritis, with good results[162,163]. Shelf procedures are performed to increase the extra-articular buttress, thereby increasing the load-bearing area of the hip. They are indicated when congruent reduction is impossible, when there is no severe osteoarthritis and when augmentation is needed after other osteotomies. The slotted-shelf procedure is recommended over the other types because of the greater resultant stability[74,164].

FOLLOW-UP

Most orthopedic surgeons agree that children with a history of DDH should be followed until skeletal maturity[1,6]. However, some studies raise doubt regarding the necessity of radiographic monitoring[165-167], while others stress its significance[17,48,168]. The incidence of residual acetabular dysplasia after successful treatment with Pavlik harness cannot be disregarded[79,169,170]. Concern has been raised about the late effects of radiation due to the long life expectancy of the patients[171,172]. A recent retrospective study established the incidence of radiographic acetabular dysplasia in children with previous DDH normalization to be 17% and 33% around the ages 6 and 12 mo, respectively. Based on this data,

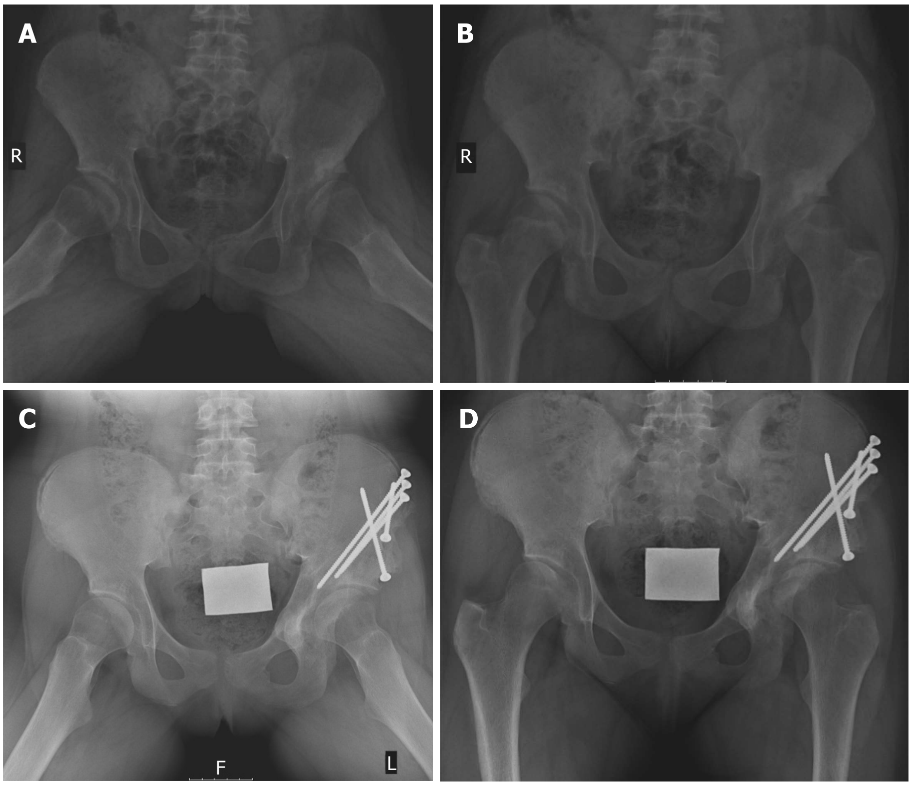

Figure 5 Female patient with developmental dysplasia of the hip that was diagnosed in early adolescence. A, B: X-rays at the time of diagnosis of DDH at the age of 13 years; C, D: X-rays taken two years after Ganz osteotomy on the left side. DDH: Developmental dysplasia of the hip.

the authors concluded that infants who normalize after treatment with Pavlik harness or spontaneously can benefit from a single-view AP radiograph of the pelvis at the age 6 and 12 mo. Follow-up at these particular ages can allow early intervention. The need for long-term radiographic follow-up after 12 mo of age cannot be inferred from this study[173]. A group from the United Kingdom reported a 4% recurrent dysplasia that required intervention after treatment of DDH to ultrasonographic normality. They recommended long-term follow-up of dysplastic hips with an early pelvic X-ray at around 6 mo[174]. Another study evaluated children with unilateral hip dysplasia for a contralateral hip dysplasia that was not apparent with thorough and recurring evaluations early in childhood. The authors showed that mild dysplasia of the hip can develop as the child grows older[175]. This emphasizes the significance of thorough and recurring clinical and radiographic examinations.

CONCLUSION

The main changes in the field of DDH during the last 20 years are summarized in Figure 6.

The normal development of the child's hip relies on congruent stability of the femoral head within the acetabulum. Early diagnosis and treatment of DDH is critical to provide the best possible functional outcome. The acetabular changes in DDH are well recognized. Recently we also gained understanding into the changes of the femoral head. The traditional risk factors for DDH were questioned and new ones were explored, and consequently we have a better understanding of the factors that are associated with this condition. The best example is probably the change that was made in some cultures, from traditional swaddling, with the lower extremities fully extended and wrapped together, to safe swaddling, with the infant hips positioned in slight flexion, leading to reduced incidence of DDH. In the future, genetic research may give us better understanding on the molecular mechanisms that lead to this condition. There is still much clinical research to be done in order to convert all of our knowledge into clinical practice.

As early diagnosis and treatment is critical in order to achieve best functional outcome, there is much interest in the search for the best screening program. Despite best efforts many young adults with dysplasia are not detected at birth. Although ultrasonography is the technique of choice for visualization of acetabular changes in children up to 4 mo of age, its role in the screening of DDH in newborns is still controversial. The recommended length of follow-up for at risk infants is also undefined. We recommend performing ultrasonographic screening to all newborns with risk factors at 4 to 6 wk of age, followed by ultrasonographic monitoring until age one year. We also recommend radiographic follow-up of all children treated because of dysplasia of the hip until at least 3 years of age.

Imaging and its role in the screening, follow-up and treatment of DDH is rapidly evolving. The role of

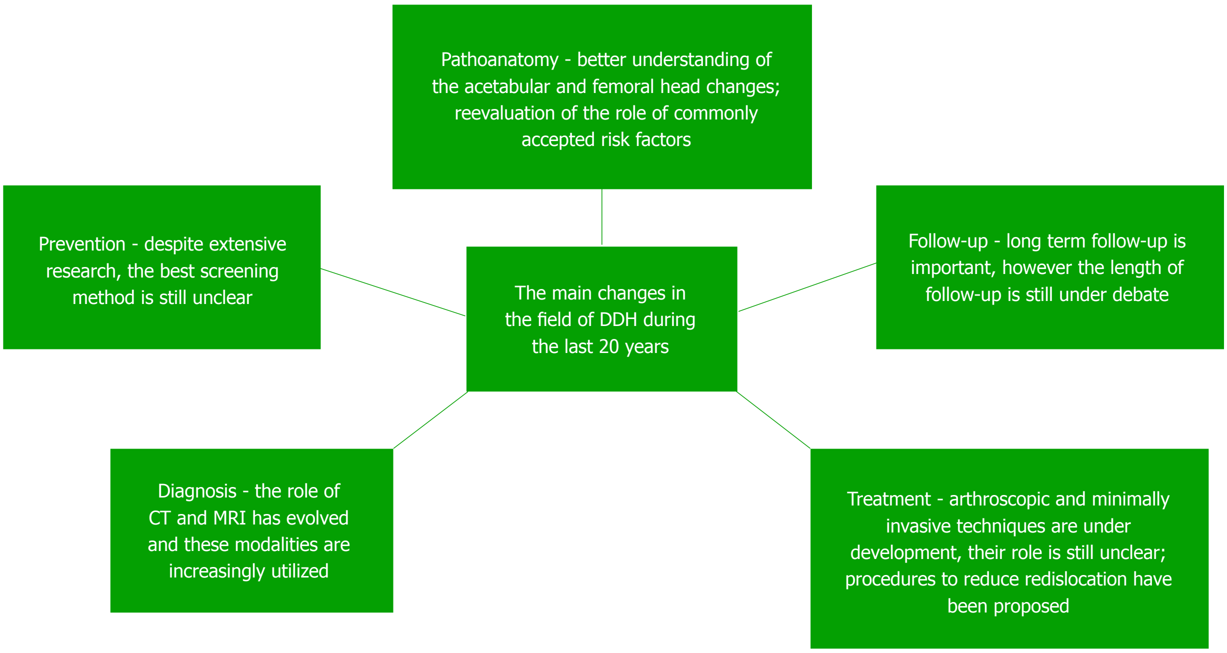

Figure 6 Summary of the main changes in the field of developmental dysplasia of the hip during the last 20 years. MRI: Magnetic resonance imaging; DDH: Developmental dysplasia of the hip; CT: Computed tomography.

ultrasonography was established as the best imaging modality for screening and follow up of infants suspected for DDH up to the age when the proximal ossific nucleus appears. Radiographs are used in order to rule out other conditions and for evaluation and follow up of older patients. CT is increasingly used especially for evaluation of dysplasia in older patients. Protocols using less radiation are developed. MRI is gaining popularity due to the fact that no radiation is involved and as it has the ability to show better soft tissue anatomy than any other imaging modality. Shorter imaging protocols were developed. Contrast enhanced MRI might also be of use in the future to assess perfusion of the femoral head after reduction and fixation.

Much research has been done in order to compare different treatment protocols and surgical procedures. The Pavlik harness still remains the main treatment for the younger infant. Patients that failed to achieve stable fixation with the Pavlik harness need closed reduction and spica casting. The introduction of the "safe zone" concept has reduced the AVN rates associated with this treatment.

Patients who fail after closed treatment need an open reduction. Patients older than 18 mo of age usually require hip reconstruction during open reduction. A vast amount of research has been performed comparing different surgical approaches and different procedures in the search for the best treatment protocol based on deformity and patient age. New procedures are being proposed and developed, such as minimally invasive and arthroscopic surgery. Some common features that led to failure of primary surgery were identified and the role of femoral shortening and derotational femoral osteotomy has been assessed. Despite substantial research, high quality comparative studies are lacking and the treatment of an older child with DDH is mainly based on the clinical experience of the treating surgeon.

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REVIEW

Rotator cuff tears: An evidence based approach

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Abstract

Lesions of the rotator cuff (RC) are a common occurrence affecting millions of people across all parts of the globe. RC tears are also rampantly prevalent with an age-dependent increase in numbers. Other associated factors include a history of trauma, limb dominance, contralateral shoulder, smoking-status, hypercholesterolemia, posture and occupational dispositions. The challenge lies in early diagnosis since a high proportion of patients are asymptomatic. Pain and decreasing shoulder power and function should alert the heedful practitioner in recognizing promptly the onset or aggravation of existing RC tears. Partial-thickness tears (PTT) can be bursal-sided or articular-sided tears. Over the course of time, PTT enlarge and propagate into full-thickness tears (FTT) and develop distinct chronic pathological changes due to muscle retraction, fatty infiltration and muscle atrophy. These lead to a reduction in tendon elasticity and viability. Eventually, the glenohumeral joint experiences a series of degenerative alterations - cuff tear arthropathy. To avert this, a vigilant clinician must utilize and corroborate clinical skill and radiological findings to identify tear progression. Modern radio-diagnostic means of ultrasonography and magnetic resonance imaging provide excellent visualization of structural details and are crucial in determining further course of action for these patients. Physical therapy along with activity modifications, anti-inflammatory and analgesic medications form the pillars of nonoperative treatment. Elderly patients with minimal functional demands can be managed conservatively and reassessed at frequent intervals. Regular monitoring helps in isolating patients who require surgical interventions. Early surgery should be considered in younger, active and symptomatic, healthy patients. In addition to being cost-effective, this helps in providing a functional shoulder with a stable cuff. An easily reproducible technique of maximal strength and sturdiness should by chosen among the armamentarium of the shoulder surgeon. Grade 1 PTTs do well with debridement while more severe lesions mandate repair either by trans-tendon technique or repair following conversion into FTT. Early repair of repairable FTT can avoid appearance and progression of disability and weakness. The choice of surgery varies from surgeon-to-surgeon with arthroscopy taking the lead in the current scenario. The double-row repairs have an edge over the single-row technique in some patients especially those with massive tears. Stronger, cost-effective and improved functional scores can be obtained by the former. Both early and delayed postoperative rehabilitation programmes have led to comparable outcomes. Guarded results may be anticipated in patients in extremes of age, presence of comorbidities and severe tear patters. Overall, satisfactory results are obtained with timely diagnosis and execution of the appropriate treatment modality.

Key words: Rotator cuff tears; Partial thickness tears; Full thickness tear; Natural history; Ultrasonography; Magnetic resonance imaging; Single row repair; Double row repair; Healing

Core tip: Close attention to history and examination enables early diagnosis in the frequently asymptomatic rotator cuff tear. Ultrasonography and magnetic resonance imaging serve as excellent visualization tools. While conservative measures are successful in elderly patients with minimal lesions and demands, regular monitoring helps in isolating the surgical candidate. Early surgery should be considered in younger, healthier, active and symptomatic patients. Lower grades of tears do well with debridement alone while more severe lesions warrant a repair. Arthroscopic double-row repairs are superior in patients with massive tears. Satisfactory results are obtained with timely diagnosis and execution of the appropriate treatment modality.

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INTRODUCTION

"Its been an ache and a joy both to look over this big shoulder of mine at all my yesterdays" - Ethel Waters. Tears of the rotator cuff (RC) have been inherited by man from his ancestors with an association leading to the great apes[1,2]. With the advent of newer techniques, good to excellent results can be expected in the appropriately selected and compliant patient[3]. The aim of this article is to provide a comprehensive review of evidence-based concepts and present understanding of the epidemiology, etiopathogenesis, natural history, clinical evaluation, imaging, management and healing of RC tears.

PREVALENCE

Abundant data from across the world has been published on the prevalence of RC tears. Yamaguchi *et al*[4], from Missouri, United States, evaluated 588 patients with unilateral (U/L) shoulder complaints. Their analysis revealed 199 (33.8%) U/L and 177 (30.1%) bilateral (B/L) RC tears with average ages of 58.7 and 67.8 years respectively. The authors found high correlation between advancing age and RC tears[4]. In 2009, a study from the same institution on ultrasonographic (USG) screening of both shoulders in 237 asymptomatic individuals revealed a 17.3% prevalence of RC tear in at least one shoulder. Age-wise prevalence observed was 20% in 60-69 years old and 40.7% in subjects 70 years of age or older[5]. In a larger cohort of 683 Japanese villagers with a mean age of 57.9 years, Yamamoto *et al*[6] observed RC tears in 36% symptomatic against 16.9% in asymptomatic subjects with an overall prevalence of 20.7%. In a recent systematic review of 30 studies, Teunis *et al*[7] analysed 6112 shoulders with 1452 cuff abnormalities. Overall prevalence of RC abnormalities ranged from 9.7% in patients younger than or 20 years and increased to 62% in patients aged 80 years and older (P < 0.001) regardless of symptoms, among the general population and in patients with a dislocated shoulder.

A German prospective study on 411 asymptomatic shoulders by Tempelhof *et al*[8] revealed 23% overall prevalence of RC tears with high occurrence in patients over the age 70 and 80 years of 31% and 51% respectively. Further, Fehringer *et al*[9] observed a 22% prevalence of full-thickness tears (FTT) of the RC in patients aged 65 and above. Other European studies have shown lower figures. In a study from Austria on 212 asymptomatic shoulders, Schibany *et al*[10] reported a 6% prevalence of FTT. Likewise, Moosmayer *et al*[11] in a Norwegian study on 420 asymptomatic volunteers aged 50-79, revealed FTT in 32 subjects (7.6%).

Cadaveric studies on the RC tears have also revealed varying results. Neer's study on 500 cadavers more than 3 decades ago observed a less than 5% occurrence of FTT[12]. In 456 cadaver shoulders (mean age = 64.7) years, Lehman *et al*[13] reported an higher, 17% prevalence of FTT. Cadavers below and above 60 years of age had tear incidences of 6% and 30% respectively[13]. Still higher rates were observed by Reilly *et al*[14] in a review comparing cadaveric against radiological studies. Overall prevalence among 30 cadaveric studies was 30.3% while 11 ultrasound studies reported a prevalence of 38.9% in asymptomatic individuals which rose to 41.4% in symptomatic patients. Further, 14 magnetic resonance imaging (MRI) based studies reported 26.2% prevalence in the asymptomatic population *vs* 49.38% in symptomatic patients[14]. The disparity between human and cadaveric studies can be attributed to differences in subject population and unknown historical and clinical backgrounds in cadavers.

Despite varied regional distribution, RC tears are prevalent in up to 39% of asymptomatic individuals. An age-related increase in incidence leaves one with the thought of whether the tears are a part of the normal aging process. Their overall prevalence in symptomatic individuals is up to 64%. Presence of pain and decreasing shoulder strength and scores, which increases with age, heralds the onset or increase in size of existing RC tears. The opposite shoulder must be evaluated in U/L complaints to rule out B/L RC tears.

PREDISPOSING FACTORS

Age

Advancing age has been consistently held accountable as one of the major risk factor for the development of cuff tears in various studies. Gumina *et al*[15] on 586 patients with a history of arthroscopic tear repair reported a mean age of 59 years. Patients older than 60 were twice as likely to develop tear which were larger and more massive[15]. The prevalence in human and cadaveric studies in patients 60 years and older ranges from 20% to 30% and touches 62% in individuals aged 80 and more[4,5,7-9,11,13]. With a 10-year increase in age, the odds of an RC tear increase 2.69 fold (P = 0.005)[8].

Sex

A study by Abate *et al*[16] on menopausal women revealed increased prevalence of asymptomatic FTT in the postmenopausal period. Both sexes have otherwise been quoted as being equally predisposed to the development of RC tears[17,18].

Hand dominance

While some evidence suggests greater risk of the dominant hand for developing RC tears, others find this predilection not significant[6,18]. Dominant shoulders in veteran tennis players were more frequently torn suggesting an association of high energy activity with RC tears[19].

Contralateral shoulder

In patients operated for ipsilateral partial-thickness tears (PTT) or FTT, opposite shoulders are at increased risks of developing the same[20]. Ro *et al*[21] reported a higher prevalence of RC tears in contralateral (C/L) asymptomatic shoulders in U/L symptomatic RC tears, medium-sized or large operated RC tears and in patients with symptomatic RC tears of the non-dominant arm. B/L tears are common in U/L symptomatic tears with 35.5% prevalence FTT on the opposite side as observed by Yamaguchi *et al*[4]. The likelihood of a bilateral tear after 60 years of age is as high as 50%[4].

Smoking

A strong dose and time-dependent association has been established between smoking and the development of RC tears. Baumgarten *et al*[22], among 586 consecutive patients with unilateral shoulder pain, found 375 patients with RC tears. A smoking history was elicited in 61.9% patients with a mean 23.4 years of smoking 1.25 packs per day and 30.1 mean pack-years. In a systematic review by Bishop *et al*[23], increased rates and sizes of RC degeneration and symptomatic RC tears were seen in smokers which could consequently increase the number of surgical procedures in these patients. In a study on 408 patients, Carbone *et al*[24] found higher frequencies of smokers with at least a type Ⅱ tear (34.8%) differing significantly from the type Ⅰ patients (23.2%) and concluded that smoking negatively affects vascularity of tendons.

Family history

Increased risk in relatives of individuals with RC disease has been identified. In a study by Tashjian *et al*[25], patients diagnosed before 40 years showed significant relatedness for individuals with RC disease in close and distant relationships (up to 3rd cousins) (P = 0.001).

Posture

In a recent cross-sectional study by Yamamoto *et al*[26], RC tears were observed in 65.8% patients with kyphotic-lordotic postures, 54.3% with flat-back postures and 48.9% with sway-back postures while only 2.9% patients with ideal alignment had RC tears. The authors found poor posture as an independent predictor of symptomatic and asymptomatic RC tears[26]. In an Italian study, Gumina *et al*[27] compared the radiologically calculated subacromial space (SAS) width in 47 patients with thoracic hyperkyphosis with normal controls. They found reduced acromio-humeral space in hyperkyphotic patients, females and patients older than 60 years. The authors attributed this decrease to less posterior tilting and dyskinesis of the scapula[27].

Others

They are history of trauma, hypercholesterolemia and occupational demands of heavy labour[6].

ETIOPATHOGENESIS

Bursal and articular sided tears

The classical description by Ellman classifies RC tears on the basis of location into articular-sided tears (AST) and bursal-sided tears (BST) which are further staged according to their depths (Figure 1)[28]. These two varieties have differing properties and vasculature.

The precarious vascularity of the articular side has been demonstrated by Lohr and Uhthoff[29] who found the predominance of a zone of hypovascularity on the on the articular side. While ASTs result more commonly from intrinsic factors alone, intrinsic and extrinsic factors

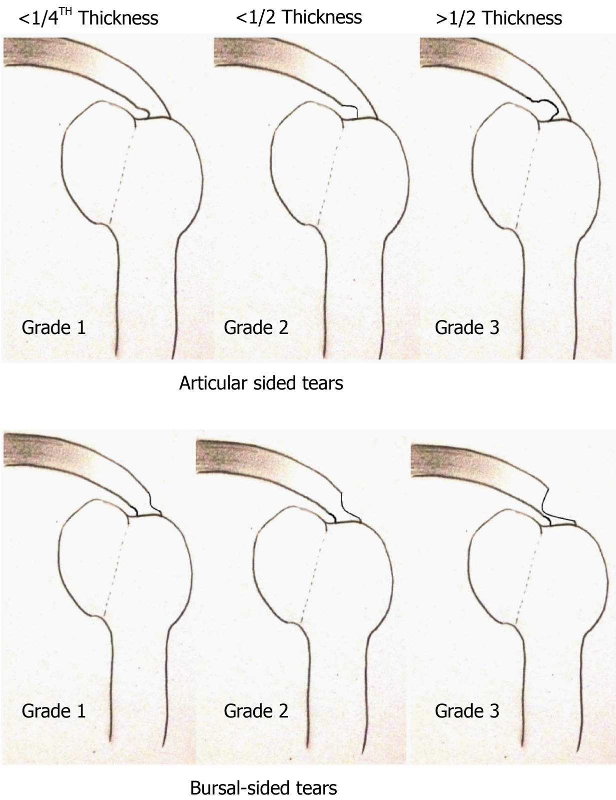


Figure 1 Types of partial thickness tears.

and greater wear and impingement more often result in BST. Ozaki *et al*[30] in a cadaveric study on 200 shoulders confirmed the association of BST with attritional lesions on the coracoacromial ligament (CAL) and anterior third of the undersurface of the acromion while ASTs had a normal acromion. Although an acromial lesion was always associated with an RC tear, the reverse was not true[30].

Extrinsic mechanisms

Tears of the RC have been theorized by Neer *et al*[31] to occur as a sequel of shoulder impingement due to repetitive translation of the cuff tendons under the acromion. Anatomical factors implicated in impingement and consequent tears of the RC include, among others, abnormalities in the coracoacromial arch. The acromion has been classified as flat, curved and hooked by Bigliani *et al*[32] (Figure 2).

Extrinsic sources arise from developmental aberrations in the form of os acromiale, hooked and keeled acromion, enthesophytes at acromial insertion of CAL and acromion-uncovered portion of humeral head (HH) leading to SSP impingement between the two[33]. Lower successful rates of nonoperative methods have been demonstrated in curved (73%) and hooked (58.3%) *vs* flat types (89%) by Wang *et al*[34]. Neer[35] in 1972 on 50 shoulders managed by anterior acromioplasty for impingement over 5 years demonstrated good results in 39. He concluded that acromioplasty provides good pain relief in mechanical impingement, exposure for SSP repair and prevents further impingement and wear. Moor *et al*[36], on the other hand, found no association between the acromion morphology and slope and RC tears. They avowed higher acromial indices, smaller lateral acromial angles and larger critical shoulder angles in degenerative RC tears. Anterior and lateral acromial bony spurs have been associated with FTT in symptomatic patients[37]. Other structures implicated in RC tears include spurs in CAL, altered coracoid morphology, increased pillar angulation, reduced inter-pillar distance or pillar length resulting in subcoracoid impingement. The subdeltoid, subcoracoid and subacromial bursae (SAB) are recognized causes of adhesions, bursitis and impingement[33]. The SAB may however, prove beneficial in tendon healing[38].

Intrinsic mechanisms

Besides extrinsic factors, the degeneration-microtrauma theory links advancing age and chronic microtrauma with PTT. Involvement of deep fibres leads to retraction, increased tension on intact fibres and conversion to FTT. Inflammatory changes and oxidative stresses causing tenocyte apoptosis along tissue remodelling are responsible for these tears[39]. Hypovascularity predisposes to development of RC tears in an age-dependent manner as shown by Rudzki *et al*[40] in 2008. A critical hypovascular zone exists 10-15 mm proximal to the RC insertion on the HH. In a study on 18 human specimens, the presence this zone close to SSP insertion was confirmed by selective vascular injection with a silicon-rubber compound. Uniformly sparse vascular distribution at the articular side against a well-vascularized bursal side could explain development of AST[29]. A few, however, have refuted this theory[41,42]. Laser Doppler flowmetry analysis by Levy *et al*[41] reported areas of increased flux at the RC tear edges suggesting areas of hypervascularity.

Internal impingement

Walch *et al*[42] in young, athletic individuals described impingement occurring between the deep side of SSP and posterosuperior edge of glenoid. Arthroscopic visualization confirmed AST involving posterior and anterior regions of the SSP and infraspinatus (ISP) respectively in the abducted and externally rotated shoulder.

Molecular basis

In a recent study, Choo *et al*[43] found patients with bursitis and tendinopathy expressing pro-myogenic genes while those with FTT expressed genes linked with fatty atrophy and fibrosis. Massive tears had down-regulation of most genes except inhibition of myogenesis which explains the difficulty in treating them. The authors also suggested earlier surgical intervention for a more favourable response.

To conclude, RC tears result from multiple etiological factors ranging from tendon injury due to narrowed SAS and anatomical aberrations, degeneration from

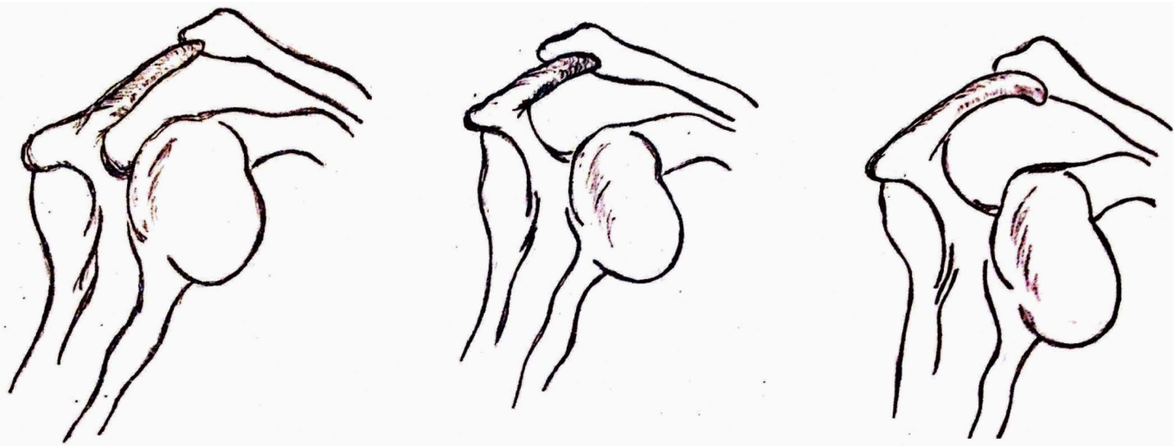


Figure 2 Types of acromion.

within the tendon and predilections resulting from non-physiological positioning in extremes of abduction and external rotation (ER). A relation of the tear process with regulation of gene expression may have a negative effect in the outcome of repairs.

NATURAL HISTORY

Symptom progression

Tears have been described as the ultimate consequence of impingement occurring in the final stage Ⅲ of RC disease[13].

Asymptomatic and symptomatic FTT

Studies in the past have revealed a substantial symptomatic conversion of asymptomatic FTT. Moosmayer *et al*[44], in a three-year follow-up of 50 patients found 18 symptomatic at the end of 3 years with significantly larger mean tear sizes (10.6 mm *vs* 3.3 mm, $P = 0.02$), faster muscular atrophy (MA), fatty degeneration (FD) and development of a pathological long head of biceps (LHB). Yamaguchi *et al*[45], while evaluating asymptomatic C/L tears in patients with U/L symptoms over 5 years, found greater symptoms and tear progression in 23 (51%) of 45 previously asymptomatic patients over a mean 2.8 years. In 2010, Mall *et al*[46] compared 44 newly symptomatic subjects over a two-year period, with 55 subjects who remained asymptomatic. The development of pain and increase in size of FTT by more than 5 mm occurred in 18% of the FTT. A 40% conversion of PTT to FTT was associated with significant reductions in the American Shoulder and Elbow Surgeons (ASES) scores. Newly symptomatic patients had significantly larger tears at initial evaluation. The development of symptoms in asymptomatic tears should, therefore, alert the surgeon towards suspecting tear enlargement[46].

The natural history of symptomatic RC tears often puzzles the reader with doubts regarding worsening and improvement of symptoms, risk of tear progression, indications and benefits of nonoperative and surgical intervention and the presence of FD and MA. Improved pain relief and arm function was seen in 19 of 33 symptomatic FTT at 3.8 years of follow-up by Hawkins *et al*[47] in 1995. Goldberg *et al*[48] in a 2.5-year follow-up of 46 nonoperatively managed symptomatic FTT, found functional improvement in 59% patients. Fucentese *et al*[49] in 24 nonoperatively managed FTT found no increase in tear size and FD over a mean 3.5 years. Tear progression, reported in 25% patients wasn't related to tear reparability. A sample containing small (mean 1.6 cm), isolated tears in patients aged around 54 years could adversely affect generalization of these results[49]. MRI monitored progression in 33 nonoperatively treated FTT by Maman *et al*[50] in 2009 demonstrated increased sizes in 52% patients. Older patients (> 60 years) with longer symptom duration (> 18 mo) and initial fatty infiltration were likely to progress (FI). Safran *et al*[51] in 2011, prospectively evaluated 61 nonoperatively managed FTT with a minimum size of 5 mm in patients younger than 60 years of age. At follow-up (mean 29 mo), 30 (49%) of the 61 tears were found to be larger with significant association with pain ($P = 0.002$).

Progression rates of symptomatic PTT to FTT have ranged from 10% to 50%[46,50]. The presence of pain has shown to be significantly indicative of an increase in tear size and should be, therefore, closely watched.

Chronic changes

Tissue quality plays an important role in RC healing[52]. Cuff pathology has effects on both muscles and tendons. Muscle retraction from FTT can alter angulations between the muscle fibres and allow adhesions and eventual FI. The twofold effects of FI produces MA and higher failure rates of surgical procedures[53,54].

The term fatty infiltration signifies infiltration of adipose cells[55,56]. Melis *et al*[57] in 1688 shoulders found statistical correlation ($P < 0.0005$) between FI, type of tendon lesion and patient age for SSP, ISP and subscapularis (SS). Severe FI was observed in extensive lesions, longer duration following rupture and increased patient age. A study involving 251 FTT revealed eighty-seven (34.7%) tears with FI having significantly greater dimensions and shorter distances posterior from the biceps than those without FI ($P < 0.0001$). The latter was the most important predictor for SSP FI. Tear width and length were found to be the most important predictors for ISP FI[58]. ISP FI has shown poorer results following repairs attributed to traction injuries of suprascapular nerve, disturbance to the anterior-posterior glenohumeral (GH) force couple and under-diagnosis[59].

As a part of the RC pathology, muscle atrophy has been documented by various authors. Swan *et al*[60] observed increases in muscle mass by 30%, fibre length by 7%, and physiological cross-sectional area by 27% in normal growing rats. The sarcomere length, however, were nearly constant. A comparative 53% SSP and 45% ISP rat RC mass reduction 30 d after tear was reported by Gumucio *et al*[61]. Barton *et al*[62] demonstrated rapid yet reversible loss of muscle mass, increase in fast muscle fibres, and fibrotic content of the muscle bed and tendon adhesions following RC tears in rats. Adhesion-induced reversal of changes may however, occur on return of load to the muscle. Ditsios *et al*[63] observed 30% and 35% reduction in SSP and ISP forces respectively in massive tears *vs* normal rat shoulders. FI and MA were more evident near the tendon on the dorsal aspect. Recently, Mendias *et al*[64] in 13 human shoulders elicited reductions in muscle fibre force production correlating with ASES scores and tear sizes. Disordered sarcomeres with lipid-laden macrophages in the extracellular matrix were seen surrounding SSP fibres. Reports exist on compensatory hypertrophy with MA. Kikukawa *et al*[65] in 2014, in a retrospective review of 279 subjects, confirmed hypertrophic changes in teres minors of patients with RC tear involving ISP. Mechanical unloading and denervation have been shown to result in FI and MA. These two independent predictors (part of the same pathological process) along with increased connective tissue content and fibrosis eventually result in decreased elasticity, viability and healing of the RC[59]. These unique, specific changes differ from denervation-induced changes after suprascapular nerve entrapment with respect to muscle border, perineural fat and overall FI distribution[66].

Tear-induced changes in GH kinematics have been described by Keener *et al*[67]. HH migration in 98 asymptomatic and 62 symptomatic RC tears showed significant correlation between PHM and RC tear size ($\geqslant$ 175 mm^2), tear extension into ISP and presence of pain. The net result, cuff-tear arthropathy occurs more commonly than realized[68]. Neer *et al*[69] ascribed this phenomenon to inactivity, disuse, synovial fluid leakage and HH migration. Next, cartilage atrophy, subchondral bone osteoporosis and impingement leads to acromial and acromioclavicular (AC) joint erosion. The collapsed HH finally erodes into the scapula from glenoid to as far as the coracoid resulting in a condition extremely difficult to manage[69].

Muscle retraction leads to tear-size, site, duration and age-dependent FI and reduction in muscle mass and force. Incongruent GH surfaces result in a challenging cuff-deprived joint. Surgical decision-making solely based on natural history seems inadequate and inappropriate due to conflicting results with nonoperative treatment. Further studies are required to establish guidelines assisting surgeons with the decision making process. Early surgical intervention in young, active adults with RC tears can avert advanced changes and GH arthropathy, both of which have poor outcomes.

CLINICAL EVALUATION

Progressive shoulder pain typically occurs around the anterolateral shoulder margin, lateral surface of the arm down to the elbow[70]. Night pain can occur in 83% patients while 41% may experience muscle weakness[71]. Local examination reveals disuse-related SSP and ISP MA. Among various tests, the empty can test is most sensitive (68.4%), drop arm and lift-off tests most specific (100%) and Neer test most accurate (75%) for RC tears overall[71].

For the SSP and ISP, the Jobe sign and the full can test have comparable accuracies[72]. High sensitivities (83% and 97%) and low specificities (23% and 5%) are reported with Hawkins sign and the painful arc test. Higher specificities (91% and 86%) have been observed with the external rotation lag sign (ERLS) and the drop-arm test (DAT) in diagnosing FTT. The sensitivity of lag tests reduces after subacromial lidocaine injection, while specificities of the Jobe, ERLS and DAT have been seen to improve[73]. A positive lift-off test is highly specific for diagnosing FTT and severe FI of SS[74]. No test in isolation however, is adequate for diagnosing an RC tear and a combination of tests improves the diagnostic yield[75].

IMAGING

Once clinically suspected, the RC tear requires radiological establishment of diagnosis. Ultrasonography (USG) is invaluable providing excellent tendon visualization. In a meta-analysis of 6066 shoulders, USG showed good sensitivity (84%) and specificity (89%) for the assessment of PTT and FTT (sensitivity 0.96; specificity 0.93)[76]. Orthopaedician-performed USG displayed better accuracy in large and massive tears against small tears (96.5% *vs* 91.6%)[77]. In a study by Iannotti *et al*[78] on 99 shoulders with RC disease, comparable sensitivities and specificities of MRI and USG were reported. Errors with USG were due to inability to distinguish between PTT and FTT around 1 cm in size[78]. FI can also be reported by USG with remarkable precision. Wall *et al*[79] have reported, as percentage-agreement with MRI, 92.5% and 87.5% accuracy in detection of FI with USG in SSP, ISP and SS respectively.

Read *et al*[80] compared preoperative and postoperative USG findings in 42 consecutively operated patients obtaining excellent sensitivity and specificity for

FTT (100% and 97%). The results were more dismal for PTT with sensitivity of 46%. A Cochrane Database review has similarly reported poor sensitivity of USG in diagnosis of PTT[81]. The 3D technique has demonstrated lower inter and intra-observer reliability than 2D USG for RC tears especially in the interpretation of small hypoechoic lesions close to the footprint as PTT[82]. Ok *et al*[83], in a prospective analysis of orthopaedician-performed USG in 51 shoulders, reported significantly poor correlation of USG-reported and arthroscopically-determined tear sizes (P < 0.05). In contrast, Roy *et al*[84] in a meta-analysis have demonstrated similar accuracy of USG by the radiologist/sonographer or orthopaedician.

A steep learning curve, operator and technique-dependence with inaccuracies in measuring tear size and PTT are few drawbacks of USG. Nonetheless it remains a reliable, fast, accurate, cost and time-saving tool in experienced hands providing excellent depiction of the RC tendon fibres. It also possesses easy availability, portability and speed, lacks motion artefacts and allows instant comparison with C/L side, dynamic evaluation of tendons and quantitative and qualitative assessment of FI[85,86].

The MRI can provide vital information and outstanding details not only on the RC tear size, extent, location retraction, FI and MA, but also on LHB, acromial morphology, AC joint and SAS[87]. A prospective follow-up of 48 patients revealed 100% PPV of MRI in detecting surgical tears[88]. Lower MRI accuracy has been reported in severe GH arthritis. Sershon *et al*[89] in 100 patients reported a 100% sensitivity, 68% specificity and 6% PPV. The MRI thus has an edge over USG in detecting smaller tears and possibly better evaluation of PTT.

Literature is flooded with studies comparing the two techniques. Teefey *et al*[90] in 124 consecutive painful shoulders reported similar accuracies of USG and MRI (87%). Likewise, Lenza *et al*[81] evaluating 20 studies with 1147 shoulders failed to illustrate any significant difference. Roy *et al*[84], in their meta-analysis, observed sensitivity and specificity of over 90% for FTT with USG and MRI. While specificity for PTT with both modalities was over 90%, lower sensitivities (67%-83%) were seen for PTT. Dinnes *et al*[91] in a systematic review found USG more cost-effective and accurate at picking up PTT than MRI. Over a 4-year period, Rutten *et al*[92] evaluated 5216 patients with shoulder symptoms and reported comparable accuracies of 95% and 100% for USG and MRI in diagnosing FTT and 89% and 67% in diagnosing PTT respectively. A smaller study on 21 patients demonstrated similar sensitivity, specificity, PPV, NPV and accuracy of USG and MRI[93].

Other, less frequently utilized and indication-specific modalities of imaging include plain radiographs with arthrography, computed tomography scans and MRI arthrography[80].

The decision regarding which to perform can be made on parameters like importance of obtaining data on lesions of the glenoid labrum, joint capsule or surrounding structures, the presence of an implanted device, patient tolerance and cost[78]. The ultimate decision needs to be based on these facts as well as availability, affordability and high-quality training of personnel performing the USG.

NONOPERATIVE MANAGEMENT

Management options RC tears includes nonsurgical measures, partial repair and/or debridement, open or arthroscopic repair, reconstruction and arthroplasty[94]. While the benefits of nonoperative measures include: avoiding surgery and its potential complications, less obvious risks include persisting and recurring symptoms, lack of healing, tear extension, fatty infiltration, muscle atrophy, tendon retraction and arthritis[5]. In a follow-up of 19 massive, nonoperatively managed RC tears, Zingg *et al*[95] observed satisfactory shoulder function for at least four years despite significant progression of degenerative structural joint changes. This risk of a reparable tear progressing to an irreparable tear needs to be averted by prompt recognition and early surgical intervention. Various modalities include analgesics, anti-inflammatory medications, physical therapy, activity modification and subacromial injections of local anaesthetics and/or steroids[96].

PTT are managed nonoperatively by tailored rehabilitation, ROM optimization and RC and scapular rotator strengthening. Anterior capsular tightness is addressed by ER stretching with the shoulder adducted while posterior capsular contractures require stretching of the abducted and internally rotated arm. With subsequent improvements, a strengthening programme is initiated of the shoulder girdle, core abdominal and thoracic muscles[97]. In a retrospective study on conservatively managed 26 PTT, Maman *et al*[50] found 2 increased and one decreased tears sizes. Contrasting reports however, exist. Hamada *et al*[98] in 1997 utilized in-situ hybridization to localize cells containing α1 type-Ⅰ procollagen mRNA in 13 PTT to determine RC healing. Maintained numbers of labelled cells at the tear and margins of concomitant intratendinous extensions led the authors to conclude that PTT and these extensions can continue to rupture after initial injury. Further, Yamanaka *et al*[99] in 40 AST observed tear reduction and disappearance in 4 cases each while tear enlargement and progression to FTT was seen in 21 and 11 patients respectively at 2 years.

Existing evidence on nonsurgical management of FTT is also conflicting. In a series by Fucentese *et al*[49], 24 symptomatic, isolated FTT of SSP were offered operative treatment only to be declined by the patients. Re-examination and MRI (at median 42 mo after diagnosis) reported high patient satisfaction and no increase in the average tear size. While 9 tears each remained constant and decreased, 2 were no longer detected at follow-up. In another 20 conservatively managed FTT, Baydar *et al*[100] observed statistically significant improvements in

ROM, pain and function scores at 6 mo follow-up. In a study by the Moon shoulder group on 452 patients with atraumatic FTT, significantly improved patient reported outcomes were observed at 6 and 12 wk after diagnosis and patients opted for surgical treatment in only 25% of instances[101]. In a long-term follow-up of 43 RC tears over 13 years, Kijima *et al*[102] observed nil or only slight pain in 90% of the patients while 70% patients had no disturbance in the ADLs. Younger patients had more significant symptoms.

Poor results with conservative treatment for FTT have been show by Maman *et al*[50]. A 52% progression in 33 FTT over a mean 20 mo demonstrated SSP atrophy in 24% patients. Safran *et al*[51], in 61 nonoperatively treated symptomatic RC tears at mean 29 mo reported increased sizes in about 50% patients.

The effects of physical therapy were prospectively analysed in a multi-center study on 389 patients with symptomatic RC tears. Higher scores were seen in females (P = 0.001), higher education (P < 0.001), active abduction (P = 0.021) and strength in forward elevation (P = 0.002) and abduction (P = 0.007). Lower scores were seen in males (P = 0.001), supra and ISP atrophy (P = 0.04, 0.003) and scapulothoracic dyskinesis (P < 0.001). The authors concluded that factors associated with pain and loss of function including scapulothoracic dyskinesis, active abduction, and strength in forward elevation and abduction should be addressed nonoperatively with therapy[103]. The Appropriate Use Criteria (AUC) developed by the American Academy of Orthopaedic Surgeons recommend nonoperative treatment is always appropriate in patients have a response to conservative care[104].

Nonoperative management should be individualised considering patient expectations, symptoms and response to previous nonoperative treatment. Our experience suggests earlier surgery in patients below 60 years or healthy symptomatic 60-70 year olds having increased demand for activity. Patients older than 70 years with low functional demands can be managed nonoperatively.

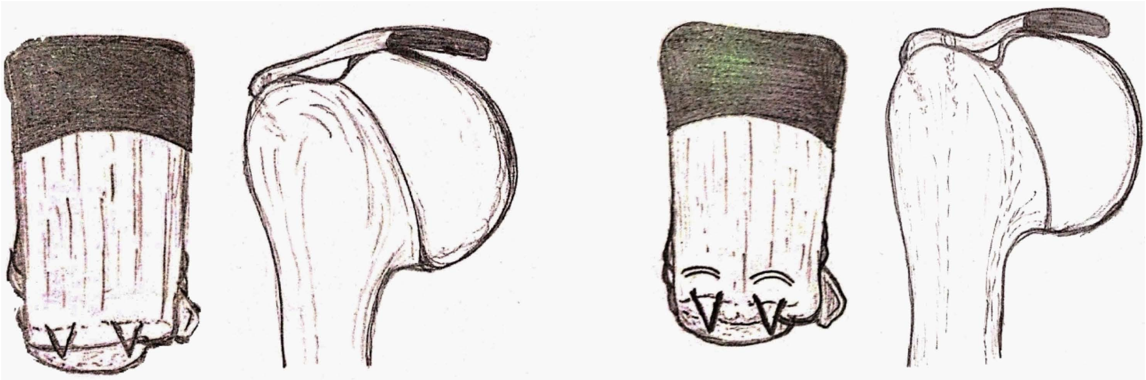
OPERATIVE MANAGEMENT

Surgical repair of the RC is a cost-effective solution for all populations and reduces the societal burden of the disease[105]. Surgical techniques have evolved from open to arthroscopic procedures[106]. Arthroscopic repairs have witnessed a dramatic 600% increase in the United States over the last decade[107]. The ideal repair of the RC tear must have the potential to withstand physiological loads while allowing simultaneous healing to occur[39]. The repair configuration opted for must be most reproducible and provide the best possible outcome and healing[94]. Predictable success, pain relief and patient satisfaction has been met with after repair of RC tears[108]. In a recent study on 103 shoulder surgeons, Robinson *et al*[109] observed overall higher overall popularity of arthroscopic repairs while open and mini-open procedures were preferred by the long-timers.

Several biomechanical factors to consider while repairing RC tears include the suture material properties which should be sufficiently strong, stiff, requiring a simple and reliable operative technique and configuration. Bioabsorbable anchors over their metallic counterparts offer no lasting foreign object, graduated loss of strength, minimum imaging artefacts and suture-abrading eyelets. Potential drawbacks include unpredictable loss of strength, eyelet rupture and foreign body reaction. Anchor insertion at standard depths (manufacturer-dependent), 0°-45° angulation with double loaded suture in the anterior and middle regions of the greater tuberosity with screw-type metal anchors for osteoporotic bones impart a good fixation[39].

PTT can be operated after a fair trial with conservative therapy. Repairs in non-overhead and overhead athletes are considered for tears more than 30%-50% and 75% respectively. Higher positional forces in throwers threaten repair integrity and preservation of motion. Options available include arthroscopic cuff debridement and open/arthroscopic repair with or without subacromial decompression[97]. Excellent postoperative outcomes have been reported, in data from 16 studies, ranging from 28.7% to 93%[110]. Thirty-nine PTT managed by acromioplasty, debridement and suturing, at a mean follow-up of 55 mo revealed satisfactory to excellent results in 33 (85%) patients. Four of six unsatisfactory results had unsuccessful previous surgery[111]. Evidence to suggest good to excellent results in more than 80% patients treated by debridement exists in literature[112,113]. Cordasco *et al*[114] in 162 patients with either normal, grade 1 (frayed) or grade 2 (< 50%) PTT in an average 4.5 years postoperatively reported significantly higher failure rates in grade 2B BST while the outcomes of in grades 1 and 2 and normal tears were not significantly different. The authors believed grade 2B BST may have been better served with primary repair.

Satisfactory results with arthroscopic BST repairs have been obtained. Koh *et al*[115] retrospectively evaluated 38 patients with a mean age of 50.8 years undergoing full-layer repair for more than 50% PTT with preservation of articular fibres. At a mean 26.9 mo of follow-up of 33 shoulders, 29 (87.9%) had intact repaired tendons with significant improvements in the patient scores. Investigators have also evaluated various techniques of AST repairs. In a prospective study by Franceschi *et al*[116], 2 arthroscopic modalities were compared. While 32 AST were repaired with TTT, 28 were converted to FTT and repaired. The authors reported significant improvements in clinical and functional outcomes and healing. Both methods were safe, comparable and effective. The addition of a biceps tendon tenotomy and augmentation to the TTT for AST has shown significant improvements in pain, function and ROM with no re-tears in preliminary results on 39 consecutive patients[117]. The direct visualization of the retracted AST layer to its insertion on the GT followed by DR fixation has been also shown to provide a stable



Single-row repair Double-row repair

Figure 3 Single and double row repairs of full thickness tears.

shoulder with good ROM[118]. A reduction in GH contact pressures has been identified with TTT for AST, in a study on 9 cadavers leading to diminished GH and SA impingement. Laxity however, can unwantedly result[119]. Reports also exist of FTT medial side tearing with TTT of AST in 21.2 mo follow-up of 7 out of 8 patients despite improved clinical outcomes[120].

Excellent healing after arthroscopic conversion of PTT to FTT has been reported by Kamath *et al*[121] in repairs of 42 PTT (after conversion to FTT). Thirty-seven (88%) shoulders had intact repairs 11 mo postoperatively which were significantly younger (average age 51.8, P = 0.02) than those with persistent defects (62.6). Overall patient satisfaction rate was 93%. No significant differences have been reported between AST and BST following conversion to FTT. A recent paper by Kim *et al*[122] comparing 20 AST with 23 BST conversions to FTT and repairs reported comparable improvements in both groups at mean 35.53 mo follow-up with higher re-tear rates in BST (9.5% *vs* 0%).

Outcomes of repaired PTT and FTT have had comparisons. Peters *et al*[123] compared 105 arthroscopically repaired small-medium FTT with 64 PTT demonstrating excellent results in both groups. Postoperative stiffness and re-tear rates were similar. Chung *et al*[124] compared repairs of 34 high-grade PTT with 21 small FTT and observed healing failure in 12 PTT related to severity of tendinosis (7.64 times higher in high-grade tendinosis). Despite good to excellent results in a majority of PTT repairs, patients operated previously with poor tendon quality and advanced age can disappoint.

The AUC recommendations suggest repair of full-thickness RC tears: maybe appropriate for reparable tears (even in patients responding conservatively), is appropriate for healthy symptomatic patients failing conservative treatment, maybe appropriate in chronic massive tears while arthroplasty maybe appropriate for healthy pseudoparalytic irreparable tears[104]. Early surgical intervention is needed in the setting of weakness and substantial functional disability[108]. Factors contributing to optimal repair include intact tendon-footprint motion and contact area, tendon and bone quality. Hypoxia, decreased vascularity, fibrocartilaginous changes and extrinsic compression along with MA and FI reduce the healing response[125].

Comparable long-term results have been demonstrated for open and all-arthroscopic modalities. Lindley *et al*[126] in a systematic review of 10 studies comparing postoperative outcomes in mini-open repair and all-arthroscopic repair techniques found no significant differences in patient demographics, RC pathology, rehabilitation protocols, ASES scores and recurrent defects. Short-term pain reduction was seen in the all-arthroscopic repairs. A recent meta-analysis on 12 studies with 770 patients failed to identify any significant differences in functional outcomes, pain scores, re-tear rates or presence of adhesive capsulitis between the 2 groups[127]. Parallel results have been demonstrated by other authors[128,129]. A randomized study on 125 patients receiving either mini-open or arthroscopic procedures for RC tears revealed similar results in both groups. Functional outcomes and re-tears were higher in FTT managed arthroscopically[130]. A lateral approach for mini-open RC repair permits improved visualization and function as described by Cho *et al*[131].

Popular among arthroscopic techniques are the single-row repair (SRR) and the double-row repairs (DRR) (Figure 3).

Varying degrees of clinical outcomes, healing and repair integrity and cost-effectiveness have been reported of DRR over SRR. A randomized controlled trial by Carbonel *et al*[132] on 160 patients revealed significantly greater improvements with DRR. Higher ASES scores, IR and ER along with lower re-tears following DRR have been reported in 2 recent meta-analyses[133,134]. A systematic review by Duquin *et al*[135] demonstrated significantly lower re-tear rates with DRR when compared to SRR for tears more than 10 mm in size. Another recent meta-analysis by Millett *et al*[136] comparing SRR with DRR revealed significantly higher re-tear rates in SRR especially in PT re-tears.

The repair of large, massive tears with DRR have shown better, though not statistically significant, functional outcome than with SRR in a systematic review by Saridakis and Jones[137]. This improvement in larger tears has been confirmed in a meta-analysis by Chen *et al*[138]. Other investigators have found equally improved outcomes after SRR and DRR[139-141]. Superiority of DRR in terms of healing rates has more clearly documented. Significantly higher healing has been observed in DRR surgeries[134,142]. This has also been confirmed in biomechanical studies. A systematic review by Wall *et al*[143] found DRR stronger than SRR with lower rates of failure and gap formation. A cadaveric study by Ahmad *et al*[144] demonstrated lesser extravasation of fluid from DRR suggesting an enhanced healing potential. Pauly *et al*[145] have also, in a systematic review demonstrated biomechanical and radiographic superiority with DRR in terms of structural integrity and reduced re-tear rates.

Few studies have criticized the DRR and proclaimed superiority for the simpler time-saving SRR method. Aydin *et al*[146], documented no significant differences in clinical outcomes and found DRR to be demanding, expensive and time consuming. Longer operating times with DRR have been supported by other studies[134,147]. The cost-effectiveness of DRR has been questioned by Genuario *et al*[148]. However, costs variations and probability of re-tear with SRR can have profound effects and prove DRR to be more cost effective in the first place. Higher re-tears with DRR have been reported. Kim *et al*[149] in a comparative analysis in 78 larger than medium-sized RC tears observed higher re-tear, lower UCLA and ASES scores in remnant tendons lengths less than 10 mm. Park *et al*[150] observed improved ultimate failure loads, better footprint restoration and stronger repairs with transosseous-equivalent (TOE) RC repair technique when compared to DRR. Gap formation was similar for both techniques.

Double-loaded suture anchors and margin-convergence sutures have been shown by Miškulin *et al*[151] to provide excellent results with significant improvements in functional parameters. The use of triple-loaded anchors in SRR has been shown to yield comparable and have shown to increase footprint coverage in cadaveric shoulders and potentially reduce costs[152]. The results of knotless self-reinforcing DRR have shown high patient satisfaction and serve as an alternative option in managing RC tears[153].

Based on the above discussion of the existing evidence, the suture technique should be chosen based on tissue properties, tear pattern and dimension and surgeon experience and comfort. PTT (BST or AST), do well with surgery. In FTT, mini-open and arthroscopic repairs provide comparable outcomes with better short-term pain control and more re-tears in arthroscopic methods. While the best biomechanical characteristics are possessed by the TOE repair, DRR may prove beneficial in tears more than 10 mm by providing stronger repairs closely replicating the native cuff at the cost of increased expenditure and failure at the MTJ which is harder to repair. Smaller (< 10 mm) tears can be repaired successfully by SRR the biomechanical superiority of which can be increased by increasing the suture limbs[104].

POSTOPERATIVE REHABILITATION

Physical rehabilitation is a vital component of postoperative patient care involving strict adherence and compliance. Poor patient cooperation, observed most frequently between 6-12 wk postoperatively, can lead to re-tears and failure[154]. Despite several reviews of rehabilitative programmes, high-level evidence is presently lacking[155]. Primary goals include restoring function while maintaining repair integrity. Gradual rehabilitation has been advocated in 4 phases beginning with 4 to 6 wk of immobilization, followed by protected passive ROM, followed by a gradual progression to active ROM and appropriate resistance exercise program[156]. Millett *et al*[157] have advocated protecting the repair initially and gradually progressing from early passive ROM through return to preoperative levels of activity.

Aggressive and early rehabilitation with continuous passive motion has been associated with improved early ROM, pain relief and outcomes[158]. In a prospective randomized controlled trial of 88 patients who underwent SRR, postoperative immobilization for 4 and 8 wk were compared. No significant differences were observed in terms of re-tears, ROM or clinical scores. Increased stiffness was however, higher in the 8 wk group (P = 0.038)[159]. Keener *et al*[160], in a study on 124 patients comparing early with delayed motion at 6 wk after DRR reported no differences in function, ROM and strength between the 2 groups. Active elevation and ER were better in early mobilization group at 3 mo. Gallagher *et al*[161] observed improved function in the first 3-6 mo with early ROM. Increased re-tears in medium to large tears, though statistically insignificant, occurred with early ROM. Identical outcomes were seen at 1 year. Lee *et al*[162] compared early and limited early passive rehabilitation in 64 patients after arthroscopic RC repair. Significant and faster improvements were seen in the early rehabilitation group in forward flexion, ER and IR at 90° of abduction and abduction 3 mo postoperatively. No significant differences were seen at 1-year follow-up. Postoperative MRI scans showed higher re-tears in the early *vs* limited early rehabilitated group (23.3% against 8.8%). The authors advocated gentler rehabilitation after arthroscopic RC repair for improved for tendon healing.

Less aggressive delayed immobilization has been associated with stiffness. Parsons *et al*[163] evaluating 43 arthroscopically repaired FTT in full-time sling immobilization without formal therapy for 6 wk found 10 patients (23%) developing initial stiffness. No difference in mean forward elevation, ER or IR and functional scores with the remaining patients at 1 year postoperatively. Lower re-tears were seen among the stiff patients. Newer modalities including combined aquatic and land-based postoperative therapy have shown encouraging results with significant improvements in both ROM and outcome scores (P < 0.001)[164].

An individualized rehabilitation approach is warranted in order to achieve a strong and mobile with maximum function and preserved repair integrity.

HEALING

Healing, as described by Mall *et al*[52], is formation of a continuous layer of tissue from the RC muscle belly to its insertion on the greater tuberosity. The evidence of spontaneous RC healing, without surgical repair, has been shown to be inadequate, inferior and limited in animal models.

Pathological changes described earlier along with delay in repair adversely influence postoperative outcomes as shown in animal studies[54,165,166]. Studies have however, reported excellent outcomes despite significant rates of recurrence, re-tearing and poor cuff healing. Deniz *et al*[167] reported excellent results in 66 out of 87 arthroscopically repaired shoulders despite re-ruptures in 26 patients. Neither the MA nor FI, over 30 mo, demonstrated any MRI documented improvements. While the MA pattern in re-tears was identical in the intact and the re-torn tendons, FI was significantly greater in the latter. Though complete healing demonstrates a greater improvement on follow-up, patient age, sizes of initial and re-tears are other factors correlating with final results[168-171]. Postoperative USG is an asset in evaluating repair integrity with 85% concordance with MRI readings and can be employed by sufficiently trained and experienced surgeons[172].

In recent literature, patient related factors affecting RC healing have been identified as demographic variables, comorbidity-status and tear-related factors. Demographic variables include: advancing patient age, longer duration of symptoms and longer follow-up[52,173-175]. Comorbidities including: Diabetes, hypercholesterolemia, smoking-status and nonsteroidal anti-inflammatory drug (NSAID) use have been shown to affect and delay bone-tendon healing[52,173,174,176]. Smoking has been associated with worsened histopathology and degenerative changes and increased apoptosis[175]. A reduced bone mineral density in a cohort study by Chung *et al*[173] was identified as an independent factor affecting postoperative RC healing. Tear-related factors with poor healing have included: Larger tears of longer duration with multi-tendon involvement. Small to medium-sized tears show higher healing rates (87%) as against large to massive-sized tears (62%)[177]. Tashjian *et al*[175] followed-up 49 shoulders at mean 16 mo postoperatively after DR-repairs identified lower healing rates (36%) in multi-tendon tears against single-tendon tears (67%). Retraction of the muscle-tendon units, tendon shortening, FI and MA along with presence of matrix metalloproteinases -1, 9 and tumor necrosis factor-alpha have also yielded poor results[52,128,173-175,177]. Medialization of the muscle-tendon junction (MTJ) is associated with significantly poorer healing rates (55%) when compared to MTJs lateral to the face of the glenoid (93%)[177]. The anterior sub-region of tendon has been associated with significantly higher gap formation[178]. Large tears with additional biceps or AC procedures have a negative impact on cuff integrity[179].

Various surgeon-associated factors influencing healing have included the choice and timing of technique, greater tuberosity preparation, acromioplasty, structural augmentation, platelet-rich plasma (PRP) and rehabilitation protocol[52]. Open *vs* arthroscopic methods have been systematically reviewed with no significant differences in the rates on healing[126,180]. While DRR has been shown to be stronger with improved healing rates as compared to single-row techniques, the functional outcomes have been equivalent in all except large and massive tears where DRR has provided a functional advantage[173]. Knotted *vs* knotless techniques have shown comparable functional outcomes and repair integrity. Mall *et al*[181], however, have reported greater hysteresis, reduced gap formation and higher ultimate load in medially knotted shoulders. Repair of chronically torn tears can result in injury at the time of repair. Davis *et al*[182] observed injury to almost 70% rat muscle fibres at the time of repair. Concomitant acromioplasty and the use of PRP have failed to demonstrate improvements in structural healing[52]. While early and delayed mobilizations continue to be debated, slower rehabilitation programmes can be safely adopted in light of improved healing and equivocal outcomes[52,173].

Compromised RC healing ability has questionable association with outcomes. Tear and patient age, comorbidities, NSAIDS, smoking-status, osteoporosis and tendon shortening and retraction adversely affect outcomes. Surgical and rehabilitation techniques have varying degrees of impact on the final result.

CONCLUSION

With increasing likelihood of occurrence RC tears with advancing age and longevity, the future poses a unique challenge to the orthopaedic surgeon. The morbidity of activity restriction added to severe pain makes matters worse for the debilitated patient. In such circumstances, it becomes essential for us to give due regard and promptly recognise cuff tears and timely intervene by providing the most appropriate treatment. Nonoperative treatment should be offered and continued in those with a good initial response and improvement of symptoms. Surgical intervention however, must not be postponed endlessly, especially in the younger and active population with worsening symptoms and progressing tears. With inherent advantages and promising outcomes, arthroscopic repair seems a propitious approach. The addition of a rehabilitation plan to the above provides the requisite nourishment and environment essential for the repaired and recovering tendons. An evidence-based and systematic modus operandi can help the surgeon in comprehensively managing RC tears with high degrees of success in the present scenario. Future directions point towards application of principles of tissue engineering to achieve enhanced repairs and functional outcomes.

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MINIREVIEWS

Current concepts in total femoral replacement

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Abstract

Total femoral replacement (TFR) is a salvage arthroplasty procedure used as an alternative to lower limb amputation. Since its initial description in the mid-20th century, this procedure has been used in a variety of oncologic and non-oncologic indications. The most compelling advantage of TFR is the achievement of immediate fixation which permits early mobilization. It is anticipated that TFR will be increasingly performed as the rate of revision arthroplasty rises worldwide. The existing literature is mainly composed of a rather heterogeneous mix of retrospective case series and a wide assortment of case reports. Numerous TFR prostheses are currently available and the surgeon must understand the unique implications of each implant design. Long-term functional outcomes are dependent on adherence to proper technique and an appropriate physical therapy program for postoperative rehabilitation. Revision TFR is mainly performed for periprosthetic infection and the severe femoral bone loss associated with aseptic revisions. Depending on the likelihood of attaining infection clearance, it may sometimes be advisable to proceed directly to hip disarticulation without attempting salvage of the TFR. Other reported complications of TFR include hip joint instability, limb length discrepancy, device failure, component loosening, patellar maltracking and delayed wound healing. Further research is needed to better characterize the long-term functional outcomes and complications associated with this complex procedure.

Key words: Hip disarticulation; Limb salvage; Revision arthroplasty; Total femur arthroplasty; Total femoral arthroplasty; Total femoral replacement; Total femur replacement; Salvage arthroplasty

Core tip: The inherent mechanical limitations of the total femoral replacement implant, the complexities of the associated surgical technique and the typically poor condition of the host soft tissue bed have contributed to the mixed outcomes and high complication rates which are reported in the literature. Although this proce-

dure could provide satisfactory long-term ambulatory outcomes by salvaging the extremity for weight bearing, prudent selection and management of the well-evaluated surgical candidate is essential to ensuring the successful achievement of this goal.

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INTRODUCTION

The total femoral replacement (TFR) represents an important surgical option in limb salvage reconstruction. Otherwise known as total femur replacement or total femoral arthroplasty, the procedure and its indications have continually evolved since its earliest descriptions in the middle of the 20th century[1]. Apart from its more recognized applications in oncologic reconstruction, the TFR has also been utilized in the non-oncologic setting as rates of revision arthroplasty continue to rise worldwide[2]. However, the inherent mechanical limitations of the TFR implant design, the complexity of the associated surgical technique and the typically poor condition of the local host soft tissue bed have contributed to the mixed outcomes and high complication rates which are reported in the literature.

This is a minireview conducted to identify current practice in TFR. Relevant articles were independently identified by two research personnel using PubMed (65 results), EMBASE (75 results) and Scopus (76 results) with the earliest retrieved article dating from September 1970. The following search parameters were used: ("total femoral arthroplasty" or "TFR") or ["total replacement" and (femur or femoral) and arthroplast*]. Both English and non-English articles were qualitatively reviewed and multiple large case series were studied to determine TFR survivorship and complication rates (Table 1).

INDICATIONS AND PATIENT SELECTION

The decision to perform TFR must be made only after careful consideration of the specific reconstructive needs and functional expectations of the patient. The most commonly considered surgical alternatives to this procedure include hip disarticulation and above knee amputation[3]. Although TFR could provide better long-term ambulatory outcomes by salvaging the extremity for weight bearing, prudent selection of the well-evaluated surgical candidate is essential to ensure the successful achievement of this goal.

In the appendicular skeleton, the femur is the most common bone to be affected by primary and secondary malignancies. Therefore, the oncologic applications of TFR have been well documented in a variety of conditions with extensive bone involvement, including: osteosarcoma, Ewing's sarcoma, chondrosarcoma, pleomorphic undifferentiated sarcoma and bony metastases[4,5]. Expandable prostheses have been implanted in skeletally immature individuals to address the challenge of limb length discrepancy due to ongoing growth of the contralateral limb[6,7]. However, the requirement for multiple lengthening revision procedures may increase the risk of deep periprosthetic joint infection with this technique. Other surgical alternatives in such situations include van Nes rotationplasty and amputation[7]. Rotationplasty involves the rotation of the tibia during reconstruction to allow the ankle to simulate functional mobility of the former knee joint. It is noted for excellent long-term functional outcomes in young, motivated individuals who would otherwise be rendered unable to perform high impact activities with a TFR[8].

As the yearly number of revision arthroplasty procedures continues to rise, it is anticipated that there will be a correspondingly greater incidence of salvage arthroplasty[9]. The performance of multiple revision surgeries predisposes to extensive bone loss which would then necessitate either partial or total endoprosthetic replacement of the femur (Figure 1)[10]. Similarly, repeated surgical debridement in the setting of periprosthetic joint infection could also lead to the dramatic reduction of femoral bone stock[11]. The orthopaedic challenge posed by these multiple revision surgeries has been labeled by some surgeons as a "shattered femur", that is a femur which cannot be reconstructed by more conventional methods[12]. Extensively comminuted periprosthetic fractures which were managed by TFR have reportedly good functional outcomes and an implant survival rate of 86% at 10 year follow-up[13]. Occasionally, TFR may provide a single surgical solution for multiple concurrent, ipsilateral orthopaedic issues. For example, in a limb requiring proximal or distal femoral replacement, the coexistence of severe knee or hip osteoarthritis, respectively, may be simultaneously managed by TFR[12].

Other clinical conditions which can alter the biomechanical integrity of the femur and predispose to pathologic fractures have been successfully managed with TFR[14]. Past use of customized curved femoral stems for the management of Paget's disease of the femur had been associated with periprosthetic fractures at the level of the prosthesis tip[15]. However, in 1965, it was shown that a vitallium endoprosthesis could be used to successfully replace a deformed Pagetic femur[1]. That case report represented one of the earliest descriptions of TFR in the orthopaedic literature[16]. Similarly, it has been shown that amputation may be avoided in radical resection of massive hemophilic pseudotumors of the femur and soft tissues of the thigh by simultaneous reconstruction with a custom total femoral prosthesis[17]. It is known that hemophilia results in extensive bone loss and cavitation along with significant joint ankylosis secondary to repeated episodes of hemarthrosis[18].

Table 1 Types of total femoral replacement prostheses

Feature	Intramedullary TFR system	Tumor-style TFR system
Basic design	Modular hip femoral component; Constrained knee femoral component with customized intercalary segments; May require strut allografts and cerclage cables	Modular and available in multiple lengths
Femoral bone stock	Possibility of preservation; can maintain muscle attachment	Absent
Distal femur resection	Can preserve distal femur or remove femoral component using standard revision techniques	Entire distal femur can be removed by subperiosteal dissection (less bleeding)
Tibial component	Suitable for constrained condylar articulation	Suitable for rotating hinge articulation

TFR: Total femoral replacement.

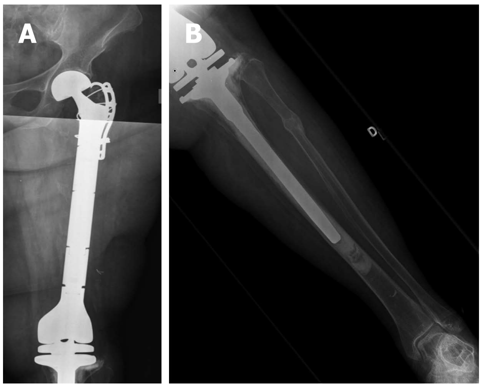

Figure 1 Total femoral replacement with intercalary body to connect proximal femoral replacement with distal rotating hinge knee implant. A: Composite radiographic images of our patient who underwent revision arthroplasty with TFR after periprosthetic infection necessitated removal of distal femoral replacement rotating hinge component and *en bloc* resection saucerization excision of remnant native proximal femur; B: Reconstruction was accomplished with intercalary body connecting proximal femoral replacement component with rotating hinge knee implant. Extensor mechanism was reconstructed and the greater trochanter repaired with a long claw cable fixation and Mersilene tapes. TFR: Total femoral replacement.

This represents yet another potential situation where TFR could treat structural deformity of the femur while concurrently managing degenerative changes in the ipsilateral hip or knee.

CURRENT PRACTICES IN SURGICAL TECHNIQUE

Given the technical complexity of this procedure, it is anticipated that TFR will require significantly longer operating time than most other revision arthroplasty surgeries. This potentially increases the risk of intra-operative wound contamination and the subsequent development of periprosthetic joint infection[19]. In recognition of this, some manufacturers have recently begun to coat their TFR prostheses with silver in order to provide an antimicrobial advantage in the local tissue bed. Of note, a recent prospective study of megaprostheses with galvanized silver coatings (including six TFR prostheses) noted that 23% of the study population developed local argyria after a median of 25.7 mo[20]. However, despite this local idiosyncratic reaction to silver metal, the study did not find clinical evidence of any systemic complications.

Also, the extensive dissection required for this procedure is likely to result in a greater volume of blood loss. However, adherence to a subperiosteal dissection will help minimize bleeding[12]. In specific situations, recent technological advancements, such as intraoperative blood salvage, bipolar sealing device and argon beam coagulation, may assist with hemostasis and lessen the requirement for blood transfusions[21-23]. Also, the frequently multiple comorbidities of the TFR patient population and the intensive physiologic demands of the procedure itself make the requirement for postoperative intensive care highly likely.

There are two varying implant designs of TFR prostheses available for consideration when limb salvage reconstruction is planned (Table 2)[12]. The intramedullary TFR (IM-TFR) represents an important alternative to the more conventional "tumor-type" TFR. The IM-TFR is based on the prosthetic linkage of previously implanted femoral components of past hip and knee arthroplasties. This can be accomplished by two different surgical approaches: either (1) the use of a custom intramedullary sleeve to link the well-fixed hip stem with a stemmed component of a total knee arthroplasty; or (2) the use of an intercalary segment to connect revised hip and knee arthroplasties *via* morse taper junctions[24]. The IM-TFR has been designed to address the central disadvantages of the conventional TFR by reducing the need for extensive dissection and by maintaining the soft tissue attachments. However, it is highly advisable to have both implant options readily available at the time of surgery[12]. With regard to surgical approach in TFR, options include a lateral incision proximally and a separate midline incision distally or a single anterolateral incision. In the prior trauma patient with past incisional scars on the lateral aspect of the thigh, a lateral parapatellar approach may be used when implanting the distal portion of the TFR, as with rotating hinge knee arthroplasty[25]. In order to ensure optimal wound closure, the surgical plan must take into consideration the preexisting surgical scars in this frequently re-operated patient population. Poor preoperative planning predisposes to inadequate wound healing which may eventually lead to secondary periprosthetic infection of the TFR[26].

Most of the TFR systems which are currently available on the market are fixed constructs and therefore the surgeon is permitted only limited control of the proximal femoral version. This key feature of the TFR implant may predispose to postoperative hip dislocation proximally

Table 2 Large case series of total femoral replacement in current literature

Ref.	Publication	*n*	Age	Indications	Follow-up (mo)	Patients living at time of publication	Survivorship	All-cause revision rate	Complications	Prosthesis used
Ahmed[28]	Arch Orthop Trauma Surg	9	47 (10-74)	Oncologic	51 (8-200)	4/9	No failures	0%	Infection (2), tibial component loosening (1)	Zimmer
Amanatullah *et al*[3]	J Arthroplasty	20	65 ± 11	Non-oncologic (revision arthroplasty)	73 ± 49	0/20	70% at 5 yr follow-up	30%	Infection (7), hip dislocation (5), limb length discrepancy (2), knee flexion contracture (1)	Biomet, Link Stryker
Berend *et al*[2]	Clin Orthop Relat Res	59	74 (39-91)	Non-oncologic (end-stage prosthetic disease)	58 (12-156)	14/59	65% at 5 yr follow-up	30.5%	Infection (8), hip dislocation (7), tibial component loosening (2), acetabular component loosening (1)	Biomet, Link
Fountain *et al*[10]	J Arthroplasty	14	63.7 (48-79)	Non-oncologic (revision arthroplasty)	90 (12-204)	13/14	NA	35.7%	Hip dislocation (5), infection (3)	Link
Friesecke *et al*[30]	J Bone Joint Surg Am	100	68 (40-94)	Non-oncologic (revision arthroplasty)	59 (1-138)	95/100	NA	21%	Infection (12), hip dislocation (6), prosthesis failure (3), patellar issues (2), hematoma (2), peroneal nerve palsy (1), delayed wound healing (1)	Link
Lombardi *et al*[12]	J Arthroplasty	75	73 (36-92)	Non-oncologic (end-stage prosthetic disease)	42 (1-158)	50/75	NA	30.7%	Infection (11), hip dislocation (7), tibial component loosening (2), acetabular component loosening (1), hematoma (1), periprosthetic fracture (1)	NA
Mankin *et al*[14]	Clin Orthop Relat Res	15	52 ± 1 (16-82)	Oncologic, non-oncologic (Paget's disease, rheumatoid arthritis)	54 (12-192)	7/15	NA	33.3%	Prosthesis failure (4), infection (1)	NA
Nerubay *et al*[26]	Clin Orthop Relat Res	19	20	Oncologic	18-96	7/19	NA	-	Wound healing problems (10), infection (1), popliteal vein injury (1), prosthesis failure (1)	NA

Steinbrink *et al*[33]	J Bone Joint Surg Br	32 (28 patients)	56 (21-81)	Oncologic, non-oncologic (end-stage prosthetic disease, revision arthroplasty, pathologic fractures, osteoporosis)	6-84	23/28	NA	9.4%	Infection (2), hip dislocation (1), prosthesis failure (1), patellar pain (1)	Custom
Ward *et al*[34]	Clin Orthop Relat Res	21	44.6 (11-91)	Oncologic, non-oncologic (revision arthroplasty, end-stage prosthetic disease)	31 (1-125)	11/21	NA	2.4%	Infection (3), hip dislocation (2), patellar pain (1)	Custom

NA: Information was not available in article.

and altered patellofemoral tracking distally. Hence, the proximal end of the TFR system is often connected to a bipolar or tripolar constrained liner to lower the risk of postoperative hip dislocation[3]. Of note, certain TFR systems are designed with interdigitating fins which allow some customizability of proximal femoral version. In oncologic settings, the native acetabulum may be retained and purse stringing of the joint capsule can be performed to provide hip joint stability. Appropriate external rotation of the tibial component is critical to facilitate patellofemoral tracking, particularly with the use of a constrained condylar articulation. Prior to wound closure, it is essential to evaluate patellofemoral tracking. Performance of lateral retinacular release with or without reefing/imbrication of the vastus medialis obliquus muscle may be required to enhance patellofemoral tracking[12].

Adequate soft tissue reattachment, particularly of the hip abductor muscle group, is a critical part of the surgical technique[10]. The TFR prostheses contain holes for passing suture material through the implant itself (Figure 2). These holes are smoothly beveled to prevent the potential fraying of suture material upon repeated friction over the metal surface. Polyester graft materials are commonly used to help reattach the muscle groups to the greater trochanter[10]. However, detecting failure of these materials can challenging because of their radiolucency.

Newer designs have tried to incorporate trabecular metal pads to increase the possibility of tissue metallic ingrowth. Proximally, clawed devices may lead to lateral trochanteric tissue irritation. The screws in these clawed devices may loosen and subsequently lead to failure of hardware fixation. This could be a potential source of long-term pain and increased instability.

REHABILITATION AND FUNCTIONAL OUTCOMES

The most compelling advantage of TFR is the achievement of immediate fixation which permits early mobilization[27]. Rehabilitation protocols described in the literature are generally similar, with most emphasizing the importance of quadriceps muscle strengthening in ensuring competence of the extensor mechanism[28]. The use of a custom-molded polypropylene brace to limit flexion and adduction has been advocated for up to 6 wk postoperatively[27]. In the setting of difficulty in hip flexion, TFR patients may perform circumduction at the hip in order to clear the foot during gait.

A recent series of oncologic TFR patients observed that mean patient-reported functional scores were significantly lower than among comparison patients who underwent only proximal or distal femoral reconstruction[29]. However, in another large series of patients who underwent TFR after multiple failed revisions, there was significant postoperative improvement in functional scores for both knees and hips[30]. Arthroplasty with the IM-TFR has been theorized to provide better functional outcomes because of the less invasive surgical technique associated with its implantation[24].

Of note, there is considerable heterogeneity in long-term outcomes among the TFR patient population, particularly between oncologic and non-oncologic patient groups[3]. Reported follow-up and survivorship in the literature is also highly variable due to differences in mortality rates between both groups in adults (Table 2). Despite this heterogeneity, all TFR patients are typically faced with a challenging rehabilitation course due to the almost invariably complex medical history and the immediate physiological demands of the surgery itself.

It is imperative that each patient’s functional expectations are carefully assessed at the preoperative visit. The possibility of future surgeries and the potential for lifelong requirement of an assistive device must be discussed with the patient[12]. However, it is clear that even a TFR with moderate functional outcomes will provide far better ambulatory capabilities than hip disarticulation[29].

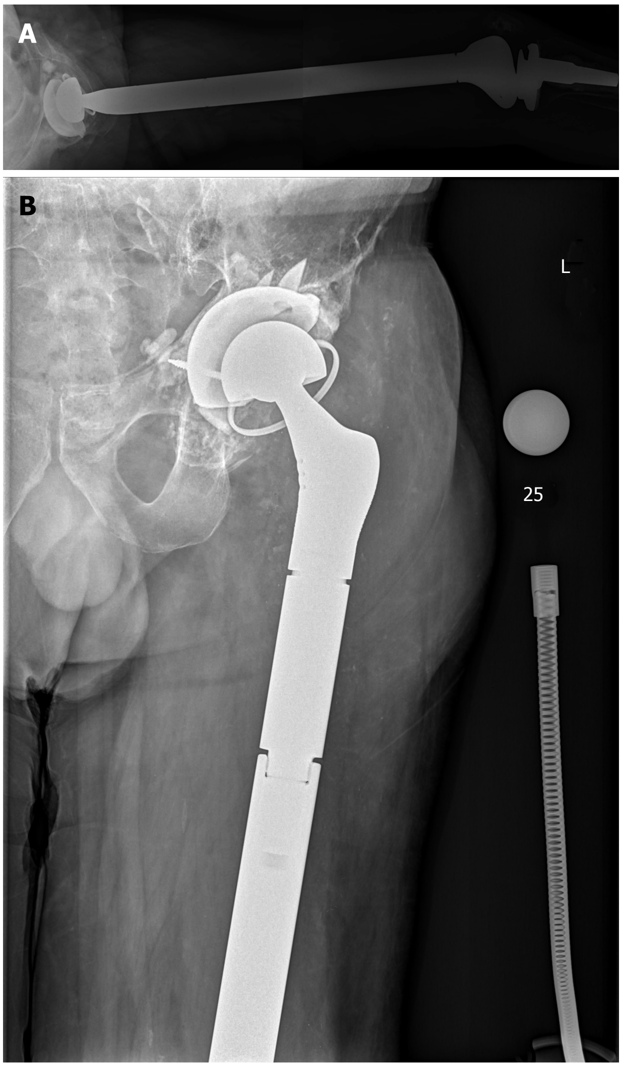

Figure 2 Total femoral replacements with constrained acetabular component and rotating hinge knee implant. A: Composite radiographic images of our patient who underwent TFR after multiplerevisions of total hip arthroplasty; B: TFR was done with constrained acetabular component, rotating hinge knee arthroplasty and patellar resurfacing. Abductor muscle repair was done by using a locking suture technique sewing into holes in the proximal femoral replacement component. Somatosensory evoked potentials were used intraoperatively to monitor sciatic nerve function during correction of a 4 cm limb length discrepancy. Potentials remained normal throughout. TFR: Total femoral replacement.

COMPLICATIONS ASSOCIATED WITH TFR

As the incidence of TFR surgeries continues to rise, a correspondingly greater need for revision TFR surgery is anticipated. One of the most common indications for revision surgery is deep periprosthetic infection. In a large series of non-oncologic TFR performed for revision arthroplasty in 100 consecutive patients who were infection-free at time of surgery, 12% developed periprosthetic infection of the TFR[30]. It was determined that seven of these patients were newly infected whereas the others five patients had a remote history of prior infection.

In the current era of multi-, extreme- and even total-drug resistance, the TFR patient is at a significantly greater risk for acquiring a life-threatening infection. There are multiple predisposing factors involved in the development of TFR periprosthetic infection, namely: extensive surgical dissection, large metal surface area, prolonged operative time, multiple patient comorbidities and repeated hospitalization for past surgical procedures in this patient population, including prior revision arthroplasty for periprosthetic infection[31]. Moreover, this risk of infection may be increased by an inadequacy of initial antibiotic therapy or a lack of thoroughness in surgical debridement (secondary to retained cement material or implant hardware). It is imperative that postoperative antibiotic therapy is of appropriate duration and intensity in order to ensure satisfactory prophylaxis, particularly in patients known to have been colonized with drug resistant strains preoperatively.

In the management of TFR periprosthetic infections, there are various options including one-stage prosthesis exchange with chronic antibiotic suppression and two-stage revision arthroplasty with cement spacer placement. However, it is reported that patients above 50 years of age or recipients of secondary TFR are at a particularly high risk for developing a periprosthetic infection which could render the TFR unsalvageable[27]. Therefore, depending on the likelihood of attaining infection clearance, it may sometimes be advisable to proceed directly to hip disarticulation without attempting salvage of the TFR[3]. When considering salvage of the infected TFR, the surgeon must be particularly mindful of the virulence and treatability of the infective organism. Recent reports of nearly untreatable periprosthetic infections in frequently re-operated patients underscore the importance of this decision[32]. In such situations, eventual infection clearance is often attained at high physical and financial cost with survivors suffering from major disability secondary to renal toxicity and unsatisfactory functional outcome of the salvaged limb.

Post-operative hip instability causing recurrent dislocations is another leading cause of TFR revision. Concomitant infection could also further complicate matters in these cases. Hip dislocations in TFR can be managed by placement of a constrained liner screw into the cup or the insertion of additional interpositional segments[30]. Limb length discrepancy is another potential complication which may require revision surgery with exchange of modular components to shorten or lengthen the TFR as required.

Other less common complications which are reported to have required additional surgery include mechanical failure of the prosthesis, acetabular or tibial component loosening, patellar complications (such as revision for patellar maltracking) and difficulty with wound healing[32,33]. Free flap coverage may be performed either at the time of TFR or later as part of a staged treatment plan. Inadequate wound coverage and the presence of local necrotic tissue may quickly lead to secondary periprosthetic infection of the TFR.

Postoperative complications associated with TFR are frequent and expensive to manage. Appropriate patient selection is necessary to minimize this risk and avoid high healthcare costs associated with failure of TFR.

CONCLUSION

TFR is anticipated to become an increasingly favored salvage option in the setting of extensive femoral bone loss. Careful patient selection, excellent surgical technique, a comprehensive rehabilitation program and the prompt management of postoperative complications are essential to ensure optimal long-term outcomes in this challenging patient population. Therefore, given the complex nature of this procedure, it would seem that TFR should probably be performed by the orthopaedic oncologist or adult reconstruction surgeon who is familiar with the unique challenges involved. In lieu of a prospectively compiled, central registry for TFR, continued research with larger patient series and retrospective cohort studies is needed to better characterize the functional outcomes and complications associated with this procedure.

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MINIREVIEWS

Posterior shoulder instability in the athletic population: Variations in assessment, clinical outcomes, and return to sport

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Abstract

Posterior instability of the shoulder is becoming an increasingly recognized shoulder injury in the athletic population. Diagnostic elements, such as etiology, directionality, and degree of instability are essential factors to assess in the unstable athletic shoulder. Concomitant injuries and associated pathologic lesions continue to be a significant challenge in the surgical management of posterior shoulder instability. Return to sport and previous level of play is ultimately the goal for every committed athlete and surgeon, thus subpopulations of athletes should be recognized as distinct entities requiring unique diagnostic, functional outcome measures, and surgical approaches.

Key words: Posterior shoulder instability; Overhead throwing athletes; Contact athletes

Core tip: This article focuses on important posterior shoulder instability diagnostic criteria, effects of concomitant injuries, discussion of variations in athletic subpopulations and effects of return to sport, surgical management and advantages of arthroscopic *vs* open techniques.

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INTRODUCTION

Posterior instability of the shoulder represents a unique entity among athletic shoulder injuries. Accurately diagnosing and treating posterior instability of the shoulder is often challenging due to the numerous confounding variables existing on the shoulder instability injury spectrum. However, despite diagnostic and surgical challenges, posterior shoulder instability is becoming increasingly recognized as a treatable shoulder injury.

Posterior shoulder instability is multifactorial and the etiology varies widely within the athletic population. Primary mechanisms of injury may include: (1) an acute traumatic posteriorly directed shearing force along the glenoid face between the posterior labrum and glenoid articular surface, resulting in capsulolabral detachment[1-3]; (2) repetitive microtrauma to the posterior capsule, ultimately leading to capsular attenuation and labral tears[4]; or (3) insidious onset of laxity of the posterior capsule and associated passive stabilizers[5-7]. Other causes of posterior instability often result from (1) excessive glenoid or humeral retroversion; (2) an engaging reverse Hill-Sachs lesion; and (3) and glenoid hyperplasia[1,5].

DIAGNOSIS OF INSTABILITY

Essential elements, such as etiology, directionality, and degree of instability are critical to assess in order to adequately manage posterior instability and prevent recurrence. Thus, it has been shown that unrecognized instability in more than a single isolated direction may be a significant contributing factor leading to poor patient outcomes. A level 2 study performed by Bradley *et al*[8] evaluated 100 athletes undergoing posterior shoulder stabilization procedures reported 62.5% (5 of 8) of their recurrences may have been a direct result of failure in diagnosis of bi-directional or multi-directional instability at the time of the index procedure. Furthermore, an earlier retrospective investigation by Wolf *et al*[9] identified similar findings in their cohort of 14 patients, in which the 1 reported failure was noted to have pronounced inferior laxity accompanying posterior instability at the time of the revision procedure.

It is also well known that patients with recurrent subluxation and/or dislocation frequently have osseous defects of the posterior glenoid rim or humeral head, which may contribute to the degree of instability. Operative intervention to address such cases may involve more aggressive and invasive procedures, such as reverse Hill-Sachs, humeral head or posterior bone allografts[10,11]. Ultimately, the degree of instability is one of many variables that should be considered in order to determine the most appropriate operative management in order to ensure successful patient outcomes.

Patients with a voluntary component to their posterior shoulder instability should also be recognized as a unique entity with the potential for less predictable outcomes. In a case series of 33 patients, Provencher *et al*[12] demonstrated that patients with voluntary instability resulted in worse outcomes. Specifically, they identified recurrent instability to be specific to patients with a voluntary instability component, whereas, all patients with involuntary instability were stable at follow-up (P = 0.025). Similarly, a case series of 20 shoulders reported by McIntyre *et al*[13] observed that 4 of 5 of their patients with a recurrence had a voluntary component to their instability.

Ultimately, failure to accurately access posterior instability both preoperatively *via* clinical examination, magnetic resonance imaging, as well as, intraoperative arthroscopic assessment to identify potential excessive capsular laxity, concurrent soft-tissue or osseous lesions, and bi- or multi-directional instability may result in unfavorable patient outcomes[8].

CONCOMITANT INJURIES

Posterior shoulder instability rarely occurs in isolation, often accompanied by microtrauma resulting from repetitive shearing forces, macrotraumatic events, prior dislocations, scapulothoracic dysfunction, and various osseous and soft-tissue abnormalities[4]. Concomitant injuries and procedures pose additional challenges in the management of posterior shoulder instability, which may lead to varied and less favorable outcomes[14]. In a retrospective case series of 14 patients, Bahk *et al*[15] reported that patients with concurrent injuries had less reliable outcomes, *e.g.,* higher pain scores (P = 0.001), lower American Shoulder and Elbow Scores (ASES) scores (P < 0.001), lower University of California, Los Angeles Shoulder Rating Scale (UCLA) scores (P < 0.001), higher subjective instability scores (P < 0.001), higher Western Ontario Shoulder Instability (WOSI) scores (P = 0.0002), or lower score for WOSI percentage of normal (P = 0.0002) at an average follow-up of 66 mo (range, 24-149 mo). Additionally, the senior author (JPB) has determined approximately 40% of his cohort of 389 patients that underwent surgical management of posterior shoulder instability had concomitant pathology at the time of the index stabilization procedure (James P. Bradley, personal communication, June 1, 2015). Furthermore, an advanced understanding of biomechanics and pathoanatomy of the posterior capsulolabral complex and all static and dynamic structures, such as the rotator interval, the anterior-superior labrum and its attached superior glenohumeral ligament, the coracohumeral ligament, the inferior glenohumeral ligament complex, and infraspinatus are also critical for precise patient evaluation and surgical management.

Higher rates of failures and less favorable patient outcomes may result from poor quality posterior capsular tissue as a consequence of prior surgical intervention. In particular, thermal capsulorrhaphy has been shown to result in failures and revisions. For instance, the level 4 retrospective case series of 33 patients by Provencher *et al*[12] determined that 71% (5 of 7) of their failures had undergone prior surgical procedures, such as thermal capsulorrhaphy (n = 3) and anterior stabilization (n = 2) and resulted in a higher chance of failure. Additionally, the level 4 retrospective investigation of 20 shoulders performed by McIntyre *et al*[13] utilized a multiple suture technique and reported 60% (3 of 5) of their

Table 1 Arthroscopic clinical outcomes of athletes - Posterior shoulder instability *n* (%)

Ref.	Evidence level	Primary procedure	No. total shoulders	No. athletic shoulders	Mean age, yr (range) Female/Male	Mean follow-up, mo (range)	Recurrence rate	Subjective stability (Stable or E/G)	Patient satisfaction	Return to sport (any level)	Return to sport (pre-injury level)
Bradley *et al*[18]	II	CLR	200	Overall: 200 Contact sport: 117 Overhead/ Throwers: 60	Overall: 24 (15-65) 42 F/158 M Contact sports: 21 (16-28) NR, F/NR, M	Overall: 37 (12-115) Contact sports: 35 (12-77)	Overall: 12 (6) failures *via* ASES 14 (7) failures *via* stability scale 7 (4) failures *via* both ASES and stability scale Contact athlete: 7 (6) *via* ASES 4 (4) *via* stability scale 3 (3) *via* ASES and stability scale	Overall: 182 (91) Contact athlete: 110 (94)	Overall: 187 (94) Contact athlete: 111 (95)	Overall: 180 (90) Contact athlete: 106 (91)	Overall: 127 (64) Contact athlete: 81 (69)
Schwartz *et al*[29]	IV	BB	19 (1 patient Ehlers Danlos)	Overall: 18 Contact sport: 13	30 (15-56) 5 F/13 M	21 (13-32)	3 (6) (1 bilateral patient with persistent instability of unknown etiology, contralateral shoulder was revised; 1 patient persistent pain due to prominent graft)	16 (84)	16 (84)	16 (89)	9 (50)
Wanich *et al*[30]	IV	10 CLR 2 DB only	12	12 Baseball "batter's shoulder"	21 (16-33) 0 F/12 M	34 (18-64)	1 (8)	NR	NR	11 (92)	11 (92)
Lenart *et al*[31]	IV	CLR	22	19	NR	NR	2 (9)	NR	NR	19 (100)	19 (100)
Bahk *et al*[15]	IV	CLR	29	28	26 (18.3-43.4) 1 F/28 M	66 (24-149)	1 (3.4)	28 (97)	28 (97)	22 (85)	17 (68)
Savoie *et al*[14]	IV	CLR	92	Overall: 81 Throwing sports: 32	26 (15-59) 21 F/69 M	28 (12-132)	2 (2)	≥ 30 yr old, lower instability scores (P = 0.041) 90 (98)	NR	NR	NR
Radkowski *et al*[19]	II	CLR	107	Overall: 107 Throwing sports: 27 Nonthrowing sports: 80	Overall: 23 F/84 M Throwing athletes: 21 (range, NR; SD ± 5.5) 7 F/20 M Nonthrowing athletes: 24 (range, NR; SD ± 9.1) 16 F/64 M	Throwing athletes: 28 (range, NR; SD ± 11.6) Nonthrowing: 28 (range, NR, SD ± 12.5)	11/107 (10)	No difference between 2 groups for postoperative stability Overall: 96/107 (90) Throwers: 24/27 (89) Nonthrowers: 72/80 (90)		Overall: 96/107 (90) Throwers: 23/27 (85) Nonthrowers: 73/80 (91)	Overall: 72/107 (67) Throwers: 15/27 (55) Nonthrowers: 57/80 (71)

Bradley *et al*[8]	II	CLR	100	Overall: 100 Contact sports: 51 Overhead/ Throwers: 28	23 (15-61) 23 F/77 M	(12-77)	Overall: 9 (9) failures according to ASES 11 (11) failures according to the standardized stability scale Contact athlete: 3 (6) failures according to ASES 5 (10) according to standardized stability scale	Overall: 89 (89) Contact athlete: 43 (84)	Overall: 92 (92) Contact athlete: 46 (90)	Overall: 89 (89) Contact athlete: 44 (86)	Overall: 67 (67) Contact athlete: 38 (74)
Bottoni *et al*[32]	IV	CLR TC	19	17	NR	40 (24-63)	1 (5)	NR	NR	NR	NR
Bisson[33]	IV	TC	14	Overall: 14 Contact sports: 7 Overhead sport: 1 swimmer Sport NR: 6	19 (15-32) Shoulders: 4 F/10 M Patients: 4 F/8 M	36 (26-53)	(3/14) (1 bilateral)	11 (79)	14 (100)	14 (100)	6 (43)
Goubier *et al*[34]	IV	CLR	13	Overall: 11 Contact sports: 1 Overhead/ Throwers: 3	33 (18-47) 5 F/8M	34 (11-80)	0 (0)	NR	13 (100)	NR	8 (89)
Kim *et al*[35]	IV	CLR	27	Overall: 27 Contact sports: 9 Overhead / Throwing: 6/6	21 (14-33) 2 F/25 M	39 (24-85)	1 (4)	26 (96)	NR	26 (96)	NR
Williams *et al*[36]	IV	CLR	27	Overall: 27 Contact sports: 11 Overhead/ Throwers: 5	29 (15-55) 0 F/27 M	61 (24-140)	2 (7)	25 (93)	25 (96)	25 (93)	NR

Wolf *et al*[9]	IV	CLR	14	Overall: 10 Contact sports: 3 Overhead/ Throwers: 2 (1 baseball pitcher, 1 tennis)	26 (14-54) 3 F/11 M	33 (24-45)	1 (7) traumatic reinjury	13 (93)	14 (100)	10 (100)	9 (90)
McIntyre *et al*[13]	IV	CLR	20	Overall: 14 Contact sports: 5 football (2 resulted in dislocations) Overhead/ Throwers: 2 baseball pitchers	22 (15-36) 4 F/15 M	31 (24-44)	5 (25) (2 recurrent dislocations, 3 subluxations)	17 (85)	NR	NR	12 (86)
Papendick *et al*[37]	IV	CLR PIGHLR	41	Overall: 36 Overhead/ Throwers: 21	23 (15-42) NR, F/NR, M	10 (4-41)	2 (4.8) recurrence (both recurrent dislocation)	NR	39 (95)	36 (100)	NR

AC: Acromioclavicular; ADL: Activities of daily living; ASES: American shoulder and elbow score; BB: Bone block; CI: Capsular imbrication; CLR: Capsulolabral repair; CP: Capsular plication; CR: Capsular repair; CS: Capsular shift; DB: Debridement; E/G: Excellent to good; GHLR: Glenohumeral ligament repair; IGHLR: Inferior glenohumeral ligament repair; LR: Labral repair; MDI: Multidirectional instability; NR: Not reported; PB: Posterior bankart; PHAGLR: Posterior humeral avulsion of the glenohumeral ligament repair; PIGHLR: Posterior inferior glenohumeral ligament repair; PSS: Penn shoulder score; ROM: Range of motion; SAD: Subacromial decompression; SANE: Single assessment numeric evaluation; SF-36: Short form health survey; SST: Simple shoulder test; TC: Thermal capsulorrhaphy; UCLA: University of California Los Angeles shoulder score; VAS: Visual analog scale; WD: Walch-Duplay; WOSI: Western ontario shoulder instability.

recurrences had also undergone prior surgery. Additional evidence of the effect of prior surgery having an effect on revision rates is supported by the level 2 cohort study of 100 athletic shoulders by Bradley *et al*[8] in which they reported 25% (2 of 8) of their revisions had undergone a prior thermal capsulorrhaphy procedure. Thus, prior surgery resulting in poor quality capsular, especially as a result of thermal shrinkage of capsular tissue may weaken the capsulolabral complex, resulting in unsatisfactory patient outcomes leading to further revision and failure[16].

CONTACT ATHLETES *VS* THROWING ATHLETES

Athletic clinical outcomes for posterior shoulder instability are summarized in Tables 1 and 2.

Posterior shoulder instability injuries can occur in contact or collision athletes *via* a single macrotraumatic episode with the shoulder in an internally rotated, flexed and adducted position (*e.g.*, wrestler takedown with outstretched arm) causing in-direct shearing forces that result in capsulolabral injury[1-3]. Additionally, repetitive microtrauma can also result in posterocapsular injuries in the contact athletes with continuous posteriorly directed axial loading of the glenohumeral joint (*e.g.*, football lineman)[10,17].

Table 2 Open clinical outcomes of athletes - Posterior shoulder instability *n* (%)

Ref.	Evidence level	Primary procedure	No. total shoulders	No. athletic shoulders	Mean age, yr (range)	Mean follow-up, mo (range)	Recurrence rate	Stability subjective (e/G)	Patient satisfaction (S or E/G)	Return to sport (any level)	Return to sport (preinjury level)
Servien *et al*[6]	IV	BB	21	19	24.8 (17-40)	72 (24-228)	3 (14)	21 (100)	21 (100)	17 (89)	13 (68)
Misamore *et al*[38]	IV	Capsulorrhaphy	14	14	19.6 (15-26)	45 (26-90)	1 (7)	13 (93)	NR	13 (93)	12 (86)
Hawkins[39]	IV	BB	10	8	26.4 (20-39)	61 (32-100)	1 (10)	9 (90)	NR	NR	NR
Hurley *et al*[40]	IV	Reverse Putti-Platt w/o bony procedure	22	22	18.3 (13-30)	60 (24-132)	16 (73)	NR	NR	15 (68)	1 (45)
Surin *et al*[41]	IV	Rotational Osteotomy of Humerus	11	6	23 (16-30)	80.73 (24-144)	0 (0)	11 (100)	10 (91)	4 (100)	3 (75)
Hawkins *et al*[42]	IV	Posterior Glenoid Osteotomy/ Capsulotendinous Plication/Reverse Putti-Platt	26	26	21 (NR)	86 (24-180)	13 (50)	NR	NR	10 (38)	NR

BB: Bone block; CLR: Capsulolabral repair; NR: Not reported.

Return to sport and return to previous level of play have been shown to be higher for contact athletes *vs* throwing athletes. A level 2 prospective cohort of 200 athletes by Bradley *et al*[18] underwent arthroscopic posterior shoulder stabilization procedures and outcomes were based on ASES scores, stability, pain, function, strength, return to sport and return previous level of play. The investigators reported no difference in the Contact Athlete subgroup compared to entire cohort for any outcome measure. An additional study conducted by the same group performed a level 2 study of 107 patients and also determined that was no difference in the Contact Athlete subgroup compared to entire cohort as well as no difference in functional outcome between traumatic *vs* atraumatic injuries[19]. However, throwing athletes should be recognized as a unique subset of athletes requiring unique diagnostic, operative intervention and shoulder outcome measures due to increased demands on the glenohumeral joint[20]. Repetitive microtrauma occurring with throwing athletes may put them at increased risk for developing posterior labral injuries *vs* other athletes[19,21]. For instance, in elite baseball pitchers, it has been reported that internal rotation of the humerus can approach velocities as high as 7000 deg/s[22]. Large compressive and distractive forces generated at the extreme ranges of motion in the late cocking phase and the high distraction forces occurring during the follow-through phase have been reported to cause weakening and contractures in the posterior inferior capsule, placing the glenoid capsulolabral complex and associated stabilizers at great risk for injury[23]. The largest study to date comparing surgical management of posterior instability in throwing athletes (n = 27) *vs* non-throwing athletes (n = 80) was a prospective level 2 study performed by Radkowski *et al*[19]. The investigators reported throwing athletes had nearly equal postoperative pain, stability, function, range of motion, strength and ASES post-operatively as non-throwing athletes. However, a lower percentage of throwers were able to return to their previous level of play (55%) compared to non-throwing athletes (71%). Ultimately, less dynamic glenohumeral demands of contact athletes compared to the throwing athlete may allow them to have higher rate of return to sport and previous level of play.

Advanced understanding of biomechanics and pathoanatomy, as well as awareness of throwing athletes requiring a more distinct functional shoulder outcome measure to assess the athletes true postoperative functioning is critical elements to consider during evaluation and treatment. Thus, although throwing athletes achieve similar improvements in pain, stability, and function compared to non-throwing athletes, experts have advised counseling the throwing athlete pre-operatively of the high probability that they are less likely to return to their previous level of play[19].

SURGICAL MANAGEMENT

Arthroscopy has evolved from being utilized strictly as a diagnostic tool to replacing many open techniques. Minimally invasive arthroscopic techniques have potential benefits and advantages compared to open procedures for posterior instability of the shoulder[18,24]. Intraoperative assessment allows for visualization of subacromial and intraarticular space and identification of abnormalities, such as rotator cuff pathology and intraarticular capsulolabral lesions. Anatomy can be restored more precisely to resemble native anatomy[14]. Concomitant injuries, such as SLAP and glenohumeral ligament complex lesions often missed during pre-operative evaluation may be identified during intraoperative arthroscopic assessment and can be addressed in the same operative setting[18,20]. Additionally, shoulder arthroscopy has been recognized as both a diagnostic and therapeutic technique with a low incidence of complications[25]. Post-operatively, increased range of motion, shorter rehabilitation, and less pain and morbidity have been reported in arthroscopic procedures compared to more invasive techniques[24]. A recent metaanalysis for the treatment of unidirectional posterior shoulder instability conducted by DeLong *et al*[26] evaluated 27 arthroscopic studies and 26 open studies and identified a trend in the current literature of arthroscopic techniques having superior outcomes compared to open techniques for stability, recurrence, patient satisfactions, return to sport and previous level of play. Ultimately, less comorbidity associated with arthroscopic surgical procedures may allow athletes to return sport faster and with less complications[24].

Recognition of pathoanatomy and choice of technique and repair to restore posterior shoulder stability is also important to consider. Appropriate evaluation of capsular laxity with or without an intact labrum and adequate capsular shift with the use of anchors has been shown to result in more favorable outcomes. The level 2 study of 200 athletes by Bradley *et al*[18] reported a significantly higher return to play in athletic shoulders that received suture anchors. The investigators concluded that techniques that utilized suture anchors increased stability and function of the posteriolabral complex and contributed to their favorable clinical outcomes and high rate of return to sport. The same group also reported an earlier study of 100 athletic shoulders in which 88% (7 of 8) of failures that had undergone capsulolabral plication without the use of suture anchors[6] and a study of 107 athletic shoulders in which 73% (8 of 11) of failures had undergone a capsulolabral repair without suture anchor[19]. Similarly, the retrospective level 4 investigation of 20 athletic shoulders by McIntyre *et al*[13] utilized an anchorless suture technique reported a high failure rate of 25% (5 of 20 shoulders). An additional level 4 report of 33 patients by Provencher *et al*[12] concluded that capsular plication rather than labral suture anchor repair had a higher chance of failure among their 7 reported failed cases (P = 0.10). Thus, arthroscopic posterior stabilization procedures utilizing suture anchors to address capsular pathology may provide the most consistent and favorable outcomes and return to sport[13,18,27,28].

CONCLUSION

Efforts should be made to identify the precise etiology, directionality, and degree of instability in the athlete with posterior shoulder instability. Isolated posterior instability is uncommon and rarely occurs in isolation and numerous and varied concomitant osseous and soft-tissue injuries create challenges in diagnosis and surgical management. However, awareness of these pathologic variables and knowledge of variances in athletic populations (*i.e.,* contact athletes compared to throwing athletes) may allow for a more precise approach to management. Finally, surgical intervention utilizing minimally invasive arthroscopy and suture anchors for capsulolabral repair may provide a significant advantage in assessment and post-operative recovery, ultimately, providing the best possible outcomes and return to sport.

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MINIREVIEWS

Serial elongation-derotation-flexion casting for children with early-onset scoliosis

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Abstract

Various early-onset spinal deformities, particularly infantile and juvenile scoliosis (JS), still pose challenges to pediatric orthopedic surgeons. The ideal treatment of these deformities has yet to emerge, as both clinicians and surgeons still face multiple challenges including preservation of thoracic motion, spine and cage, and protection of cardiac and lung growth and function. Elongation-derotation-flexion (EDF) casting is a technique that uses a custom-made thoracolumbar cast based on a three-dimensional correction concept. EDF can control progression of the deformity and - in some cases-coax the initially-curved spine to grow straighter by acting simultaneously in the frontal, sagittal and coronal planes. Here we provide a comprehensive review of how infantile and JS can affect normal spine and thorax and how serial EDF casting can be used to manage these spinal deformities. A fresh review of the literature helps fully understand the principles of the serial EDF casting technique and the effectiveness of conservative treatment in patients with early-onset spinal deformities, particularly infantile and juvenile scolisois.

Key words: Early-onset scoliosis; Infantile scoliosis; Juvenile scoliosis; Elongation-derotation-flexion casting; Conservative

Core tip: Infantile and juvenile scoliosis still pose challenges to pediatric orthopedic surgeons. Elongation-derotation-flexion (EDF) casting is a technique that uses a custom-made thoracolumbar cast based on a three-dimensional correction concept. EDF can control progression of the deformity and-in some cases-coax the initially-curved spine to grow straighter by acting simultaneously in the frontal, sagittal and coronal planes. A critical literature review is needed in order to understand the principles of the technique and the effectiveness of conservative treatment using the specific EDF casting technique in young and very young patients.

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INTRODUCTION

Scoliosis is a three-dimensional deformity of the spine with lateral, anteroposterior and rotational components. In most cases, scoliosis is idiopathic and concerns adolescents (AS), but there are rarer cases of infantile (IS) and juvenile scoliosis (JS) where onset is prior to age 5 and 10 years, respectively. On top of age at onset, IS and JS also present differently to AS in epidemiology, rate of deformity progression, and associated anomalies[1,2].

In young and very young patients, a progressive spinal deformity interferes with the regular and harmonious growth of the vertebral column and thoracic cage. In this subgroup of patients, the distorted spinal growth will lead to an underdeveloped thoracic cage, a short trunk and height, and a disproportionate body habitus[1,2]. IS and JS therefore rank among the most challenging conditions in pediatric orthopedics, as pathologic changes induced on a growing organism by an early-onset spinal deformity can prove dramatic, even leading to death in the most severe cases[2-6].

The goal of any treatment is to correct as soon as possible all distortions secondary to altered spinal growth: underdeveloped thoracic cage, short trunk and height, disproportionate body habitus, low weight, respiratory and cardiac dysfunctions. Tachypnea, dyspnea, chronic obstructive pulmonary disease, tracheomalacia, tachycardia and weight loss often prove more worrisome than the deformity of the spine itself[2,4,5,7,8].

The ideal treatment for early-onset scoliosis (IS and JS in particular) has not yet been identified. In particular, care providers (surgeons, pediatricians, pneumologists, anesthesiologists, physiotherapists) still have to overcome multiple challenges including preservation of thoracic motion, spine and cage, and protection of cardiac and lung growth and function[2,4,6-8].

Arthrodesis carried out in the thoracic spine at an early age is unable to control the negative effects of the deformity on thoracic cage shape, lung parenchyma development or preservation of cardio-pulmonary function. Early spine fusion is not the solution when progressive spinal deformities occurring in young and very young patients have to be managed. Moreover, early arthrodesis of the thoracic spine, is a cause of respiratory insufficiency and adds loss of pulmonary function to the pre-existing spinal deformity[2,6-8].

Elongation-derotation-flexion (EDF) casting is a technique that uses a custom-made thoracolumbar cast based on a three-dimensional correction concept. EDF can control progression of the deformity and-in some cases-coax the initially-curved spine to grow straighter by acting simultaneously in the frontal, sagittal and coronal planes[9,10]. In particular, the EDF cast can be used as a "positive" force to influence spinal growth[10] as it counteracts the negative effects of the spinal deformity on the future spinal development of the growing organism[4,9,10].

Here we provide a comprehensive review of how infantile and JS can affect normal spine and thorax and how serial EDF casting can be used to manage these spinal deformities. A fresh review of the literature helps fully understand the principles of the serial EDF casting technique and the effectiveness of conservative treatment in children with IS and JS.

ABNORMAL SPINAL GROWTH

The first five to ten years of life are a critical period for thoracic cage and spinal column development and growth[2-5,8]. This period is marked by a series of complex phenomena that follow in very rapid succession, and these events need to be well synchronized to preserve harmonious limb and spine relationships, as growth does not progress at the same rate in the different body segments[4,8].

Alterations of the spinal column development and growth can lead to a malformation or deformity. As a result, standing and sitting height, thoracic cage dimensions, and lung development are negatively affected. Patients with progressive early-onset spinal deformity will experience a reduction of longitudinal trunk growth and a loss of normal trunk proportions, leading to disproportionate body habitus. Moreover, in severe scoliosis, growth tends to become asymmetrical due to growth plate disorganization. As a result, this disorganization of the growth plate leads to progressive changes of vertebral bodies' anatomy. Those changes are responsible for secondary thoracic cage shape modifications, reduction of thoracic motility and altered lung growth[1,2]. This succession of events is similar to a domino. A "domino effect" means that not only is spinal growth affected but size and shape of the thoracic cage are modified as well. This modification of the thoracic cage will subsequently interfere with lung development. Constriction of the thoracic cage as a result of a spinal deformity significantly restricts lung growth and can contribute to serious pulmonary complications such as thoracic insufficiency syndrome, Cor pulmonale and, in the most severe cases, death[2,4-7].

It has been reported that the loss of vital capacity in patients with untreated early onset spinal deformities is about 15% greater compared than adolescent idiopathic scoliosis patients. Pehrsson *et al*[11] analyzed the mortality and causes of death in 115 untreated scoliosis patients. They compared their findings to the rates expected according to official Swedish statistics, and found that mortality was significantly higher in IS and JS but not AS[11]. In addition, Karol *et al*[7] reported that a thoracic spine height of at least 18 to 22 cm

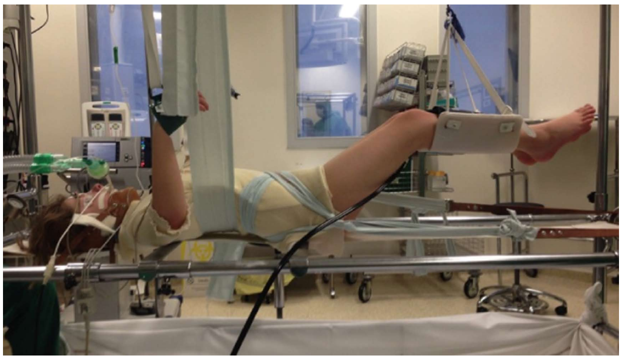

Figure 1 Positioning a patient on a Cotrel frame. Lateral view. Proximal point of traction is the chin and distal point is at the iliac crests. Harnesses and straps are employed, and amount of traction is controlled.

is necessary to reduce the risk of severe respiratory insufficiency[2,5,7].

SERIAL EDF CASTING

History

The North-American orthopedic surgeon Joseph Risser introduced the cast frame that bears his name to treat scoliosis with casting. The technique is based on the principles of elongation and derotation in order to correct the spinal curvature[12].

In 1964, French surgeons Cotrel and Morel[9] improved the Risser technique by adding the third dimension, called flexion, and subsequently popularized the EDF casting technique.

Between 1975 and 2000, United Kingdom physician Min Mehta modified Cotrel and Morel's original EDF technique and introduced the concept of serial casting. Under Metha's protocol, EDF casts are changed every 8 to 12 wk under general anesthesia[9,10].

Technique

EDF stands for elongation, derotation, and flexion. It is a method of orthopedic reduction of the scoliotic deformity on a specific reduction frame by traction, postero-lateral compression and rotation, the application of a thoraco-lumbo-sacral plaster cast, and, finally, lateral manual compression[9].

The reduction apparatus is the Cotrel frame that is used to realize an axial correction of the spine, with chin and occiput providing the proximal point of traction and iliac crests providing the distal point of traction. The technique employs harnesses and straps, and the amount of traction is controlled[9] (Figures 1 and 2).

The EDF cast can be performed under general anesthesia[13] or, alternatively, with the patient awake[14]. Both options are effective[13-15]. Canavese *et al*[13] recently reported that serial EDF casting done under general anesthesia and neuromuscular-blocking drugs improves outcome in patients with JS, specifically by enabling more effective control of curve progression in IS and JS patients compared to EDF casting under

Figure 2 Positioning a patient on a Cotrel frame. Bottom view.

general anesthesia alone or no anesthesia. Canavese *et al*[13] hypothesized that complete muscle relaxation helps the surgeon better derotate the spine while straightening it. Moreover, adding neuromuscular-blocking drugs to the protocol improves immediate outcome and slows curve progression at 24-mo follow-up[13].

The patient lay on two horizontal metal bars, one supporting the shoulders and the other supporting the pelvis. A strap wrapped around the patient on the convex side of the scoliotic curve is tensioned to reduce it by simultaneously applying a lateral and a posterior reduction force. In cases presenting an "S" curve, a second strap can be applied in the opposite side and direction, level with this second convexity (Figure 3). The two support bars can then be removed to apply the plaster over the straps, making sure it is well-molded, especially at the iliac crests. While the plaster is still malleable, one-hand lateral pressure is applied on the convexity side and two-hand counter-pressure is applied on the concavity side as close as possible to the end vertebrae, and both pressures are maintained until the plaster hardens (Figure 4). Next, a few layers of synthetic fiberglass are added to reinforce the cast, and a thoraco-abdominal window is cut to enable decompression of the anterior abdomen (stomach and bowels) and better expansion of the thoracic cage (Figure 5). The casts are subsequently changed every 8-12 wk.

At first sight, the cast may look like a constrictive force on the thorax, limiting its expansion, but in fact, if well-molded, it does not compress the thoracic cage and allows comfortable respiratory movement (Figure 6). Dhawale *et al*[16] reviewed data from 37 serial EDF casts to investigate the effects of casting on ventilation in IS,

Figure 3 Positioning a patient on a Cotrel frame. Top view. The patient is initially supported by two metal bars, one under the shoulders and the other under the pelvis. At the same time, a strap wrapped around the patient on the convex side of the scoliotic deformity is tensioned in order to reduce it by simultaneously applying lateral and posterior reduction forces.

Figure 4 Spinal deformity correction. While the plaster is still malleable, one-hand lateral pressure (dotted arrow) is applied on the convexity side (apical vertebra) and two-hand counter-pressure is applied on the concavity side as close as possible to the end vertebrae, and both pressures are maintained until the plaster hardens (red arrows).

and found that casting led to only transient pulmonary restriction: peak inspiratory pressure increased by 106% at cast application but fell back to near-baseline values once the thoraco-abdominal straps were cut free[13].

Delaying tactic or definitive treatment option?

The big challenge for the growing spine is to preserve

Figure 5 Elongation-derotation-flexion plaster. Final result.

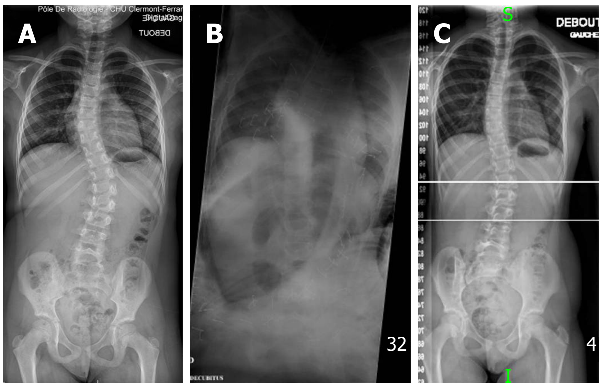

Figure 6 Pre-operative (A) and postoperative (B, C) radiographs in a 7-year-old girl with infantile and juvenile scoliosis. Forty degree lumbar deformity with 25° thoracic compensatory curve (A); after cast application, the spine is fully corrected (B); Two point five years after cast removal, the deformity has reduced to 20° in both the lumbar and thoracic spine (C).

thoracic cage, thoracic spine and lung development without altering spine and thoracic cage motion. Morbidity tied to surgical procedures has sparked a comeback of conservative treatment, *i.e.*, serial EDF casting.

EDF casting is a non-surgical option that can be considered in the management of patients with early-onset spinal deformities, particularly IS and JS. The key to successful treatment is to anticipate curve progression, recognize poor prognosis and apply prophylactic treatment, *i.e.*, serial EDF casting. Factors influencing management and outcome are numerous and heterogeneous in nature: age, curve magnitude, cardiac function, respiratory impairment, nutritional status, neurological examination, presence of pain, loss of function, and patient's and/or parents' concerns over self-esteem due to spine and chest deformity.

Serial EDF casting can be used as a delaying tactic, to stop further progression of the deformity for a few years until to definitive fusion, or as a definitive treatment option. Patients aggressively casted before age 20 mo for curves averaging 30 degrees go on to present zero net progression and/or up to a 10-degree reduction in scoliosis at skeletal maturity[9], whereas children undergoing cast treatment after age 30 mo for curves averaging 50 degrees did not go on to gain significant correction, although their spinal curvature did not progress[10]. Fletcher *et al*[15] confirmed previous findings, especially in children with moderate spinal deformities, and concluded that serial casting can contribute to postpone surgery in selected cases. van Hessem *et al*[14] recently found that serial casting is also effective for the management of JS patients. They showed that serial casting can stop curve progression and even eliminate the need for surgery[13].

The main advantage of EDF casting is that the spine is left alone. The EDF cast can control the progression of the deformity and-in some cases-coax the initially-curved spine to grow straighter by acting simultaneously in the frontal, sagittal and coronal planes[9,10]. In particular, the EDF cast can be used as a "positive" force to influence spinal growth[10] as it counteracts the negative effects of the spinal deformity on future spinal development of the growing organism[3,8,9]. Serial EDF casting plays a central role in delaying or in some cases even eliminating the need for growth-sparing surgery[10,15], but it is not effective in all patients with early-onset scoliosis. However, unlike surgery, it does not potentially interfere with spine and thoracic cage growth. In particular, it has been shown that fitting growth-sparing devices near and/or on the spine can alter spinal growth and lead to auto-lusion of ribs and vertebral bodies[4,6,7,10]. These changes will contribute to make definitive fusion more challenging with less satisfactory outcomes[17,18].

COMPLICATIONS OF EDF CASTING

Serial EDF casting should be considered as a valuable low-risk treatment strategy for patients with IS and JS[15,16,19,20]. The learning curve is rapid, reported rate of complications is low, and most reported complications are relatively minor[9,10,12,16,19]. Potential side-effects of serial EDF casting include dry or itchy skin, skin rash or irritation, blisters, weak muscles, joint pain or stiffness after the cast is removed, and sleep problems (cast intolerance)[20-22].

As reported by Sanders *et al*[21], the most important issue is temporary procedural chest pressure making ventilation difficult while the cast is setting. However, as soon as the anterior or antero-lateral window is open, respiratory airflow drops back to normal. Sanders *et al*[21] suggest intubating patients undergoing EDF casting under general anesthesia. Dhawale *et al*[16] reported that peak inspiratory pressure increased due to transient pulmonary restriction at cast application but fell back to near-baseline values once the window was cut way. They concluded that patients with underlying pulmonary disease are at risk of respiratory complications during the casting process, making it necessary to follow casting with a proper period of observation[16].

Badlani *et al*[19] reported a subclavian vein thrombosis after EDF cast application for the treatment of progressive infantile kyphoscoliosis. This is the only published case in the English literature. Badlani *et al*[19] stressed that early and accurate diagnosis of this complication allowed effective treatment and avoided further morbidity for the patient, prompting them to suggest that clinicians performing EDF casting in young patients should be aware of the possibility of this rare complication and know how to quickly diagnose and treat it[19].

A COMPREHENSIVE LITERATURE REVIEW IS MANDATORY

The ideal treatment of IS and JS has not been identified. Management strategies must consider the patient's full lifespan as well as the effects of treatment on spinal and chest growth of a patient with early-onset scoliosis.

Advancements in growth-friendly surgical procedures now offer orthopedic surgeons an array of treatment options for children with IS and JS, including distraction-based techniques (dual-growing rods, magnetic growing rods, vertebral expandable prosthetic titanium ribs), compression-based techniques (vertebral body stapling) and growth-guided techniques (Luque trolley, Shilla technique). However, due to a lack of evidence-based research, the ideal treatment for patients with early-onset scoliosis has not been yet found. Moreover, a significant variation among surgeon' surgical strategies has been reported[23].

In most cases, growth-sparing surgery is not an isolated intervention and is peppered with numerous complications. Reported rates of surgical complications ranges from 8% to 50%: reported complications include skin problems, wound complications, device migration and/or fractures, anesthetic complications, hardware failure, auto-fusion, infections, and decompensation. Mackenzie *et al*[24] reported that surgical site infection rate in patients with infantile deformities treated with growth constructs increased from 0% at insertion to up to 29% during lengthening and/or revision procedures[23,24]. Moreover, repeated hospitalizations for lengthening and unplanned surgical procedures increase the child's time away from school and can have repercussions on the child's psychological well-being[17,25].

Despite these findings, various articles published over the last few years consider growth-sparing surgery as the gold standard for the management of severe scoliosis in patients younger than 10 years of age[20,23].

However, unlike surgery, it does not potentially interfere with spine and thoracic cage growth. In particular,

Table 1 Outcome of patients with infantile and juvenile scoliosis treated by serial casting (to date, there are only two studies available reporting outcomes in patients with juvenile scoliosis[12,13])

Ref.	IS or JS	No. of patients	Idiopathic/non-idiopathic	Delay in surgery	% of surgery
Scott and Morgan[26]	IS	28	-	NA	NA
James *et al*[28]	IS	212	-	NA	NA
Lloyd-Roberts and Pilcher[29]	IS	100	-	NA	NA
Conner[27]	IS	61	-	NA	NA
Mehta[30]	IS	64	64/0	NA	NA
Ceballos *et al*[31]	IS	113	113/0	3.5 yr	NA
Mehta[10]	IS	94[1]/42[2] (136)	100/36	11[1] yr 8[2] yr	0%[1] 35.7%[2]
Sanders *et al*[21]	IS	55	41/14	2.1 yr	17%
Smith *et al*[34]	IS	17	NA	NA	30%
Fletcher *et al*[15]	IS	29	12/17	3.3 yr	28%
Baulesh *et al*[32]	IS	36	19/17	2.1 yr	31%
Waldron *et al*[22]	IS	20	8/12	18 mo	40%
Johnston *et al*[33]	IS/JS	27	11/16	20 mo	55%
van Hessem *et al*[14]	JS	7	7/0	4.6 yr	0%
Canavese *et al*[13]	JS[3]	44	36/8	2 yr	15%[4] 25%[5] 33%[6]
Demirkiran *et al*[46]	Congenital scoliosis[7]	11	NA	2.1 yr	0%

[1]Children treated before age 2 years; [2]Children treated after age 2 years and 6 mo; [3]Preliminary results; [4]Cast under general anesthesia and neuromuscular-blocking drugs; [5]Cast under general anesthesia alone; [6]Cast with patients awake; [7]Preliminary results; average patient age at time of cast application was 3 years and 4 mo. IS: Infantile scoliosis; JS: Juvenile scoliosis; NA: Not available.

it has been shown that fitting growth-sparing devices near and/or on the spine can alter spinal growth and lead to auto-lusion of ribs and vertebral bodies[4,6,7,10]. These changes will contribute to make definitive fusion more challenging with less satisfactory outcomes[17,18].

Unlike surgery, serial EDF casting does not potentially interfere with spine and thoracic cage growth. In particular, it can be used as a "positive" corrective force to influence spinal growth[10] as it counteracts the negative effects of the spinal deformity on future spinal development of the growing organism[4,9,10]. However, although serial EDF casting can in some cases delay and/or eliminate the need for surgery, it cannot completely arrest curve progression nor erase the potential need for surgery in all types of curves.

Serial EDF casting should be considered a valuable low-risk treatment strategy[14,16,18] and an alternative to surgery for patients with early-onset scoliosis, in particular for those with IS and JS (Table 1). It has been proven effective in controlling curve progression, but there is still a lack of papers reporting outcomes of serial EDF casting in patients with IS and JS. In particular, there are less than 15 papers reporting on clinical and radiological outcomes in patients with IS and JS treated by serial casting (Table 1) *vs* over a hundred papers reporting on surgical outcomes in this patient population.

In the early 1950s and late 1960s, Scott and Morgan[26] reported that resolving curves are not uncommon while Conner showed that early-onset deformities associated with developmental anomalies are likely to progress[27]. However, neither James *et al*[28] nor Lloyd-Roberts and Pilcher[29] were able to identify absolute criteria distinguishing between resolving and progressive curves.

In 1972, Mehta[30] showed that patients aggressively casted before age 20 mo for curves averaging 30 degrees go on to present zero net progression and/or up to a 10-degree reduction in scoliosis at skeletal maturity[10], whereas older children (30 mo of age) with curves averaging 50 degrees had the curve stabilized[10,30]. In a later work, Mehta reviewed 136 children with IS and found that although all children received the same treatment, the results followed different patterns. In the 94 children treated before 24 mo of age, the scoliosis resolved, whereas in the 42 patients treated after age 30 mo, treatment could only reduce but not resolve the deformity. Rate of surgery in this subgroup was 35.7%. Mehta[10,30] highlighted that avoiding delay in treatment was critically important.

Ceballos *et al*[31] confirmed Mehta's prognostic criteria. They reviewed 113 patients with IS and concluded that relationship of rib head and corresponding vertebral body at the apex of the curve is the most reliable prognostic sign[31].

In Sanders *et al*[21]'s review of 55 patients with progressive IS treated with derotational casting, 46 of 55 patients (83%) responded to treatment and did not require surgery at the time of publication[21]. Sanders *et al*[21] confirmed Mehta's findings[9,20,30] and reported that cast correction at younger age, moderate curve size, and an idiopathic diagnosis carry a better prognosis than casting at an older age, curve over 60 degrees, and a non-idiopathic diagnosis[21].

Waldron *et al*[22] reviewed 20 consecutive patients with early-onset scoliosis treated by a Risser cast performed under general anesthesia and found that at the time of publication, 13 of the 20 patients (65%) did not require surgery. They concluded that serial Risser casting under general anesthesia is a safe and effective time-buying strategy for patients with early-onset spinal deformity: relatively large curves can be stabilized and patients are allowed to reach a more suitable age for other forms of treatment[22]. Similarly, Fletcher *et al*[15] reported a group of 29 patients with IS treated by derotational casting with an average 39-mo delay to surgery, and found that at the time of publication, 21 of the 29 patients (72%) did not require surgery[15]. Although a cure could not be obtained in this cohort of patients, Fletcher *et al*[15] confirmed that serial casting can postpone surgical intervention and, in some cases, it can be considered as a valid alternative to surgery[15]. Baulesh *et al*[32] reported that serial casting can preserve normal longitudinal thoracic growth in children with early-onset spinal deformity and can have positive effects on pulmonary function. They reviewed 36 patients with early-onset spinal deformity, and reported a 25-mo delay of surgery in 25 of these 36 patients (69%)[32]. More recently, Morin and Kulkarni[20] reported that serial EDF casting for the treatment of progressive idiopathic IS is an effective tool for Metha's benign-type curves[10,24], avoiding spinal fusion in about 2/3 of cases[20]. Johnston *et al*[33] reported that serial casting is a valuable delaying tactic for children with early-onset scoliosis. They reviewed 27 patients with IS and JS treated with serial casting and found that mean Cobb angle remained stable after a mean 2.4 years of treatment. Johnston *et al*[33] concluded that although serial casting cannot control all spinal deformities, it does not compromise spinal length and avoids surgical complications associated with early growth-sparing surgery[32]. In Smith *et al*[34]'s review of 31 patients with IS, 17 of the 31 were treated with serial casting and 30% progressed to surgery (5/17), prompting the authors to conclude that serial casting is particularly indicated in patients with smaller and flexible spinal curves[34].

On the other hand, casting and especially bracing has been less successful in JS compared to IS, with reported rates of surgery ranging from 27% to 100% after conservative treatment[13,14,35,36].

JS is a rare disease with diverse clinical presentation, so there are logically scarce few studies reporting clinical and/or radiological outcomes of patients with JS treated by serial casting. Most relevant studies published to date have evaluated the efficacy of rigid brace systems (Table 1). These studies reported a gradually slow loss of correction from the fitting point until the end of the treatment as well as a worsening of the curve after the weaning point[36-38].

Tolo and Gillespie[39] reported that 27% of patients treated with the Milwaukee brace underwent surgery. Similarly, Dabney and Browen[38] reported 33% rate of surgery in patients treated with rigid brace system for scoliosis. Coillard *et al*[40] using a SpineCor orthosis reported 37% surgeries in patients with JS. Higher percentages of surgery (40% to 100%) have been reported by Kahanovitz *et al*[41] and Robinson *et al*[42].

However, recent reports from van Hessem *et al*[14] and Canavese *et al*[13] point to more more favorable results in patients with JS treated by serial casting.

van Hessem *et al*[14] reviewed 7 patients with JS treated by casting and/or bracing and found that casting with patients awake is an effective JS management approach. They reported that Cobb's angle was reduced 32%, decreasing from 37 degrees to 25 degrees, and none of the patients required surgery at a mean follow-up of 4.6 years[14].

More recently, Canavese *et al*[13] reviewed a cohort of 44 patients with JS and reported that serial EDF casting under general anesthesia plus neuromuscular-blocking drugs (curare) more effectively controls curve progression in JS patients compared to EDF casting under general anesthesia alone or no anesthesia[13]. They posit that complete muscle relaxation helps the surgeon better derotate the spine while straightening it. Moreover, adding neuromuscular-blocking drugs to the protocol improves immediate outcome and slows curve progression at 24-mo follow-up[13]. Canavese *et al*[13] found that curve magnitude according to Cobb[43], rib vertebral angle difference according to Mehta[30] and apical vertebral degree according to Nash and Moe[44] were all improved. Rib vertebral angle difference and apical vertebral degree are expressions of vertebral rotation and can be used to better characterize the spinal deformity and/or evaluate effects of brace or surgical treatment[45].

Demirkiran *et a*[46] have recently applied the principles of serial derotational casting to young and very young patients with congenital spine deformities. Demirkiran *et al*[46] reviewed 11 children with progressive congenital scoliosis. They reported that none of the patients required surgery for curve progression or developed complications during the treatment period. Demirkiran *et al*[46] concluded that serial derotational casting is an effective and safe delaying technique to postpone surgery in congenital deformities in the short-term follow-up.

CONCLUSION

There is a patent lack of papers reporting outcomes of serial EDF casting in patients with IS and JS. At the time of writing, there are less than 15 papers reporting clinical and radiological outcomes in patients with IS and JS treated by serial casting *vs* over a hundred papers reporting on surgical outcomes in this patient population.

EDF casting is a safe technique that can modify the natural evolution of infantile and juvenile-type scoliosis by reducing and slowing curve progression in both frontal and transverse planes.

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MINIREVIEWS

Diagnosing, planning and evaluating osteochondral ankle defects with imaging modalities

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Abstract

This current concepts review outlines the role of different imaging modalities in the diagnosis, preoperative planning, and follow-up of osteochondral ankle defects. An osteochondral ankle defect involves the articular cartilage and subchondral bone (usually of the talus) and is mostly caused by an ankle supination trauma. Conventional radiographs are useful as an initial imaging tool in the diagnostic process, but have only moderate sensitivity for the detection of osteochondral defects. Computed tomography (CT) and magnetic resonance imaging (MRI) are more accurate imaging modalities. Recently, ultrasonography and single photon emission CT have been described for the evaluation of osteochondral talar defects. CT is the most valuable modality for assessing the exact location and size of bony lesions. Cartilage and subchondral bone damage can be visualized using MRI, but the defect size tends to be overestimated due to bone edema. CT with the ankle in full plantar flexion has been shown a reliable tool for preoperative planning of the surgical approach. Postoperative imaging is useful for objective assessment of repair tissue or degenerative changes of the ankle joint. Plain radiography, CT and MRI have been used in outcome studies, and different scoring systems are available.

Key words: Cartilage; Subchondral bone; Imaging; Ankle; Talus; Radiography; Computed tomography; Magnetic resonance imaging; Outcome assessment

Core tip: This current concepts review aims to summarize the literature on imaging modalities in the diagnosis, preoperative planning, and follow-up of osteochondral ankle defects. There have been recent developments in this field, including the use of sophisticated methods for diagnosis [such as single photon emission computed tomography (CT)] and the use of imaging for outcome assessment (such as CT and certain magnetic resonance imaging techniques). These are all discussed in the article, which may help the reader to optimize his/her preoperative and postoperative strategy.

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INTRODUCTION

Osteochondral defects (OCDs) of the ankle mostly affect the talus and involve the articular hyaline cartilage and the subchondral bone. These defects often cause deep ankle pain on weight bearing, impairing sports and daily activities of the young and active population. The diagnosis is often delayed because of low index of suspicion and the possible absence of radiographic signs on standard radiographs[1]. Deep ankle pain that persists months after supination trauma should alert the physician of a possible OCD of the talus.

Various imaging studies are available to diagnose ankle OCDs. Plain radiographs are a common initial diagnostic tool but may not depict the OCD[2]. Computed tomography (CT) and magnetic resonance imaging (MRI) are more accurate[1]. In recent years, alternative imaging methods have become available, including ultrasonography and single photon emission computed tomography (SPECT)[3,4].

The choice of treatment of OCDs depends on the duration of symptoms, the size, location, and stability of the defect, and whether it concerns a primary or secondary OCD[5]. In general, OCDs smaller than 15 mm (diameter) are amenable for arthroscopic debridement and bone marrow stimulation (BMS) techniques, while bigger or secondary OCDs (those after failed primary surgical treatment) require a more invasive strategy, such as osteochondral autograft transfer[5-7]. For preoperative planning of the surgical procedure and the surgical approach it is important to determine precisely the extent and localization of the OCD[8-10].

After treatment, not only is the subjective functional outcome of importance, but also has objective assessment of repair tissue become of interest. Plain radiography, CT and MRI have been used in outcome studies, and different scoring systems are available.

This current concepts review outlines the role of various imaging modalities in the diagnosis, preoperative planning and follow-up of osteochondral ankle defects.

DIAGNOSIS

Radiography

Conventional radiographs usually consist of anterior-posterior (AP) mortise view and lateral weight-bearing views of the ankle. The AP mortise view is not a true AP projection but the patient's leg is projected in 15 degrees of internal rotation to optimize visualization of the ankle joint (Figure 1). The radiographs may show an area of detached bone surrounded by radiolucency but initially the damage may be too small to be visualized[11].

Routine radiological examination fails to detect 30%-50% of OCDs[1,12-14]. Thompson and Loomer[15] hypothesized that most of the missed OCDs were located posteriorly. They developed a heel-rise view to visualize the posterior part of the talar dome. This view is projected as an AP mortise view with a heel rise of 4 cm (Figure 1). Verhagen *et al*[1] prospectively compared the efficacy of diagnostic methods in the evaluation of OCDs. They demonstrated that a heel-rise view doubled the diagnostic odds ratio in comparison with standard radiographs (Table 1).

The frequent absence of radiological changes has led to the use of more sensitive methods[16].

CT

CT is a technology that uses computer-processed X-rays. A helical or spiral CT is mostly used. This permits continuous rotation of the X-ray source and detector while the patient is moved slowly through the X-ray ring. The scanning protocol for ankle CTs involves "ultra high resolution" axial slices with an increment of 0.3 mm and a thickness of 0.6 mm. Multiplanar coronal and sagittal reconstructions should be 1 mm[5].

Verhagen *et al*[1] showed a sensitivity and specificity of 0.81 and 0.99, respectively, for detecting OCDs on a helical CT (Table 1). The size and location of the bone defect and the detachment of a fragment can be visualized (Figure 2). CT is the most effective method for evaluating the osseous anatomy but it lacks the ability to visualize cartilage directly. However, focus on the condition of the subchondral bone plate seems more important in diagnosing and treating OCDs, because the pain of an OCD originates in the subchondral bone, and the integrity of the subchondral bone plate is crucial for the vitality of articular cartilage[17,18]. Nakasa *et al*[19] showed that the evaluation of subchondral bone using CT correlates with chondral damage in OCDs. There was no significant difference between CT findings and International Cartilage Repair Society grade or arthroscopic findings in their evaluation of 31 ankles[19].

MRI

MRI uses a radiowave frequency that causes the hydrogen nuclei to resonate. Multiple transmitted radiofrequency pulses can be used to differentiate between different tissues because they have different relaxation times. It is possible to suppress tissue (*e.g.*, fat) on MRI. A cartilage-sensitive pulse sequence visualizes the articular cartilage. MRI has the capability of detecting cartilage damage and subchondral bone, which may not be visible on conventional radiographs. Also, MRI has the advantage of not utilizing ionizing radiation and gives a superior detail of the surrounding soft tissue[20].

Table 1 Accuracy of different imaging techniques in diagnosing talar osteochondral defects[1]

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Standard radiography	0.59	0.91	0.70	0.86
Heel-rise radiography	0.70	0.94	0.79	0.90
Computed tomography	0.81	0.99	0.96	0.94
Magnetic resonance imaging	0.96	0.96	0.89	0.99

The differences between computed tomography and magnetic resonance imaging were not statistically significant (P = 0.33).

Figure 1 Weight-bearing radiographs [lateral (A), anterior-posterior mortise (B), and 4-cm heel-rise (C) views] showing an osteochondral defect (arrows).

A high accuracy of diagnosing OCD with MRI has been reported in the literature. Verhagen *et al*[1] reported a sensitivity and specificity of 96% (Table 1). Mintz *et al*[21] analyzed patients who had an MRI and in whom arthroscopy was performed. They reported a 100% specificity and a 95% sensitivity of the MRI to identify OCDs[21]. Additionally, De Smet *et al*[22] showed that MRI is a reliable diagnostic and an accurate predictor of stability of the fragment. However, due to bony edema, the true extent of the lesion can be overestimated, which may affect the treatment decision (Figure 3)[23,24].

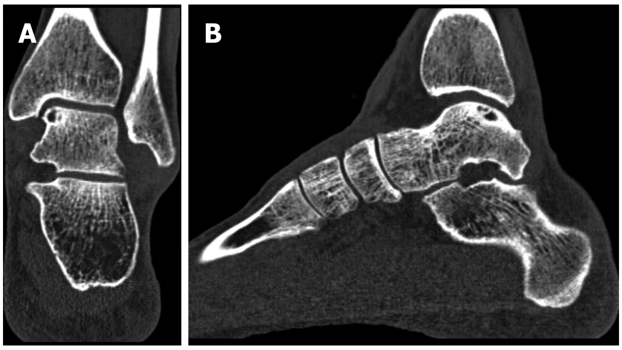

Figure 2 Coronal (A) and sagittal (B) computed tomography scans of a left ankle, showing an osteochondral defect of the posteromedial talar dome. Note the clear visualization of the cyst with an intact subchondral bone plate.

Alternative imaging modalities

Arthrography: CT and MRI scans can be supplemented with intra-articular contrast[25]. The contrast may improve assessment of OCD stability by situating between the osteochondral fragment and underlying bone. In a comparative study, Schmid *et al*[25] concluded that CT arthrography is more reliable than MR arthrography in the detection of cartilage lesions of the ankle. In comparison with conventional MRI, MR arthrography is more accurate in the evaluation of the stability of osteochondral lesions and the detection of intra-articular bodies[26,27]. However, in our opinion, there is no indication for arthrography as it is an invasive technique with risk of complications, and does not influence the treatment decision.

SPECT: SPECT is a nuclear tomographic imaging technique using gamma rays and is able to provide a 3-dimensional visualization due to the radiation distribution of bone-specific radioactive tracers in combination with the CT. Meftah *et al*[3] assessed the role of SPECT-CT in the management of OCDs. Twenty-two patients with OCDs of the talus had a SPECT-CT and an MRI. With the SPECT-CT they were able to differentiate between an active area and a non-active area of the OCD, which is useful when a patient has chronic OCD and pain after

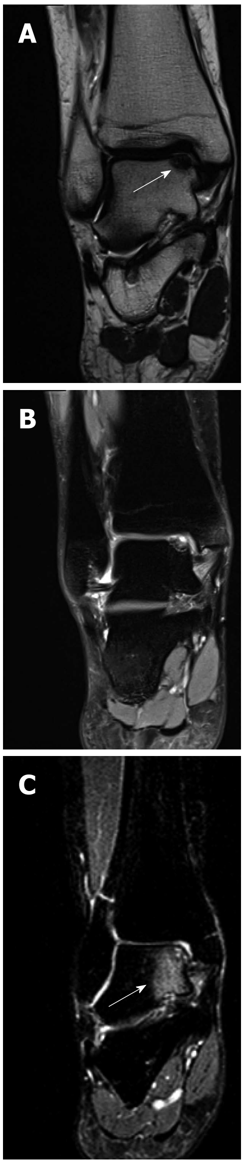

Figure 3 Magnetic resonance imaging scans of coronal T1 (A) and T2 (B) and bone edema on a T2 image (C). Coronal T1 (A) and T2 (B) magnetic resonance imaging scans of a right ankle with an osteochondral lesion of the medial talar dome. Note that the extent of the bony defect is difficult to assess precisely due to the bone edema on a T2 image (C).

recent trauma. In two patients the MRI showed minimal subchondral edema, while the SPECT-CT showed a significant activity over the subchondral surface, which can implicate an early onset of the OCD[3]. Leumann *et al*[24] evaluated SPECT-CT in comparison with MRI with respect to decision-making in the treatment of talar OCDs. In this study, the area of activity in SPECT-CT was 56% smaller in the coronal plane and 52% smaller in the sagittal plane than the bone edema in MRI[24]. Thus, SPECT-CT can be of additional value for surgical decision-making when there is a complex case with co-existing pathology.

Ultrasonography: Ultrasound can detect typical OCD morphology, such as cortex irregularities and loose fragments, and is noninvasive and cost-effective, which

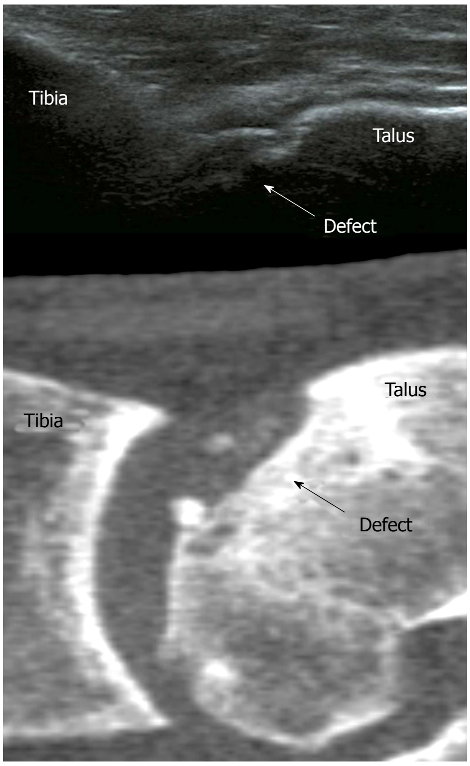

Figure 4 Ultrasound image (top) showing an osteochondral talar defect. A computed tomography scan (bottom) is shown for comparison.

makes it an interesting alternative (Figure 4)[4,27]. In a human cadaveric study there was a high sensitivity and specificity for detection of 3 to 15-mm artificially created cartilage defects[28]. However, with ultrasound, only anterior and central lesions can be detected even with maximum plantar flexion of the ankle[9]. However, although ultrasound is not yet generally applicable for detecting OCDs in the ankle, it already has the potential to act as a good noninvasive monitoring tool for the healing of an OCD after treatment.

PREOPERATIVE PLANNING

For planning the optimal treatment and surgical approach, different (combinations of) diagnostic techniques as described above can be used. We typically use plain radiography and CT. Alternatively to CT, MRI can be obtained, especially in suspected concomitant soft tissue pathology. However, CT is preferred to measure the precise OCD size and localization. To plan the surgical approach, the ankle is scanned in maximum plantar flexion.

CT plantar flexion

A diagnostic CT scan is usually made with the ankle in a plantigrade position. van Bergen *et al*[9,10] described the use of a CT scan made of the ankle in full plantar flexion for preoperative planning (Figure 5). A CT of the ankle in full plantar flexion mimics the situation of the ankle during anterior arthroscopic treatment. The scanning technique was shown to determine preoperatively the

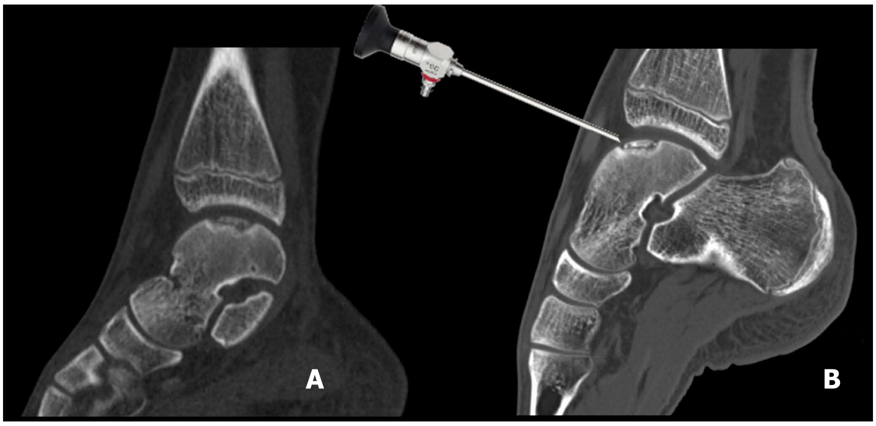

Figure 5 Sagittal computed tomography images of a 14-year-old patient with an osteochondral defect of the medial talar dome. Normal helical CT (A) and a CT made in full plantar flexion (B) showing arthroscopic accessibility. CT: Computed tomography.

Figure 6 Radiograph of a left ankle with an ostechondral defect in the lateral talar dome, preoperative (A) and postoperative (B).

in-situ arthroscopic location and accessibility of a talar OCD[9]. With use of the CT, the anterior arthroscopic reach was shown to be 48.2% and 47.8% of the medial and lateral talar dome, respectively[10]. The anterior arthroscopic reach was dependent on the degree of plantar flexion movement of the ankle. We recommend the use of this technique for planning surgical treatment of OCDs localized in the posterior half of the talus and of OCDs in ankles with limited range of motion.

POSTOPERATIVE IMAGING

In order to obtain objective assessment of repair after OCD treatment, postoperative imaging is important to evaluate the outcome following surgical procedures. However, in the literature, follow-up imaging is used inconsistently[29,30]. A systematic review showed that 58% of studies reported follow-up radiographs and 25% reported MRI after microfracture treatment[29]. After osteochondral autograft transfer, postoperative radiographs, CT and MRI were described in 65%, 80% and 20%, respectively[30]. More awareness of postoperative imaging possibilities thus seems crucial.

Radiography

Radiographs are frequently obtained in the postoperative assessment of talar OCDs (Figure 6), especially to evaluate degenerative changes in the joint. Several radiographic grading systems have been developed for the osteoarthritic (OA) ankle joint[31-33]. The purpose of the scales is to allow objective assessment of OA changes. The scales focus on the presence of osteophytes and joint space narrowing. The Kellgren-Lawrence system was not designed specifically for the ankle[31]. The five OA grades were originally described as None (0), Doubtful (1), Minimal (2), Moderate (3), and Severe (4), without further detail[31]. Kijowski *et al*[34] published a more detailed description of the Kellgren-Lawrence scale (Table 2). The Takakura system focuses mainly on the medial joint space[32]. Tanaka *et al*[35] further classified Takakura stage 3 (Obliteration of the joint space with subchondral bone contact medially) into stage 3a and 3b (Table 2). The van Dijk OA classification is used to evaluate the complete talocrural joint, and has been used for the evaluation of talar OCD in outcome studies[2,36].

Moon *et al*[37] compared the van Dijk scale[33], the modified Kellgren-Lawrence scale[34], and modified Takakura scale[35], and concluded that all these scales were reliable and valid[35]. Interobserver and intraobserver comparisons (weighted Kappa) of each scale were found to be satisfactory (Kellgren-Lawrence, 0.51 to 0.81; Takakura, 0.65 to 0.88; van Dijk, 0.64 to 0.89). However, the predictability of the scales for cartilage damage, as observed by arthroscopy, was only moderate (intraclass correlation coefficients, 0.42 to 0.51)[37]. Therefore, postoperative radiography appears to be useful for the assessment of degenerative changes but less useful for the assessment of OCD repair tissue.

CT

To objectively assess the bone repair, multislice helical CT scans can be obtained during the postoperative follow-up (Figure 7)[38]. CT has been shown to be accurate in the follow-up of talar OCDs[39]. The scanning protocol is the same as in the preoperative situation[5]. One can measure the completeness, thickness, and level of the subchondral plate (*i.e.*, flush, depressed, or

Table 2 Overview of several radiographic and magnetic resonance imaging scoring systems for the ankle joint

Van Dijk Scale[33]	MOCART[41]
(0) Normal joint or subchondral sclerosis	Degree of defect repair and filling of the defect
(1) Osteophytes without joint space narrowing	Complete (on a level with adjacent cartilage)
(2) Joint space narrowing with or without osteophytes	Hypertrophy (over the level of the adjacent cartilage)
(3) (Sub)total disappearance or deformation of the joint space	Incomplete (under the level of the adjacent cartilage; underfilling)
	> 50% of the adjacent cartilage
	< 50% of the adjacent cartilage
Modified Takakura Scale[35]	Subchondral bone exposed (complete delamination or dislocation and/or loose body)
(1) No joint space narrowing but early sclerosis and osteophyte formation	Integration to border zone
	Complete (complete integration with adjacent cartilage)
(2) Narrowing of the joint space medially	Incomplete (incomplete integration with adjacent cartilage)
(3a) Obliteration of the joint space limited to the facet of medial malleolus with subchondral bone contact	Demarcating border visible (split-like)
	Defect visible
(3b) Obliteration of the joint space advanced to the roof of the talar dome with subchondral bone contact	< 50% of the length of the repair tissue
	> 50% of the length of the repair tissue
(4) Obliteration of the whole joint space with complete bone contact	
Modified Kellgren-Lawrence Scale[34]	Surface of the repair tissue
(0) No radiographic findings of osteoarthritis	Surface intact (lamina splendens intact)
(1) Minute osteophytes of doubtful clinical significance	Surface damaged (fibrillations, fissures and ulcerations)
(2) Definite osteophytes with unimpaired joint space	< 50% of repair tissue depth
(3) Definite osteophytes with moderate joint space narrowing	> 50% of repair tissue depth or total degeneration
(4) Definite osteophytes with severe joint space narrowing and subchondral sclerosis	
	Structure of the repair tissue
	Homogenous
	Inhomogenous or cleft formation
	Signal intensity of the repair tissue
	Dual T2-FSE
	Isointense
	Moderately hyperintense
	Markedly hyperintense
	3D-GE-FS
	Isointense
	Moderately hypointense
	Markedly hypointense
	Subchondral lamina
	Intact
	Not intact
	Subchondral bone
	Intact
	Non-intact (edema, granulation tissue, cysts, sclerosis)
	Adhesions
	No
	Yes
	Effusion
	No
	Yes

MOCART: Magnetic resonance observation of cartilage repair tissue; FSE: Fast spin-echo; 3D: Three-dimensional; FS: Fat-suppressed.

proud), as well as bone volume filling of the defect and postoperative loose bony particles[38,40]. However, to our knowledge, a postoperative grading system based on CT is unavailable.

MRI

MRI evaluation of OCD repair tissue has gained popularity in recent years, as the development of high-field MR systems and the use of dedicated coils have improved the visualization of the articular cartilage morphology. The scanning protocol can incorporate several sequences. Proton density-weighted fast spin-echo (FSE-PD) and three-dimensional (3D) fat-suppressed (FS) T1-weighted gradient-echo (3D-FS T1W GRE) sequences are the ones most commonly used[41,42]. New innovative quantitative MRI techniques, like T2 mapping and delayed Gadolinium-Enhanced MR Imaging of Cartilage (dGEMRIC), are frequently used to depict early cartilage degeneration before morphologic cartilage loss occurs. These techniques have been applied increasingly in recent years to evaluate the cartilage status after cartilage repair surgery[43].

T2 mapping: T2 mapping evaluation is a biochemical

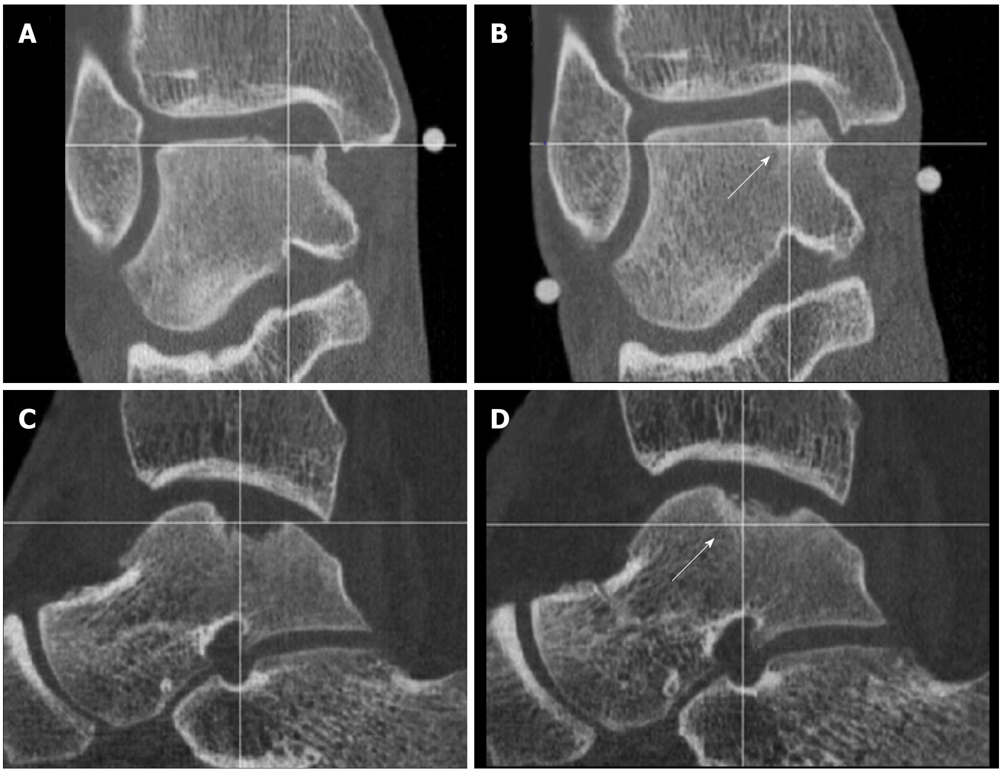

Figure 7 Coronal (A) and Sagittal (C) computed tomography-scans obtained 2 wk postoperatively, showing a medial osteochondral defect of the talus treated with arthroscopic debridement and microfracturing, these can be compared with 1-year postoperative computed tomography scans (B, D). Note the partial bony ingrowth of the defect.

imaging technique that is complement to morphological imaging in monitoring the biomechanical properties of cartilage repair tissue[44-46]. This technique does not require the injection of contrast medium and is sensitive to the collagen fiber network, including the concentration, orientation and integrity of collagen, as well as to the water content in repair tissue. Good organization of collagen is considered to indicate the maturation of repair tissue and is associated with a good clinical outcome[47], while poor cartilage organization predicts poor clinical outcomes[46,48]. A recent study demonstrated also that T2 mapping is an effective noninvasive tool for evaluating cartilage repair after microfracture treatment for full-thickness cartilage defect models in rabbit knee joints[49].

dGEMRIC: dGEMRIC is also a qualitative MR imaging technique that is recognized as a reliable tool for the assessment of cartilage status[50]. This technique was first described in 2001 and is able to provide a direct measurement of the concentration glycosaminoglycan (GAG) in articular cartilage by using the T1 relaxation time[51]. dGEMRIC requires the injection of a negatively charged intravenous gadolinium-based contrast medium and depends on the distribution of this negatively charged contrast agent through the extracellular matrix of hyaline cartilage[50]. The diffusion of intravenous gadolinium in inverse proportion to the GAG content of cartilage tissue results in a proportionate change in the T1 relaxation times measured by MRI. Several studies have shown that dGEMRIC has the potential to assess the cartilage quality in repair tissue after cartilage repair techniques[43].

Magnetic resonance observation of cartilage repair tissue: Some investigators have quantified MRI results by self-developed criteria[52,53], but a more objective, well-known, and frequently used method is the magnetic resonance observation of cartilage repair tissue (MOCART) (Table 2)[41,54]. Nine variables describe the morphology and signal intensity of the repair tissue compared with the adjacent native cartilage, the degree of filling of the defect, the integration to the border zone, the description of the surface and structure, the signal intensity, the status of the subchondral lamina and subchondral bone, the appearance of adhesions and the presence of synovitis[41]. This system has good interobserver reliability, with intraclass correlation coefficients of > 0.81 in eight of nine variables[54]. However, the association of the MOCART with the clinical situation is not exactly clear. In a study by Aurich *et al*[55] there was no relation between the MOCART and clinical outcome after matrix-associated chondrocyte implantation of the talus. In another study, three out of five variables of the modified MOCART showed good correlation with second-look arthroscopy after autologous chondrocyte implantation in the ankle, while two out of five variables showed poor correlation[56].

CONCLUSION

In the initial evaluation of patients with acute or chronic ankle pain, conventional radiographs can be useful. However, the sensitivity of detecting OCDs is limited. Although a heel-rise view improves the sensitivity, the use of more sensitive diagnostic methods is essential. Radiographs are frequently obtained in the postoperative assessment of OCDs but are primarily used for the assessment of degenerative changes to the joint.

CT is the most effective for the assessment of osseous structures. Size, location, detachment of a fragment, as well as the integrity of the subchondral bone can be assessed. The appearance of subchondral bone in CT is correlated with cartilage damage at arthroscopic evaluation. SPECT-CT allows a 3D localization of osteoblastic activity, providing additional information about the involvement of the subchondral bone, and can be of additional value in complex cases with co-existing pathology. A plantar flexion CT can be a viable tool to assess preoperatively the arthroscopic accessibility of an OCD. The use of intra-articular contrast can be helpful in the assessment of OCD stability but arthrography is an invasive method.

MRI has the advantage of not utilizing ionizing radiation and gives a superior detail of the surrounding soft tissue. However, the true extent of the OCD may be obscured by concomitant bone-marrow edema. New innovative quantitative MRI techniques, like T2 mapping and dGEMRIC, are frequently used to depict early cartilage degeneration before morphologic cartilage loss occurs.

Ultrasound can detect cortex irregularities and loose fragments, and is noninvasive and cost-effective, which makes it an interesting alternative. However, only anterior and central lesions can be detected.

FUTURE DIRECTIONS

Because of advancements in imaging sensitivity, OCDs of the talus are increasingly detected. Conservative treatment options are available, but a review by Tol *et al*[57] showed that the average success rate of nonoperative treatment was only 45%. Current surgical treatment options consist of either reparative or restorative techniques. Arthroscopic debridement and BMS is a widely used first-line reparative treatment for OCDs. While Zengerink *et al*[6] reported that the short- and medium-term results of BMS are successful in 85% of cases, authors have questioned the long-term results. In particular the long-term viability of fibrocartilage, with fibrillation and fissuring being recognized by cartilage sensitive imaging modalities[58]. Biological adjuncts, like concentrated bone marrow aspirate and platelet-rich plasma, may promote hyaline-like tissue development and improve the biological environment in which cartilage can heal. Also, new surgical techniques to restore the natural congruency of the subchondral bone and to preserve hyaline cartilage are developed. Kerkhoffs *et al*[59] showed promising results with an arthroscopic fixation technique. For this "lift drill fill fix" technique, more long-term follow-up research is needed to confirm the excellent short-term results and to show more pitfalls.

We believe that restoration of the subchondral bone and the preservation or restoring of hyaline cartilage will be the main focus of the treatment of OCDs in the future. The subchondral bone should be addressed to support the overlying cartilage[17]. Imaging modalities like CT, MRI T2 mapping and dGEMRIC, will play an important role in the postoperative assessment of the subchondral bone plate and cartilage and may lead to new insights in the treatment of OCDs of the talus.

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MINIREVIEWS

Current concepts in the management of radial head fractures

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Abstract

Fracture of the radial head is a common injury. Over the last decades, the radial head is increasingly recognized as an important stabilizer of the elbow. In order to maintain stability of the injured elbow, goals of treatment of radial head fractures have become more and more towards restoring function and stability of the elbow. As treatment strategies have changed over the years, with an increasing amount of literature on this subject, the purpose of this article was to provide an overview of current concepts of the management of radial head fractures.

Key words: Elbow; Fracture; Management; Radial head; Trauma

Core tip: The radial head is one of the most debated subjects of the elbow. As treatment strategies have changed over the years, with an increasing amount of literature on this subject, the purpose of this article was to provide an overview of current concepts of the management of radial head fractures.

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INTRODUCTION

Fractures of the radial head are the most common fractures in the elbow[1]. Although it has been 80 years since one of the first reports on radial head fractures was published in the New England Journal of Medicine; the radial head is still a topic for debate in the orthopedic and trauma literature[2]. Over the last decades, the radial head is increasingly recognized as an important stabilizer of the elbow[3,4]. In order to maintain stability of the injured elbow, the main goal in the treatment of radial head fractures is to restore the anatomy of the radial head and surrounding tissues. The purpose of this article was to discuss current aspects in the etiology and management of radial head fractures in adults.

EPIDEMIOLOGY

Fractures of the radial head are common, with an estimated incidence of 2.5 to 2.8 per 10000 inhabitants per year. They account for approximately one-third of all elbow fractures. The mean age of patients that sustain a radial head fracture varies between 44 to 47.9 years[5-7]. Male-female ratios vary between 1:1, 2:3 and 3:2[1,6,8,9]. Female patients are significantly older compared to male patients (37-41 years *vs* 48-54 years)[6,7]. The peak incidence in men is between the age of 30 and 40 years and in women it is between 50 and 60 years[6]. Once the age rises above 50 years, the number of female patients with a radial head fracture is significantly larger than the number of male patients[6]. This typical distribution can be explained by a correlation with the presence of osteoporosis in female patients above the age of 50 years and higher energy trauma in young males[10].

BIOMECHANICS

The radial head is an important secondary stabilizer in valgus and external rotation. The issue of the individual contributions of the radial head and soft-tissue stabilizers of the elbow is very complex. Several biomechanical studies have been conducted to quantify elbow stability for simulated fractures, radial head excision, and radial head replacement, with and without the integrity of the collateral ligaments[3,11].

Radial head excision alters the kinematics and varus-valgus laxity of the elbow with intact ligaments and that stability is improved after radial head arthroplasty[11-13]. Also an increase in external rotation of the ulna with respect to the humerus during passive motion with the forearm in supination was observed after radial head excision when both ligaments were intact[12].

A significant decrease in elbow stability was noted if the radial head was excised in elbows with an associated disruption of the lateral collateral ligament (LCL). Elbow laxity was improved following radial head arthroplasty; however, these elbows were still unstable relative to those with intact ligaments[12]. These findings suggest that repair of the disrupted LCL complex is essential in order to restore elbow stability following open reduction and internal fixation (ORIF) of the radial head or radial head arthroplasty.

Pomianowski *et al*[14] reported that laxity was increased after radial head excision in elbows with disruption of the medial collateral ligament (MCL). Radial head arthroplasty restores valgus stability in elbows with disruption of the MCL to a state similar to that seen in elbows with a native radial head[14,15]. Other studies observed an improved but not normal stability after radial head arthroplasty with MCL insufficiency[12,16]. However, the amount of instability was very small, possibly because of the stabilizing effect of the biceps and brachialis.

CLASSIFICATION

Mason[1] observed, back in 1954, the fracture patterns of the radial head in 100 patients and divided them in three groups. Mason Type Ⅰ fractures (73%) of the radial head involved fractures without displacement, type Ⅱ fractures (19%) were marginal sector fractures with displacement, and type Ⅲ fractures (8%) were comminuted[17]. In 1962, Johnston[18] added fractures of the radial head that were associated with a dislocation of the elbow, as a type Ⅳ to the system. Subsequently, Broberg and Morrey[19] and Hotchkiss[20] further quantified the amount of dislocation for type Ⅱ fractures. More recently, Rineer *et al*[21] suggested that the stability of the fracture can be determined based on the detail whether there was cortical contact between the fragments, or not. The various classifications are summarized in Table 1 and Figure 1. The interobserver agreement for diagnosing a 2 mm gap (κ = 0.55) or cortical contact (κ = 0.43) on standard radiographs was moderate[22]. Two- or three-dimensional computed tomography (CT) scans improved sensitivity for diagnosis in another study, though the interobserver agreement was still only moderate for most fracture characteristics[23]. Potential benefit of CT reconstructions is to determine the location of the fracture in the radial head (most commonly anterolateral quadrant with the forearm in neutral position), which may be associated with change on associated injuries and elbow instability[24,25].

ASSOCIATED INJURIES

When treating patients with a fracture of the radial head, special attention has to be given to the detection and treatment of associated injuries of the injured extremity. van Riet *et al*[7] found an incidence of associated injures in 39% in a retrospective evaluation of 333 patients with a radial head fracture. Loss of cortical contact and comminution of the radial head fracture are strongly related to a high incidence of associated injuries[7,21]. Associated injuries as ligamentous injuries, or bone bruise of the capitellum can be found using magnetic resonance imaging (MRI) in 76% to 96% of the patients with a radial head fracture[26,27]. In 9 of 14 patients with a Mason type Ⅰ radial head fracture Hausmann *et al*[28] found partial lesions of the interosseous membrane (IOM) with MRI. Seven of these patients reported pain

Table 1 Classification and description of radial head fractures

	Description of classification according to various authors				
Type	Mason	Johnston	Hotchkiss	Broberg and Morrey	Rineer
Ⅰ	Without displacement	Without displacement	< 2 mm dislocation	< 2 mm dislocation	
Ⅱ	With displacement	With displacement	> 2 mm dislocation	> 2-3 mm dislocation and involves > 30% of radial head	Cortical contact between fragments > stable No cortical contact between fragments > unstable
Ⅲ	Comminuted	Comminuted	Comminuted	Comminuted	
Ⅳ	-	Fracture associated with dislocation of the elbow		Fracture associated with dislocation of the elbow	

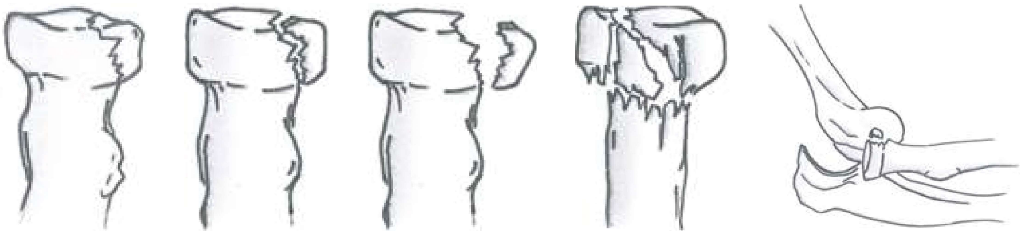

Figure 1 Different types of radial head fractures and possible associated injuries.

in the region on the distal IOM[28]. On the other hand, McGinley *et al*[29] only found incomplete or complete tears of the IOM in 5 patients with a Mason type Ⅱ or Ⅲ radial head fracture, the IOM was intact in all 13 patients with a Mason type Ⅰ fracture[29]. Overall, the clinical relevance of associated injuries found with MRI is likely to be limited[30].

Ligamentous injuries

Using MRI in 61% to 80% of the patients with a radial head fracture ligamentous injuries are seen; although these findings were not always clinically relevant[30]. Persistent symptoms after LCL injuries were seen in 11% of the patients with a radial head fracture, and in 1.5% of the patients with a MCL lesion. Lesions of both the MCL and LCL are found in 6%[7]. Ligamentous injuries of the elbow occur as the radial head fractures with the elbow in flexion and pronation with the hand fixed on the ground. As a result of the forced supination of the forearm the LCL ruptures when the body rotates internally on the elbow under axial compression. A posterolateral dislocation with or without rupture of the MCL can occur if rotational and axial forces continue. Also as a result of a valgus moment the MCL can rupture[31,32].

Elbow dislocation and coronoid process fractures

Posterolateral dislocation of the elbow accompanies 3% to 14% of radial head fractures and can occur after a fall on the (nearly) extended arm[6,7]. In the trauma mechanism as mentioned above, the coronoid process is forced under the trochlea of the humerus and can cause a shear fracture. The combination of an elbow dislocation, radial head fracture and coronoid fracture is called "the terrible triad of the elbow". Severe elbow instability and many post-traumatic complications are associated with this terrible triad[33].

Ulnar fractures

Ulnar fractures occur in 1.2% to 12% of the patients with a radial head fracture[6,7]. This includes the Monteggia lesion, which is a radial head dislocation in combination with a fracture of the distal one third of the ulna[34]. The trauma mechanism is a fall on the outstretched arm with the forearm in hyperpronation. A dislocation of the fractured radial head can also occur in complex proximal ulna fractures[35].

Capitellar injuries

(Osteo) chondral lesions of the capitellum occur as the radial head is forced on the capitellum under the axial loading. In MRI studies injury to the capitellum is seen in 39% to 96% of the patients[26,27]. Capitellar fractures occur in 2%[7].

Other associated injuries

A rare associated injury of radial head fractures is a rupture of the IOM between radius and ulna and rupture of the triangular fibrocartilage complex. It is also known as an acute longitudinal radioulnar dissociation or Essex-Lopresti injury[36]. Neurovascular injuries can also occur. Neurologic injuries occur in 20% of elbow dislocations of which the ulnar and median nerve are most commonly affected[37]. Severe anterior displacement of the radial head can cause injury to the radial nerve. Posterior interosseous nerve injury has also been reported[38,39]. Brachial artery injury accompanies 0.3% to 1.7% of elbow dislocations[40].

MANAGEMENT OF NONDISPLACED FRACTURES

In general, the treatment of Mason type Ⅰ fractures is conservative with a pressure bandage and sling for support, and active mobilization as early as possible[41]. Aspiration of the intra-articular haematoma leads to a decrease in intra-articular pressure and pain[42]. Though there is no significant difference in pain between groups of patients in which the haematoma was aspirated compared to patients in whom aspiration was combined with bupivacaine injection in the elbow joint[43]. The natural course of Mason type Ⅰ fractures is in general benign, however, in some studies persistent complaints have been reported in 20% of cases[44]. In several series, patients with the shortest period of immobilization had the best patient-reported outcome measure scores (PROMs) at follow-up[44,45]. Shulman *et al*[46] recently evaluated the follow-up of patients with a Mason type Ⅰ fracture, and concluded that "orthopaedic surgeons are likely over treating patients with Mason-Johnson Type Ⅰ radial head fractures by recommending frequent radiographic follow-up without modifying treatment, leading to unnecessary patient visits, radiation exposure, and increased costs".

MANAGEMENT OF STABLE PARTIAL ARTICULAR DISPLACED FRACTURES

There is currently no consensus on the treatment of patients with isolated, displaced, stable, partial articular fractures of the radial head. Surgical repair of radial head fractures became popular after the introduction of new techniques and implants for the fixation of small articular fracture fragments[47-52]. Later, enthusiasm grew with reports of good results on surgical treatment of these Mason type Ⅱ fractures[49-51,53]. On the other hand, articles on the conservative treatment of Mason type Ⅱ fractures also report favorable outcomes[54,55]. Lindenhovius *et al*[56] reported on the long-term outcome of ORIF for stable displaced partial articular fractures of the radial head with an average 22 years follow-up. Although the results were good, complications were seen in 44% of patients. Furthermore, they compared their results with the 19 years follow-up of the same type of fractures that were treated conservatively by Akesson *et al*[54] and concluded that ORIF is not superior in the long-term. These results are in accordance to a recent retrospective comparative study by Yoon *et al*[57], in which nonoperative management was compared to ORIF. They found no clinically significant difference in PROMs, ROM and strength between the groups[57]. However, more complications [failure of hardware and heterotopic ossifications (HO)] were seen following ORIF, and younger patients scored worse on PROMs. Helling *et al*[58] found no significant difference in outcome between ORIF with metal screws *vs* biodegradable polylactide pins for the treatment of displaced radial head fractures.

Kaas *et al*[59] performed a systematic review on the treatment of Mason type Ⅱ fractures and concluded that, based on 9 included retrospective series, there was insufficient evidence to determine which treatment is superior[59]. Currently, the inclusion of patients for a multicenter randomized controlled trial is initiated to define whether stable partial articular displaced fractures of the radial head are best treated by ORIF or nonoperative management[60].

MANAGEMENT OF COMMINUTED FRACTURES

Although Mason[1] originally advised to perform a resection of the comminuted fractured radial head, numerous other surgical techniques have been described last decades. In cases of isolated comminuted radial head fractures, without associated instability of the elbow, resection of the radial head may lead to satisfactory results[61]. Replacement of the radial head by silicone implants was performed with the idea to restore elbow stability, but resulted in several implant-related problems and complications[62]. Subsequently, management by ORIF became more popular. Good results were reported after ORIF for stable radial head fractures[51]. However, Ring *et al*[63] established that ORIF for Mason type Ⅲ fractures with more than three articular fragments was more likely to result in unsatisfactory outcomes compared to fractures with only 2 or 3 simple fragments[63]. These severely comminuted unstable fractures of the radial head are difficult to restore and are prone to result into hardware failure or nonunion. Moro *et al*[64] therefore advised to use metallic radial head prosthesis (RHP) if a stable internal fixation of the comminuted radial head cannot be achieved. A literature search revealed only one randomized study by Chen *et al*[65], which compared ORIF *vs* arthroplasty for comminuted unstable radial head fractures. After two years of follow-up patients in the replacement group had significantly better PROMs. Furthermore, more complications (limitation in motion, nonunion, malunion, HO, infection) were seen following ORIF (11/23) compared to arthroplasty (3/22). The authors concluded that replacement is more effective than ORIF in clinical practice. However, they justly noted that prosthesis have problems with ageing, loosening and wear, which are not seen in the short-term follow-up of that study. The main problem with of current RHP designs is that only short- to mid-term results are known. RHP may be classified according to the different materials used: (silicone, polyethylene, pyrocarbon, metal), into differences in modularity (monoblock *vs* modular), polarity (uni- or monopolar *vs* bipolar) or fixation method (cemented *vs* uncemented press fit *vs* intentional loose fit). Despite the growing amount of data, evolving surgical technique and improving implant design and rationale; prosthetic radial head replacement is far from what should be

Table 2 Summery of treatment options for different types of radial head fractures

Mason type	Indication	Treatment options[1]
I	All	Conservative with early motion
II	Stable	Conservative with early motion or ORIF
	Unstable	Conservative with early motion or ORIF
	Block with rotation	ORIF
III	2-3 simple fragments	ORIF
	> 3 unstable fragments	Arthroplasty
IV	See above	See above

[1]The treatment options for the radial head are listed here. It is essential to recognize associated injuries that may require surgical treatment such as lateral collateral ligament ruptures and impaction damage of the capitellum. ORIF: Open reduction and internal fixation.

considered an established and routine procedure. It is currently unknown whether one fixation technique has superior outcomes over the others. The same question accounts for material and design of the implants. Future research should therefore compare the various types of RHP and obtain long-term results of the implants.

MANAGEMENT OF ASSOCIATED INJURIES

The treatment of complex elbow trauma is based on 2 principles[35]. The first principle is that elbow function should be maintained by restoring the ulnohumeral joint. Fractures of coronoid, olecranon or distal humerus should therefore be treated by osteosynthesis. The second principle is that elbow stability should be reestablished. As described above, the radial head is an important secondary stabilizer of the elbow, and radial head fractures are commonly concomitant to ligamentous injuries. Lesions of the LCL and MCL should therefore be repaired in most cases[35].

CONCLUSION

The radial head is important secondary stabilizer of the elbow, and fractures of the radial head (and its associated injuries) can result in pain, posttraumatic osteoarthritis and impaired elbow function. Management of radial head fractures should therefore be directed to achieve a stable and functional elbow joint (Table 2). Nondisplaced fractures should be treated by early active motion. The best treatment of stable partial articular fractures is currently unclear, and can be either conservatively by early motion, or ORIF and early motion. Comminuted unstable fractures that consist of 2 or 3 simple fragments can be treated by ORIF. However, if stable internal fixation is not obtained, or the fracture consists of more than 3 fragments, radial head arthroplasty results in better outcomes in the short-term. Long-term results of RHP are still unknown. In all cases of surgically treated radial head fractures it is of utmost importance to adequately assess and treat associated injuries of the coronoid, olecranon and ligaments.

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ORIGINAL ARTICLE

Basic Study

Platelet-rich plasma increases transforming growth factor-beta1 expression at graft-host interface following autologous osteochondral transplantation in a rabbit model

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Author contributions: Boakye LA was chief in creating the manuscript and running all pertinent experiments as well as documenting and analyzing the data; Ross KA was chief in the original animal surgeries, microscopic analysis and editing of the manuscript; Pinski JM assisted the experiments and contributed to editing of the manuscript; Smyth NA and Haleem AM helped to design the original animal model and were crucial in performing the original animal surgeries; additionally, Smyth NA was key to the designing pertinent modes of inquiry; Hannon CP contributed significantly to editing the manuscript; Fortier LA made significant contributions to the initial and subsequent literature reviews while providing edits to the manuscript; Kennedy JG provided primary mentorship regarding project design as well as edits to the manuscript.

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Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at Dryad repository, who will provide a permanent, citable and open-access home for the dataset.

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Abstract

AIM: To explore the effect of platelet-rich plasma on protein expression patterns of transforming growth factor-beta1 (TGF-β1) in cartilage following autologous osteochondral transplantation (AOT) in a rabbit knee cartilage defect model.

METHODS: Twelve New Zealand white rabbits received bilateral AOT. In each rabbit, one knee was randomized to receive an autologous platelet rich plasma (PRP) injection and the contralateral knee received saline injection. Rabbits were euthanized at 3, 6 and 12 wk post-operatively. Articular cartilage sections were stained with TGF-β1 antibody. Histological regions of interest (ROI) (left, right and center of the autologous grafts interfaces) were evaluated using MetaMorph. Percentage of chondrocytes positive for TGF-β1 was then assessed.

RESULTS: Percentage of chondrocytes positive for TGF-β1 was higher in PRP treated knees for selected ROIs (left; P = 0.03, center; P = 0.05) compared to control and was also higher in the PRP group at each post-operative time point ($P = 6.6 \times 10^{-4}$, 3.1×10^{-4} and 7.3×10^{-3} for 3, 6 and 12 wk, respectively). TGF-β1 expression was higher in chondrocytes of PRP-treated knees (36% ± 29% *vs* 15% ± 18%) ($P = 1.8 \times 10^{-6}$) overall for each post-operative time point and ROI.

CONCLUSION: Articular cartilage of rabbits treated with AOT and PRP exhibit increased TGF-β1 expression compared to those treated with AOT and saline. Our findings suggest that adjunctive PRP may increase TGF-β1 expression, which may play a role in the chondrogenic effect of PRP *in vivo*.

Key words: Platelet rich plasma; Transforming growth factor-beta; Autologous osteochondral transplantation

Core tip: Despite the prevalence of platelet rich plasma (PRP) in both practice and literature, there is a dearth of data exploring the specific factors crucial to its role as an adjunct to cartilage repair surgeries. Our results suggest that the increased expression pattern of transforming growth factor-beta1 in PRP-treated rabbit femoral condyles, compared to saline treated controls, is associated with enhanced cartilage repair at the graft-host interface following autologous osteochondral transplantation. Our results serve as an initial step in building a body of evidence behind the specific growth factors crucial to cartilage repair and promise to help us understand how formulations of PRP are effective in musculoskeletal healing.

Boakye LA, Ross KA, Pinski JM, Smyth NA, Haleem AM, Hannon CP, Fortier LA, Kennedy JG. Platelet-rich plasma increases transforming growth factor-beta1 expression at graft-host interface following autologous osteochondral transplantation in a rabbit model. *World J Orthop* 2015; 6(11): 961-969 Available from: URL: http://www.wjgnet.com/2218-5836/full/v6/i11/961.htm DOI: http://dx.doi.org/10.5312/wjo.v6.i11.961

INTRODUCTION

The poor regenerative response of articular cartilage to mechanical injury is largely attributed to its avascularity and hypocellularity[1]. Thus, trauma to the articular surface of joints, particularly to the knee and ankle, may lead to osteochondral lesions (OCL). Few articular cartilage lesions heal without surgical treatment and most OCLs require intervention in hopes of preventing the eventual onset of post-traumatic osteoarthritis[2]. Generally, smaller defects are repaired with arthroscopic bone marrow stimulation (microfracture and drilling)[3]. Replacement procedures, including autologous osteochondral transplantation (AOT) are reserved for larger size lesions. In the ankle, AOT has excellent short to medium term clinical outcomes[3,4]. However, recent concern over poor graft host interface incorporation leading to subchondral bone voids and graft failure, has prompted investigators to identify biological adjuncts that may improve the cartilage graft-host interface incorporation[5-8].

Platelet rich plasma (PRP) may act as a biologic stimulant to influence cartilage repair at the graft-host interface. Although the exact combination of growth factors essential to the regenerative properties of PRP is unknown, transforming growth factor-beta1 (TGF-β1) has been suggested to stimulate mesenchymal stem cells (MSC), chondrocyte proliferation and inhibit catabolic activity[9-11]. Several *in vivo* and *in vitro* studies have attempted to investigate the milieu of growth factors that play a role in articular cartilage deposition, repair, and survival[9,12]. PRP contains concentrated platelets as well as growth factors that are three to five fold greater in concentration than whole blood[13,14]. Smyth *et al*[15] found that PRP improved osteochondral graft integration at the cartilage interface and decreased graft degeneration in an *in vivo* AOT rabbit model. Other reports have demonstrated that PRP promotes type Ⅱ collagen deposition and chondrocyte proliferation *in vitro* substantiating the chondrogenic potential of PRP[14,16].

The potential chondrogenic effects of PRP are attributed to cytokines and growth factors released from the alpha granules of circulating platelets, which suppress inflammation, promote angiogenesis and support collagen synthesis[14]. These growth factors include TGF-β1, vascular endothelial growth factor, basic fibroblast growth factor, and a host of other factors[14]. The role of TGF-β1 remains to be defined, however it is known that it assists in recruiting cells that mediate injury repair and has the capacity to promote chondro-

Figure 1 Intraoperative photograph of autologous osteochondral transplantation following graft placement.

genesis *in vivo*[15]. Thus, it is of interest to understand whether TGF-β1 is crucial to the reparative properties of PRP. The aim of the current study was to explore the effect of PRP on expression patterns of TGF-β1 in a previously published rabbit femoral condyle OCL AOT study. We hypothesized that TGF-β1 would have an increased expression pattern in the PRP treated rabbit femoral condyles compared to saline treated controls.

MATERIALS AND METHODS

Experimental design

The Institutional Animal Care and Use Committee at our institution approved the pre-cursor study (HSS Project # 09-11-03B) by Smyth *et al*[15]. The current study utilized unaltered archived samples obtained from the same cohort as the prior study. All appropriate measures were taken to minimize pain or discomfort of the rabbits during the interventions. The rabbits were cared for at the HSS veterinary facilities.

Twelve New Zealand white rabbits were treated with bilateral AOT as previously described by the current authors (Figure 1)[15]. After giving each rabbit adequate anesthesia, 27 mL of blood was aspirated from the great aural artery, combined with 4 mL of anticoagulant citrate dextrose solution A. One milliliter was set aside for cytological analysis and the remainder of the blood was used to prepare the platelet concentrated solution. Surgical procedures and PRP preparation (Magellan Autologous Platelet Separator; Arteriocyte Inc., Cleveland, Ohio) were performed as previously described[15]. Knees were randomly treated with an injection of 0.5 mL of either PRP or saline. Each rabbit received treatment in one knee, and saline in the contralateral knee to serve as its own control following wound closure. Osteochondral grafts were also soaked in PRP or saline for 10 min prior to implantation.

Rabbits were a mean weight of 4 kg (range, 3.7 to 4.2 kg) and a mean age of 23 wk. Rabbits were allowed unrestricted cage activity in individual cages for 7 d postoperatively, with rabbits euthanized (n = 4) at 3, 6 and 12 wk following surgery. Both knees were then removed *en bloc* and prepared for histological processing. A sample of synovium was also retrieved from each knee. Surgical protocol for harvesting of samples is as reported by Smyth *et al*[15]. Following the procedures, the rabbits were each given a fentanyl skin patch (12 mcg/h) and were granted free range within a cage. Rabbits were then euthanized with intravenous pentobarbital (100-150 mg/kg) at 3, 6, and 12 wk after the initial surgery.

Immunohistochemical staining

Following euthanasia and removal of knees, specimens were fixed in 10% formalin for 7 d. Decalcification protocol included placing specimens in sodium citrate-formic acid solution for a further seven days. Specimens were then embedded in paraffin and cut into 8-μm sections. TGF-β1 antibody (R and D Systems Inc., Minneapolis, Minnesota) was used to stain articular cartilage and synovial sections.

All slides were first dewaxed and rehydrated *via* 3-5 min treatments with xylenes, 5 min in 100% EtOH, 5 min in 95% EtOH, 5 min in 70% EtOH and 5 min in distilled water. Next, slides were blocked with H_2O_2 (3% in 1 × phosphate buffered saline (PBS)-10 mL H_2O_2 and 90 mL PBS), placed three times in PBS for 5 min each, retrieved without treatment, rinsed in deionized water twice for 5 min each, treated with protein block for 20 min, and exposed to antibody (1:20 in 1 × PBS-5 μL/slide), covered in parafilm, and left to react overnight in humidity chambers at room temperature. Samples were then rinsed three times in 1 × PBS. Anti-mouse immunoglobulin G was added and allowed to react for 1 h. After 45 min an Avidin Biotin Complex was prepared and added to the washed (3 × in PBS) samples for an hour. Samples were washed and then treated with 225 μL DAB and 3 mL PBS + 4 μL H_2O_2 until the cells darkened at about 7 min. Samples were then rinsed and counterstained in Harris Hematoxylin for 7 min. A mouse array containing various tissue samples served as a positive control and a negative control was not used.

Histological assessment

Samples were visualized *via* confocal microscopy (Carl Zeiss, Inc., New York) and images were taken of predetermined regions of interest (ROI) in each graft sites in each knee at 400 × magnification. ROI included the interface between graft and unaltered cartilage on either side of the defect, the center of the autologous graft, and unaltered tissue remote from the repair sites. All samples were first analyzed qualitatively for area and density of apparent staining. A total of 144 samples were reviewed and the results of 120 histological sections were included in the study. The excluded images were not included due to poor or inadequate visualization of both femoral condyles and all ROIs. Two reviewers, who were blinded to the treatment groups, independently reviewed the histological sections and

Table 1 Comparison of average percentage of chondrocytes positive for transforming growth factor-beta1 in plateletrich plasma *vs* saline in all regions of interest

Region of interest	Platelet rich plasma	Saline	*P*-value
Left	45 ± 36	15 ± 17	0.03
Center	30 ± 31	7 ± 12	0.05
Right	36 ± 24	11 ± 23	0.72
Unaltered	24 ± 25	11 ± 12	0.19
All ROIs	32 ± 31	15 ± 19	2.60×10^{-3}

ROI: Selected regions of interest.

Table 2 Average percentage of chondrocytes stained positive for transforming growth factor-beta1 antibody in platelet rich plasma and saline groups at each point of euthanasia

Time	Platelet rich plasma	Saline	*P*-value
3 wk	42 ± 19	12 ± 7	6.6×10^{-4}
6 wk	30 ± 11	7 ± 8	3.1×10^{-4}
12 wk	44 ± 19	21 ± 8	7.3×10^{-3}

assessed percentage of chondrocytes staining positive for TGF-β1. Samples were evaluated quantitatively using computer software MetaMorph (Molecular Devices, Inc., Sunnyvale, California) to count the total number of chondrocytes and total number of chondrocytes expressing TGF-β1[17]. Analysis focused on the percentage of cells stained positive for TGF-β1 as the overall cellularity of each sample varied. Synovial sections were analyzed qualitatively. The presence of any synoviocytes staining positively with TGF-β1-antibody, or lack of any stained synoviocytes within the synovial specimen, was recorded. The International Cartilage Repair Society (ICRS) histological scoring system was originally developed in 2001 as a universal and standardized scoring system to aid in the assessment of cartilage repair[18]. An analysis of ICRS Score and overall percentage of chondrocytes positive for TGF-β1 with TGF-β1 for each specimen was performed using the Spearman Rho Coefficient to determine if higher ICRS scores correlated with a higher percentage of chondrocytes positive for TGF-β1.

Statistical analysis

Statistical review of the study methods was performed by a biomedical statistician. A Student's *t*-test was used to determine whether there was a significant difference in TGF-β1 staining between samples. The percentage of chondrocytes stained positive for TGF-β1 in the PRP and saline groups in all ROI and all time intervals were compared. A value of $P \leqslant 0.05$ was considered significant. Comparison of data distribution between observers was calculated *via* a two-sample independent *t*-test. The intraclass correlation coefficient (ICC) was calculated to measure interobserver reliability. Statistical analysis was performed using commercially available software (Epi Info7™, Centers for Disease Control and Prevention, Atlanta, Georgia).

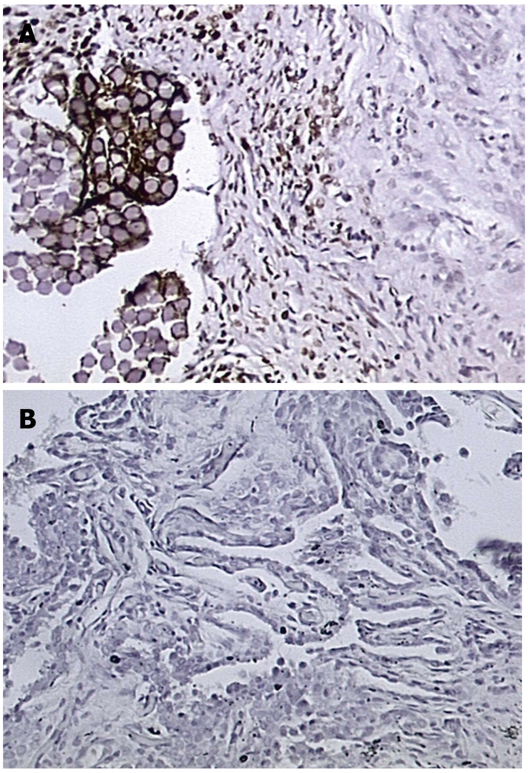

Figure 2 Synovial sections harvested six weeks following surgery (400 ×). Transforming growth factor-beta1 antibody staining is positive in cells that appear brown. A: Treated with platelet-rich plasma; B: Treated with saline.

RESULTS

Histological assessment-articular cartilage

Qualitative microscopic analysis showed differences in the expression pattern of TGF-β1, with stronger (a higher percent concentration of chondrocytes) staining in the superficial cartilage of PRP treated joints. PRP treated knees showed strong TGF-β1 staining at all time periods (3, 6 and 12 wk). The mean modified ICRS histological score was significantly higher for all PRP-treated samples with a value of 18.2 ± 2.7 *vs* 13.5 ± 3.3 for saline treated controls ($P = 0.002$)[17]. A statistically insignificant correlation of percentage of TGF-β1 stained chondrocytes to ICRS scoring existed for the samples ($r = 0.06$, $P = 0.77$). Two-sample independent *t*-test indicated that there was no difference in distribution of the data between observers ($P = 0.79$). There was good reliability between observers (ICC, 0.79).

The results of staining quantification are detailed in Tables 1 and 2. Total mean percentage of chondrocytes positive for TGF-β1, when combining data from all ROIs and time points, indicated that TGF-β1 expression was higher in the PRP group compared to saline treated group, with values of 36% ± 29% *vs* 15% ± 18% ($P = 1.8 \times 10^{-6}$) (Figures 2-5). Mean percentage of chondrocytes positive for TGF-β1 was also higher in PRP treated knees at each individual ROI when combining data from all

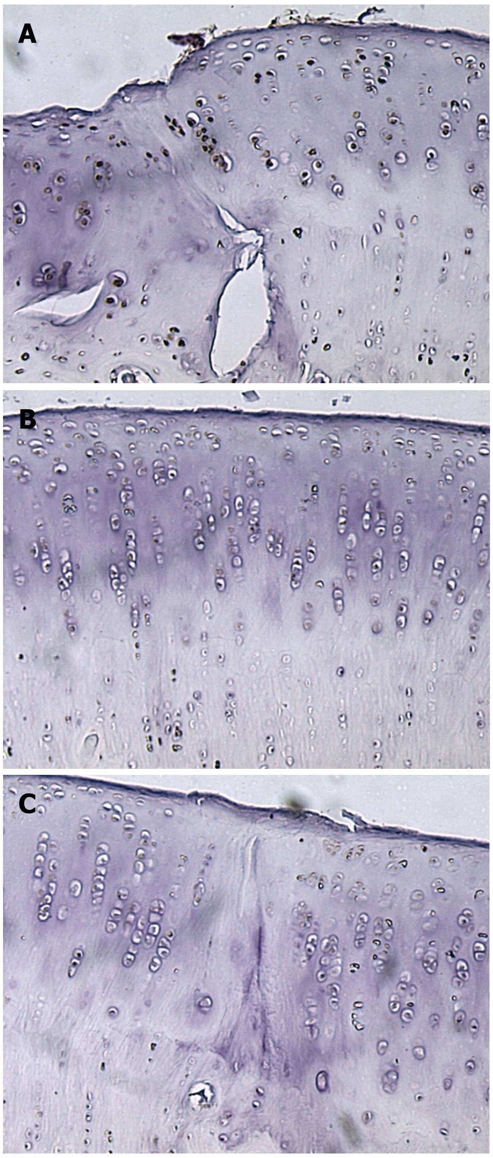

Figure 3 Sagittal sections of an osteochondral graft treated with platelet-rich plasma 12 wk following surgery (400 ×). Transforming growth factor-beta1 antibody staining is positive in cells that appear brown. A: Left interface between the graft and host cartilage; B: Central aspect of the graft; C: Right interface between the graft and host cartilage.

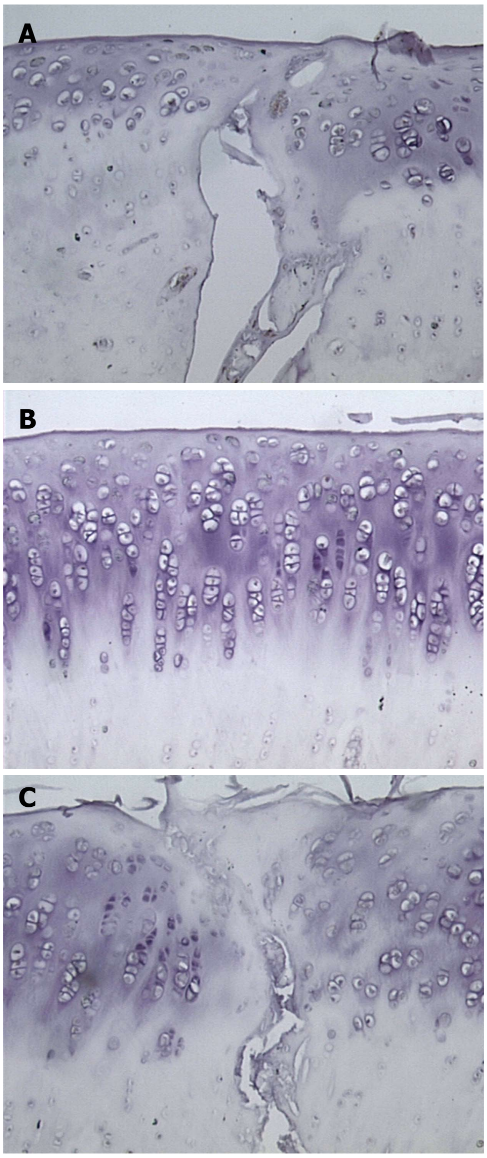

Figure 4 Sagittal sections of an osteochondral graft treated with saline 12 wk following surgery (400 ×). Transforming growth factor-beta1 antibody staining is positive in cells that appear brown. A: Left interface between the graft and host cartilage; B: Central aspect of the graft; C: Right interface between the graft and host cartilage.

post-operative time points. Findings for each ROI are detailed in Table 1. Staining was significantly higher left of the graft interface and in the center of the graft (P = 0.03, P = 0.05), but the difference at the right interface of graft and host tissue was not significant (P = 0.72). The percentage of chondrocytes positive for TGF-β1 was higher in the PRP treated group at each euthanasia time point ($P = 6.6 \times 10^{-4}$; 3.1×10^{-4} and 7.3×10^{-3} for 3, 6 and 12 wk, respectively). Findings based on time from surgery to euthanasia are detailed in Table 2. Data from all ROIs combined were utilized for calculations by post-operative time point.

Percentage of chondrocytes positive for TGF-β1 in unaltered cartilage remote from the graft site was higher in the PRP group (24% ± 25%) than the saline group (11% ± 12%) but this difference was not statistically significant (P = 0.19) (Table 1).

Histological assessment-synovium

Synovial samples that stained positively for TGF-β1 were associated with a lower mean ICRS score (14.6 ± 29.3) than those that did not stain positively (18.3 ± 4.9, P = 0.008). The mean percentage of chondrocytes stained positive for TGF-β1 in the samples with a positive synovial TGF-β1 stain was (29.3% ± 22.5%) compared to (44.9% ± 24.6%) for synovial samples without positive TGF-β1 staining- thus a difference was not statistically different (P = 0.80). Synovial tissue specimens demonstrated hypertrophy in the PRP treated group when compared to the saline treated

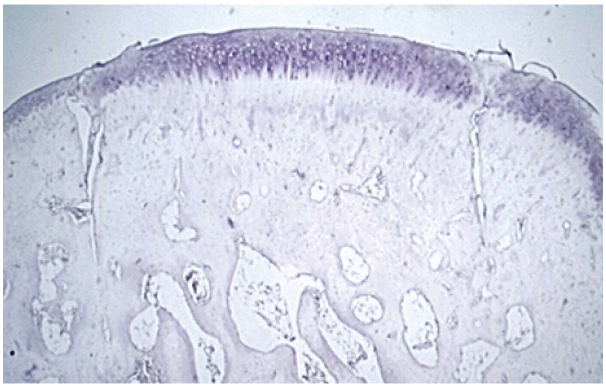

Figure 5 Sagittal section of the same osteochondral graft (20 ×). The graft was treated with saline and the knee was harvested 12 wk following surgery. The interface between host and graft tissue is integrated at points but considerable gapping remains.

group microscopically. This was more pronounced at the 6-wk time point than either of the other two experimental time points. An analysis of the synovial samples staining positively for TGF-β1 showed only 6 of 12 stained positively for TGF-β1 in the PRP treated group and four of the 12 stained positively in the saline treated group. This was not a statistically significant difference.

DISCUSSION

The current study is the first to investigate the effect of PRP on TGF-β1 expression in the setting of cartilage repair in an *in vivo* model. It follows a previous study indicating PRP was chondrogenic using the same animals. The current results indicate that PRP increases expression of TGF-β1 in the same model[15]. Increased expression of TGF-β1 appears to be present at 3, 6 and 12 wk after surgery. Platelet-rich plasma also appears to increase the presence of TGF-β1 in synovium, primarily 6 wk after surgery, although this was only qualitatively assessed, as images were not amenable to quantitative analysis of number of synoviocytes stained.

Increased TGF-β1 expression was noted in both PRP and saline treated knees. This was expected as the saline treated knees underwent AOT surgery. TGF-β1 expression was more prevalent in AOT repair sites treated with PRP compared to the saline control groups. An increase in TGF-β1 expression in histological sections exhibiting better graft integration could potentially indicate that TGF-β1 participates in this chondrogenic process in a rabbit model. The samples treated with PRP showed higher TGF-β1 expression and when compared to results published previously by Smyth *et al*[15] had higher ICRS macroscopic scores (Figure 6). In the previously published investigation, the authors showed, using the same rabbit femoral AOT model, that PRP facilitated chondrogenic integration at the graft-host interface using immunohistochemistry and safranin-o staining evaluation and quantitative data showed that

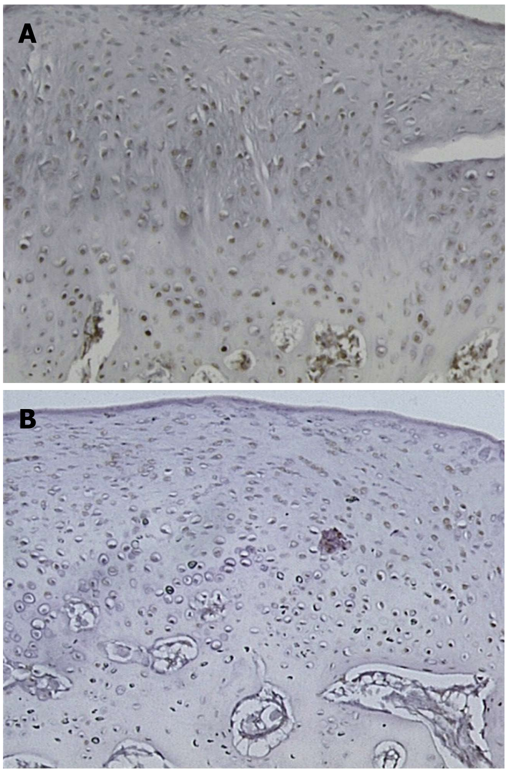

Figure 6 Sagittal sections femoral condyle articular cartilage remote for the autologous osteochondral transplantation graft site (400 ×). Transforming growth factor-beta1 antibody staining is positive in cells that are stained brown. The top section was in the left knee which was treated with platelet-rich plasma and had the second highest ICRS score (20) and the bottom section is taken from the right knee which received saline with the lowest ICRS score (7). ICRS: International Cartilage Repair Society.

PRP treated AOT produced a better infill at the graft site[15]. As this data is considered in light of the current data, we believe the effect of PRP is in large part as a result of TGF-β1 expression.

A number of other studies have investigated the role of TGF-β1 in articular cartilage synthesis with comparable results. Fortier *et al*[9] compiled the findings of several prevalent studies investigating the role of various growth factors *in vitro* and *in vivo* and found that TGF-β1 has effects on chondrocytes, cartilage, synovium and MSC. TGF-β1 stimulates MSCs and chondrocytes to facilitate chondrogenic proliferation and inhibits the catabolic activity of interleukin-1 (IL-1) and matrix metalloproteinases, which prompt degradation of cartilage extracellular matrix (ECM)[10]. TGF-β1 has also been shown to stimulate the synthesis of the ECM and downregulate type Ⅰ collagen deposition, which is associated with fibrosis and potential scar formation[9]. However, TGF-β1 has also been associated with chemotaxis of inflammatory cytokines and synovial proliferation and fibrosis[9]. These potential drawbacks have served to create some ambiguity regarding TGF-β1's interactions with ECM components.

More specifically, Qiao *et al*[19] studied *in vivo* growth factor expression in a rabbit model by exposing chondrocytes from articular cartilage of 7-week-old New

Zealand white rabbits samples to recombinant TGF-β1 activated kinase1 (TAK1), TGF-β1 activated kinase1 antagonist (TAK1a), or over-expression of TAK1 *via* transfection with adenovirus. Results demonstrated enhanced synthesis of type Ⅱ collagen protein by TGF-β1 and bone morphogenic protein-2. Möller *et al*[20] found that chondrocytes retrovirally transfected with TGF-β1 demonstrated a 96% increase in proteoglycan synthesis and a 304% increase in collagen synthesis (predominantly type Ⅱ) compared to untreated samples, thereby providing significant stimulation of ECM synthesis and hyaline cartilage deposition. Galéra *et al*[11] found that TGF-β1 successfully increases collagen synthesis *via* enhanced gene expression based on mRNA encoding of type Ⅱ procollagen of rabbit articular cartilage in monolayer culture. TGF-β1 may also contribute to mediating catabolic and inflammatory processes within the joint[9]. Smith *et al*[21] found that although IL-1 reduced proteoglycan synthesis by 50% on its own, treatment with TGF-β1 was able to restore proteoglycan synthesis to control levels.

In contrast to the aforementioned studies, PRP was the source of TGF-β1 in our study, rather than direct exposure of TGF-β1. The molecular effects of PRP have been shown to have a temporal sequence, with a maximal TGF-β1 expression at about 5 d, which is associated with the anabolic components of chondrocyte proliferation and maturation[22].

The effect of PRP is mediated therefore largely by its anabolic and anti-inflammatory effects[23]. A recent systematic review of the basic science literature found that 17 of 21 studies reported that PRP had a positive effect on cartilage repair[24]. An *in vitro* study by Park *et al*[22] assessed the effect of treating isolated primary chondrocytes with 0.1%-20% PRP. Results of reverse transcription-polymerase chain reaction and cytochemical staining indicated increased TGF-β1 expression and proteoglycan expression, along with a number of other growth factors[22]. Other animal studies have shown direct enhancement of articular cartilage repair using PRP[25-27].

This study had several limitations. Firstly, the use of PRP limited our ability to understand the effect of TGF-β1 in isolation from other growth factors and cytokines introduced by PRP. However, the purpose of our study was to investigate the effect of PRP on TGF-β1 expression patterns, rather than the effect of TGF-β1 on cartilage repair. Secondly, a lack of overall staining and ability to quantify percentage of synoviocytes or synovial fibroblasts stained positive for TGF-β1 antibody limited our ability to draw conclusions regarding the effect of PRP on synovial TGF-β1 expression. Lastly, the surgeon was not blinded to the treatment group at the time of operation, leading to possible bias during graft implantation. However, histological observers were blinded during data collection.

Several studies have reported that PRP may be an effective peri- or post-operative adjunct for cartilage injury, but there is a paucity of data elucidating the exact milieu of factors and cytokines essential to forming hyaline-like repair cartilage. The results of our study demonstrate that PRP increases TGF-β1 expression in AOT and may play a role in enhancing cartilage repair. Further evaluation of TGF-β1's restorative capacity and temporal sequence of activity would help to optimize PRP's use as an adjunctive therapy. Future research should focus on determining the specific role of growth factors and inflammatory cytokines to determine the most effective PRP formulation for musculoskeletal healing.

The results of the current study indicate that repair cartilage treated with PRP exhibits increased TGF-β1 expression compared to saline treated controls in a rabbit model. This finding, along with enhanced repair in the PRP group previously reported in the same model, indicates that TGF-β1 may play a role in the chondrogenic effect of PRP *in vivo*.

ACKNOWLEDGMENTS

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COMMENTS

Background

Trauma to the articular surface of joints may lead to osteochondral lesions (OCL) due to poor regenerative potential. Most OCLs require intervention in hopes of preventing subsequent post-traumatic osteoarthritis. There are options for repair and/or replacement of articular cartilage. Replacement procedures, including autologous osteochondral transplantation (AOT) are reserved for larger size lesions. Although AOT has shown excellent short to medium term clinical outcomes, concern regarding poor graft host interface incorporation has prompted investigators to identify biological adjuncts that may improve the cartilage graft-host interface incorporation. Platelet rich plasma (PRP) may act as a biologic stimulant to influence cartilage repair at the graft-host interface. The potential chondrogenic effects of PRP are attributed to cytokines and growth factors released from the alpha granules of circulating platelets, which prevent inflammation, promote angiogenesis and support collagen synthesis. Although the exact combination of growth factors essential to the regenerative properties of PRP is unknown, transforming growth factor-beta1 (TGF-β1) has been suggested to stimulate mesenchymal stem cells, chondrocyte proliferation and inhibit catabolic activity.

Research frontiers

The use of biologic adjuncts in articular cartilage repair or replacement surgeries is a burgeoning field as there remains a dearth of information of what factors are most influential in the effectiveness of the most commonly used adjuncts. In an effort to align clinical practices with evidence-based research, much of the recent research on articular cartilage has focused on the pathophysiology of adjuncts.

Innovations and breakthroughs

The study was driven by an interest in addressing the paucity of data elucidating the exact milieu of factors and cytokines essential to forming hyaline-like repair cartilage. The aim of the current study was to explore the effect of PRP on expression patterns of TGF-β1 in a previously published rabbit femoral condyle OCL AOT study. The results of the study demonstrate that PRP increases

TGF-β1 expression in AOT and may play a role in enhancing cartilage repair.

Applications

Further evaluation of TGF-β1's restorative capacity and temporal sequence of activity would help to optimize PRP's use as an adjunctive therapy. Future research should focus on determining the specific role of growth factors and inflammatory cytokines to determine the most effective PRP formulation for musculoskeletal healing.

Terminology

PRP: An autologous blood product rich in cytokines and growth factors increasingly studied as an adjunct to cartilage repair and replacement procedures. Above baseline quantities of platelets or at least 1.1 × 10^6 platelets/μL as well as growth factors that are 3 to 5-fold greater in concentration than whole blood; AOT: Replacement of the articular cartilage defect with a tubular unit of viable hyaline cartilage and bone from a donor site in the ipsilateral knee joint.

Peer-review

The manuscript is well written and has scientifically relevant data.

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ORIGINAL ARTICLE

Case Control Study

Effect of early surgery in high surgical risk geriatric patients with femoral neck fracture and taking antiplatelet agents

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Author contributions: Sa-ngasoongsong P and Chanplakorn P contributed equally to this work; Sa-ngasoongsong P and Chanplakorn P designed the research, analyzed the data and prepared the manuscript; Pinsiranon N collected the data; Kulachote N and Sirisreetreerux N contributed to the study design; Sa-ngasoongsong P, Kulachote N, Sirisreetreerux N, Kawinwonggowit V and Suphachatwong C were the surgeons who performed the surgery and reviewed the data critically; Laohajaroensombat S and Wajanavisit W assisted in preparation of the manuscript and reviewed the manuscript critically; and Woratanarat P reviewed data and performed statistical analysis; all authors read and approved the final manuscript.

Institutional review board statement: The study was approved by the ethical clearance committee of Human Rights Related to Research Involving Human Subjects of the Faculty of Medicine Ramathibodi Hospital, Mahidol University.

Informed consent statement: All study participants in the prospective cohort group provided informed written consent. According to ethical approval, no informed consent was necessary from individual patients in the retrospective group since all data were gathered retrospectively from medical records.

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

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding authors at pongsthornc@yahoo.com.

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Abstract

AIM: To investigate the effect of early surgical intervention on the high surgical risk elderly patients who sustained femoral neck fracture (FNF) and taking concomitant antiplatelet agents.

METHODS: Between 2010 and 2012, a prospective study was conducted on 49 geriatric patients, who took antiplatelet agents, sustained FNF and underwent surgery within 72 h [early surgery (ES) group], and these were compared with a retrospective consecutive case series of patients with similar characteristics (45 cases) who had delayed surgery (DS group) after 72 h during an earlier 3-year period. Postoperative outcomes were followed for one year and compared.

RESULTS: There were non-significant differences in perioperative blood loss, blood transfusion, intensive care unit requirement and postoperative mortality (P > 0.05 all). There were 2 patients (4%) in the DS group who died after surgery (P = 0.23). However, the ES group showed a significantly better postoperative outcome in terms of postoperative complications, length of hospital stay, and functional outcome (P < 0.05 all).

CONCLUSION: Early hip surgery in geriatric hip fracture patients with ongoing antiplatelet treatment was not associated with a significant increase of perioperative blood loss and postoperative mortality. Moreover, ES resulted in a better postoperative surgical outcome. In early hip surgery protocol, the antiplatelet agents are discontinued and the patient is operated on within 72 h after admission, which is safe and effective for the medically fit patients.

Key words: Early hip surgery; Blood loss; Elderly hip fracture; Antiplatelet agents; Displaced femoral neck fracture; Hip arthroplasty

Core tip: In this cohort controlled study, a prospective study was conducted on geriatric femoral neck fracture patients, who took antiplatelet agents, and underwent hip replacement within 72 h which was compared with a retrospective case series of patients with similar characteristics who had delayed surgery. Our results supported the benefits of early surgery on these high surgical risk elderly patients in terms of significantly better postoperative complications, length of hospital stay, and 1-year functional outcome without significant difference in perioperative blood loss and postoperative mortality.

Sa-ngasoongsong P, Kulachote N, Sirisreetreerux N, Chanplakorn P, Laohajaroensombat S, Pinsiranon N, Woratanarat P, Kawinwonggowit V, Suphachatwong C, Wajanavisit W. Effect of early surgery in high surgical risk geriatric patients with femoral neck fracture and taking antiplatelet agents. *World J Orthop* 2015; 6(11): 970-976 Available from: URL: http://www.wjgnet.com/2218-5836/full/v6/i11/970.htm DOI: http://dx.doi.org/10.5312/wjo.v6.i11.970

INTRODUCTION

Recent studies have shown that early surgical intervention in elderly hip fracture significantly reduces postoperative mortality and morbidity, and increases the proportion of patients recovering to pre-injury ambulation status[1-3]. However, postoperative mortality and morbidity risk is different in an individual geriatric patient due to many other associated factors, such as comorbidities and medical conditions, perioperative blood loss, the necessity of blood transfusion, and postoperative complications[4-6]. Therefore, the effect of early surgery (ES) in a subgroup of patients who have multiple comorbid diseases and high risk for perioperative blood loss, such as elderly patients taking antiplatelet agents, could be different from a general elderly population who had no significant comorbidity[7,8]. This patient subgroup with comorbidities requires specific perioperative management to avoid the bleeding-related complication (from impaired platelet function) and thrombotic complications (from prolonged drug withdrawal). Although the safety of early hip surgery in patients taking anti-platelet medications has been introduced[9], the true benefit of it in geriatric hip fracture patients who need hip replacement surgery is still debatable[10-19]. This is because most of the previous studies were retrospective studies with small sample size or had mixed type of fracture and operation[10-13], and used patients without anti-platelet medications as a control group[13-19].

Nevertheless, current scientific evidences have demonstrated that more than 50% of platelet function will already have returned after drug withdrawal for at least 48-72 h[20,21], so considered safe for hip surgery[22]. To our knowledge, there still is no universal guideline for management of hip fracture patients taking antiplatelet agents, and whether the patients should continue or stop these drugs during the perioperative period[23-25]. We assumed that ES with short drug withdrawal (< 72 h) should result in a comparable perioperative blood loss and other better postoperative outcomes compared with delayed surgery (DS) with prolonged drug withdrawal. The aim of this study was to compare the outcomes between ES with short drug withdrawal (< 72 h) and DS with prolonged drug withdrawal (> 72 h) in elderly femoral neck fracture (FNF) patients who received preoperative antiplatelet medication and underwent hip replacement in terms of blood loss and bleeding-related complications, postoperative mortality, morbidity, and functional outcome.

MATERIALS AND METHODS

This study was designed as a single-centered, prospective cohort study, between 2010 and 2012, which was compared with a retrospective consecutive case series within the same center from an earlier 3-year period (2007-2009). The prospective arm directly followed the retrospective arm when the study was initiated. Before the introduction of this study, our hospital guideline indicated that patients should have had their antiplatelet agents stopped for at least 5 d before operation. Patients, after the study protocol introduction, stopped their antiplatelet agents after admission and then were operated on within 72 h after admission (Figure 1). The inclusion criteria were: (1) patients aged 60 years or older with displaced FNF from

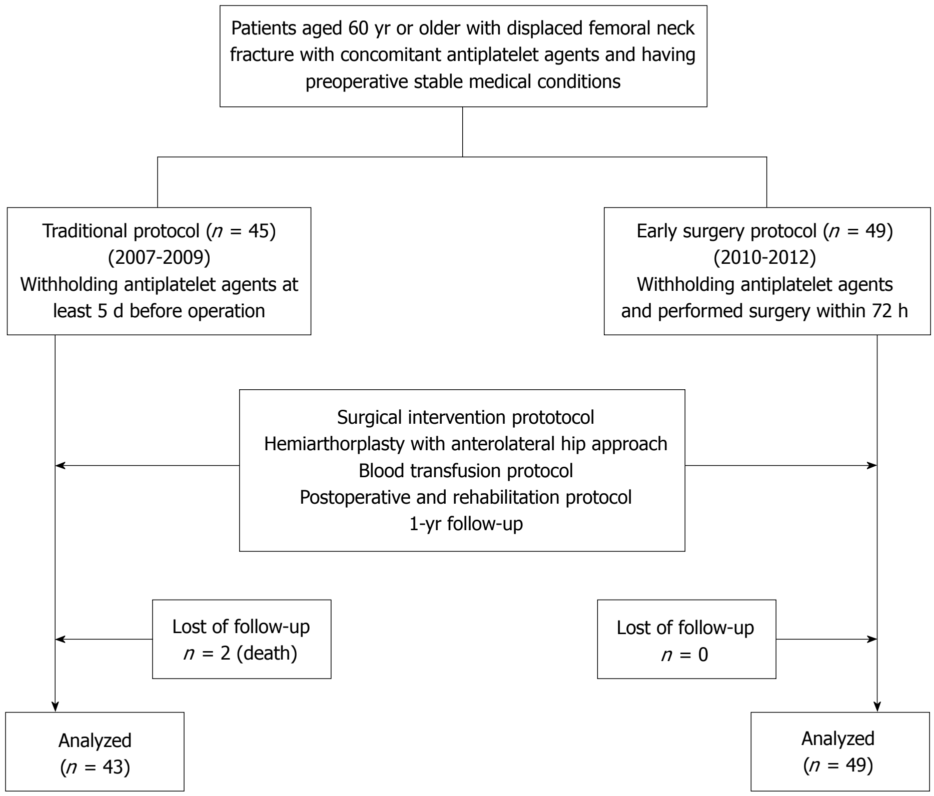

Figure 1 Flow diagram of the study; patients in the early hip surgery protocol stopped the antiplatelet agents after admission and then were operated within 72 h after admission compared with the patients in the delayed hip surgery protocol who stopped the antiplatelet agents at least 5 d before the operation.

low energy trauma and planned for hemiarthroplasty; (2) previously taking at least one antiplatelet agent or more; (3) having high surgical risk with American Society of Anesthesiologists (ASA) physical status[26] grade 3 or more; and (4) having stable medical condition and able to perform early surgical intervention within 72 h after admission. The exclusion criteria were: (1) other pathological fracture such as malignancy or stress fracture; (2) concomitant fractures; and (3) undertaking anticoagulant therapy such as warfarin. Prior approval was obtained from our institutional board review, and informed consent was obtained from all prospective patients, who participated in this study, before the surgery was scheduled.

Patients' characteristic data such as age, gender, height, weight, fracture side, comorbid diseases, pre-injury walking ability, ASA physical status, time to surgery, type of operation, anesthetic technique, operative time, and preoperative laboratory values were collected by the fourth author (Table 1). Body mass indexes (BMI), were then calculated. Time to surgery was defined as the number of days between admission and operative day.

Postoperative data such as intraoperative blood loss (IBL) and drainage volume (DV), amount of blood transfusion, intensive care unit (ICU) requirement, and length of hospital stays (LOS) were recorded. All patients had 1-year follow-up postoperatively for postoperative mortality, morbidity, and ambulatory status (Table 2). Postoperative morbidity was defined by complications which occurred after and related to their hip fracture, which included infection (pneumonia, urinary tract infection), pressure sore, cardiac complications (myocardial infarction, congestive heart failure, and new-onset cardiac arrthymia), thromboembolic events [symptomatic deep vein thrombosis (DVT), pulmonary embolism, and acute stroke], fracture treatment complication (surgical site infection, periprosthetic fracture, and implant failure or loosening), and incidence of readmission due to hip fracture related complications.

All patients were treated with hemiarthroplasty, performed by one or more trauma experts, using the same surgical approach which was anterolateral hip approach with anterior hemimyotomy[27]. The decision on hip prosthesis, cemented or cementless femoral stem, was based on proximal femur morphology. The choice on anesthetic technique, general or regional anesthesia, depended on the anesthesiologists. Blood transfusion protocol followed ASA guideline, and packed red cell transfusion was considered when Hb was less than 6 gm% or the patient had positive anemic symptom (dyspnea, tachypnea and hypoxemia)[28].

Postoperative care and rehabilitation were managed by the same postoperative protocol. The patients were encouraged to exercise as soon as possible (to prevent thromboembolism, and other complications). The patients were allowed to have weight bearing exercise with walker as tolerated. All the patients were followed,

Table 1 Patients' characteristic data

		ES group (n = 49)	DS group (n = 45)	P value
Age[1], yr		80 ± 8	81 ± 8	0.67
Female gender		34 (69)	35 (78)	0.36
BMI[1], kg/m^2		22.6 ± 2.8	23.3 ± 4.4	0.40
Fracture right side		24 (49)	24 (53)	0.67
No. of comorbid diseases				
	0-1	18 (37)	11 (24)	0.25
	2 or more	31 (63)	34 (76)	
ASA physical status				
	3	39 (80)	28 (62)	0.07
	4	10 (20)	17 (38)	
Time to surgery[1]		1.6 ± 0.9	8.9 ± 3.6	< 0.01
Type of antiplatelet agents				
	Aspirin alone	42 (86)	36 (80)	0.59
	Clopidogrel	7 (14)	9 (20)	
Preinjury ambulation status				
	Walk independently	42 (86)	36 (80)	0.67
	Walk with gait aid	7 (14)	8 (18)	
	Wheel chair or bed ridden	0 (0)	1 (2)	
Preoperative laboratory value[1]				
	Hemoglobin, g/dL	12.0 ± 1.6	11.2 ± 1.2	< 0.01
	Platelet count, × 10^3/mm^3	241 ± 85	284 ± 96	0.03
	Creatinine clearance, mg/dL	1.3 ± 1.1	1.7 ± 1.7	0.92
	Serum albumin, g/L	35.6 ± 4.4	34.9 ± 5.3	0.53
	aPTT, s	27.5 ± 3.6	26.6 ± 4.3	0.34
	PT, s	11.9 ± 1.1	12.4 ± 2.5	0.23
Regional anesthesia		31 (63)	31 (69)	0.66
Type of operation				
	Cemented	26 (53)	37 (82)	< 0.01
	Cementless	23 (47)	8 (18)	
Operative time[1], min		98 ± 27	102 ± 34	0.48

[1]Value presented as mean ± SD; value presented as no. of patients (percentage). BMI: Body mass index; ASA: American Society of Anesthesiologists; aPtt: Activated partial thromboplastin time; PT: Prothrombin time.

by telephone interview or at the clinic, for at least 1 year.

Primary outcome was perioperative blood loss measured by three methods; total apparent blood loss (TABL), total hemoglobin loss (THL), and calculated total blood loss (CTBL). TABL was calculated by summation between IBL and DV. THL and CTBL were calculated by using preoperative and postoperative Hb and Hct on the fourth day[29,30]. Secondary outcome measures were blood transfusion needed, postoperative ICU requirement and LOS, postoperative mortality and morbidity, and walking ability at 1-year period.

Statistical analysis

Statistical analysis was performed using Stata software version 11.0 (Stata Corp, College Station, Texas, United States). Continuous data were presented as mean and standard deviation, and compared with *t*-test. Categorical data were presented as proportion and compared with Fisher's exact test or χ^2 test as appropriate. Significant difference was considered if *P*-value < 0.05.

Sample size estimation was calculated by using data on actual perioperative blood loss from the retrospective controlled arm (mean blood loss ± SD = 507 ± 250 mL). We assumed that the significant difference in blood loss should exceed 30% (152 mL) compared with control group. Setting the pre-study power of pre-study power of test as 0.8, significant difference as 0.05, and the ratio of sample size in each group as 1:1, gave the sample size of each group was 43 patients.

The statistical methods of this study were reviewed by Patarawan Woratanarat, MD, PhD (Clinical Epidemiology) from Department of Orthopedics, Faculty of Medicine Ramathibodi Hospital, Mahidol University.

RESULTS

There were 49 patients included into the ES group (42 aspirin group and 7 clopidogrel group), and 45 patients included into the DS group (36 in aspirin group and 9 in clopidogrel group) (Figure 1). Demographic data were shown in Table 1. The mean time to surgery was 1.6 ± 0.9 d in ES group compared with 8.9 ± 3.6 d in DS group (P < 0.001). There were non-significant differences in age, gender, BMI, fracture side, number of comorbid diseases, ASA physical status, type of antiplatelet agents used, preinjury ambulation status, preoperative laboratory value, anesthetic technique, and operative time between both groups (P > 0.05 all). However, the ES group showed significantly higher preoperative hemoglobin, lower platelet count and

Table 2 Blood loss outcomes

Bleeding outcome	ES group (n = 49)	DS group (n = 45)	P value
Blood loss[1], mL			
Intraoperative blood loss	291 ± 136	315 ± 224	0.52
Drainage blood loss	201 ± 131	178 ± 91	0.33
Total apparent blood loss	492 ± 210	493 ± 229	0.97
Calculated blood loss	292 ± 222	303 ± 187	0.8
PRC transfusion[1], UI	0.6 ± 0.9	0.7 ± 0.8	0.49

[1]Value presented as mean ± SD.

higher proportion of patients receiving cementless hemiarthroplasty compared to DS group (P < 0.05 all).

Perioperative and postoperative outcomes were shown in Tables 2 and 3. During perioperative period, there were non-significant differences in perioperative blood loss and blood transfusion, number of patients requiring ICU, and postoperative length of hospital stay (P > 0.05 all). However, the overall length of hospital stay in the ES group was significantly lower than those in the DS group (P < 0.001). At postoperative one-year period, none of the patients in the ES group died, while 2 of the DS group died (P = 0.24). Both patients died at 2-mo postoperatively due to sepsis after pneumonia (1) and urinary tract infection (1). The ES group showed significantly lower overall complications and higher one-year ambulation status compared with the DS group (P = 0.02 both). Cardiac complications occurred in 3 patients of the DS group (2 congestive heart failure, 1 myocardial infarction). Two patients in each group had symptomatic DVT, on the injured side, proven by duplex ultrasonography, and then were treated with warfarin. Postoperative infections occurred in 9 patients of the ES group and 16 patients in the DS group (Table 3). No postoperative hematomas which required surgical evacuation were detected in this study.

DISCUSSION

Hip fracture is a common injury in elderly population leading to significant mortality and morbidity. Generally, this condition requires an urgent diagnosis and prompt surgical treatment, as early as possible, in order to reduce postoperative mortality, morbidity, and improve functional outcome[1-3]. However, geriatric patients have a wide range of comorbidities and are increasingly taking anti-platelet medication for treatment of their existing medical comorbid diseases or for medical prevention[31-33]. However, uninterrupted antiplatelet medication while undergoing early hip surgery would increase surgical bleeding and bleeding-related complications[10,12,16,17,19], whereas prolonged drug withdrawal would result in higher mortality and morbidity from DS and risk of lethal complications related to a rebound effect such as acute coronary syndrome and thromboembolic complication[4,34-37]. Moreover, though the safety of ES in the patients undertaking antiplatelet agents has been introduced[9], there is still no universal guideline for perioperative management for this subgroup[23-25] and the exact benefit of ES on postoperative outcomes in these patients is still unknown. Recent studies have demonstrated that stopping these drugs at least 48-72 h was sufficient for improving platelet function and safe for hip surgery[20-22]. Moreover, the peaked incidence of acute coronary syndrome, due to the rebound effect, occurred between days 4 and 8 after withholding antiplatelet medications[37]. Therefore, our study aimed to evaluate the outcomes after early *vs* delayed hip replacement surgery with drug withdrawal protocol in elderly patients who had displaced FNFs with ongoing anti-platelet agents to clarify the safety of ES with shorter drug withdrawal strategy in this subgroup of geriatric hip fractures.

Table 3 Postoperative mortality and morbidity

Postoperative outcome	ES group (n = 49)	DS group (n = 45)	P value
Mortality	0 (0)	2 (4)	0.23
Postoperative complications			
Overall	12	28	0.02
Pneumonia	2	5	
Urinary tract infection	7	11	
Pressure sore	0	2	
Cardiac	0	3	
Thromboembolic complication	2	2	
Delirium	1	5	
ICU requirement	19 (39)	14 (31)	0.39
LOS[1], d	7 ± 3	14 ± 9	< 0.0001
PLOS[1]	6.1 ± 3.4	7.4 ± 7.8	0.28
Readmission	1 (2)	6 (13)	0.052
One-year ambulation status	n = 49	n = 43	
Walk independently	18 (37)	7 (16)	0.03
Walk with gait aid	30 (61)	33 (77)	
Wheelchair	0 (0)	3 (7)	

[1]Value presented as mean ± SD; value presented as no. of patients (percentage). Value presented as no. of incidence. ICU: Intensive care unit; LOS: Length of hospital stay; PLOS: Postoperative length of hospital stay.

Our study showed that most demographic data was comparable between the ES and DS groups (Table 1). However, the proportion of cemented hemiarthroplasty was significantly higher in the DS group which should be from the tendency to shift of hip replacement in elderly patients from cemented hip replacement to cementless hip replacement in recent years[38]. We also found that the preoperative hemoglobin level was higher in the ES group, which might be explained by ongoing blood loss in DS compared to ES, which resulted in improved functional recovery in the ES group[39].

The results from this study showed that all perioperative blood loss parameters (intraoperative, drainage, TABL, and CTBL) and blood transfusion were not significantly different between both groups (P < 0.05 all), which was comparable to previous studies[13-15] (Table 2). Therefore, this data supported our hypothesis that ES with shorter drug withdrawal was sufficient for hip replacement surgery. Our results also supported the benefits of ES protocol in geriatric patients undertaking antiplatelet agents in terms of significantly lower overall postoperative complications (P = 0.02) and length of hospital stay (P < 0.001), and higher one-year ambulatory status (P = 0.02) without any significant difference in postoperative ICU requirement or readmission rate (P > 0.05 both) (Table 3). This could be explained because early surgical intervention resulted in early rehabilitation in order to prevent postoperative complications such as venous thromboembolism, or infection. Moreover, this study could detect higher postoperative complication trend due to the rebound phenomenon, although not statistically significant, in cardiac complications in the DS group (3 patients) compared with the ES group (none). This confirmed that cessation of antiplatelet therapy perioperatively increased the risk of thrombotic events[40-42].

Based on our study, we found that there were positive effects in early hip replacement surgery in the geriatric hip fracture patient with ongoing antiplatelet treatment. Unfortunately, our study population was mainly on aspirin, for more than 80% of our study population. However the previous studies on clopidogrel effects on the hip fracture surgery revealed a similar trend that ES should be more beneficial than delayed hip surgery[13-17]. Therefore we have concluded that early hip surgery in geriatric hip fracture patients with ongoing antiplatelet treatment was not associated with a significant increase of perioperative blood loss and postoperative mortality. Moreover, ES resulted in better postoperative surgical outcomes. Early hip surgery protocol and discontinuation of antiplatelet agents and operation within 72 h after admission, is safe and effective for the medically fit patients.

COMMENTS

Background

To evaluate the perioperative blood loss and postoperative complications in the high surgical risk geriatric patients [elderly who sustained femoral neck fractures (FNF) and taking antiplatelet medications] following early surgical intervention with short drug withdrawal protocol compared with those having delayed surgical intervention with prolonged drug withdrawal protocol.

Research frontiers

The benefit of early hip replacement surgery in FNF patients and taking antiplatelets became clearly visible.

Innovations and breakthroughs

Early hip replacement in FNF patients and taking antiplatelet medication would result in significantly less postoperative complications, length of hospital stay and better postoperative functional outcome without significant difference in postoperative mortality.

Applications

The standard hip fracture protocol should include the geriatric hip fracture patients taking antiplatelet medications and having stable medical conditions to receive early surgical intervention within 72 h after admission.

Terminology

Early hip fracture surgery: Patients receiving surgical management within 72 h after admission.

Peer-review

This study is a good comparative clinical study which showed the benefits of early surgery in the hip fracture patients who receive antiplatelet medication.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Cost benefit analysis of the use of tranexamic acid in primary lower limb arthroplasty: A retrospective cohort study

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Abstract

AIM: To examine the cost benefit conferred by the perioperative administration of intravenous tranexamic acid (TXA) in lower limb arthroplasty.

METHODS: This study evaluates the use of TXA in 200 consecutive lower limb arthroplasties performed in a single surgeon series. The initial 100 patients (control group) underwent surgery without perioperative administration of TXA while the subsequent 100 patients (TXA group) all received 1 g TXA at the time of induction of anaesthesia. Pre- and post-operative haemoglobin, platelet count, haematocrit, the use of blood product post-operatively, length of stay were examined. A financial analysis of both groups was then undertaken.

RESULTS: The mean age of patients in both groups was 63 ± 13 years. There were no significant differences between groups in terms of gender (P = 0.47), proportion of total hip replacement to total knee replacement (P = 0.25) or pre-operative haemoglobin (P = 0.43). In the control group, the transfusion rate was 22%. In the TXA group, the transfusion rate dropped to 2% (P < 0.001). The mean post-operative haemoglobin was 10.82 ± 1.55

g/dL in the control group *vs* 11.33 ± 1.27 g/dL in the TXA group (*P* = 0.01). The total cost of transfused blood products was €11055 and €603 respectively. The mean length of stay in the control group was 6.53 ± 5.93 d *vs* 5.47 ± 4.26 d in the TXA group (*P* = 0.15) leading to an estimated financial saving of €114586. There was one pulmonary embolus in the control group and one deep venous thrombosis in the TXA group.

CONCLUSION: Intravenous TXA reduces blood loss in lower limb arthroplasty. This leads to lower transfusion rates, shorter length of stay in hospital and significant financial savings.

Key words: Arthroplasty; Hip; Knee; Tranexamic acid; Cost-benefit analysis

Core tip: Worldwide the demand for lower limb arthroplasty procedures is increasing in the context of a diminishing economic climate. Total hip replacement and total knee replacement have traditionally been associated with large volume blood loss and the need for transfusion. Use of perioperative intravenous tranexamic acid (TXA) has been shown to be a cost effective measure, which reduces the need for transfusion. In this study, TXA was found to significantly reduce the number of patients requiring blood transfusion post-operatively, which has both clinical and economic significance.

McGoldrick NP, O'Connor EM, Davarinos N, Galvin R, Quinlan JF. Cost benefit analysis of the use of tranexamic acid in primary lower limb arthroplasty: A retrospective cohort study. *World J Orthop* 2015; 6(11): 977-982 Available from: URL: http://www.wjgnet.com/2218-5836/full/v6/i11/977.htm DOI: http://dx.doi.org/10.5312/wjo.v6.i11.977

INTRODUCTION

An aging population globally, coupled with an expansion of the indications for total hip replacement (THR) and total knee replacement (TKR) has meant that the demand for lower limb arthroplasty is expected to increase in the future[1]. Against this, the economic climate worldwide has resulted in reduced healthcare funding whilst expecting increased productivity from the orthopaedic surgeon.

Surgical procedures such as THR and TKR may require allogeneic blood transfusion post-operatively[2,3]. Perioperative transfusion of blood products not only adds expense to the procedure, but also places the patient at increased risk of wound infection, immune suppression and allergy, transfusion-related lung injury and transmission of viral pathogens[4-6]. Efforts have therefore focused on maintaining post-operative haemoglobin levels and minimizing the need for blood transfusions. Such measures may reduce overall surgical morbidity and length of in-hospital admission, while minimizing the burden of additional blood tests.

Perioperative tranexamic acid (TXA) has emerged as a useful adjunctive agent in reducing blood loss and the need for blood transfusion in lower limb arthroplasty. TXA is a synthetic derivative of the amino acid lysine, and exerts antifibrinolytic activity by competitively binding the lysine sites on plasminogen. It is thought that this makes blood clots more resistant to degradation, thereby preventing further blood loss.

Several recent studies have reported favourable outcomes for intravenous administration of TXA in both THR and TKR[7,8]. Studies examining oral and topical administration of TXA have also demonstrated promising results[9,10].

The primary aim of this study was to evaluate whether the use of intravenous TXA in elective primary THR and TKR in a single surgeon series resulted in reduced transfusion rate of packed red blood cells. Secondary aims included examining the effect of TXA on post-operative haemoglobin, haematocrit and platelet count, length of stay in hospital, rate of deep venous thrombosis (DVT) and pulmonary embolism and to assess whether its use is cost effective.

MATERIALS AND METHODS

This study was a retrospective review of a cohort of 200 consecutive primary total knee and hip replacements performed by a single orthopaedic surgeon at a single institution between September 2013 and March 2015. The initial 100 joints were all performed without perioperative administration of TXA (control group). The subsequent 100 joints were all performed with additional perioperative TXA (TXA group). Revision joints, arthroplasties performed for fracture, and simultaneous bilateral procedures were excluded from the analysis.

Preoperative antibiotic prophylaxis followed local institutional protocol and consisted of intravenous cefuroxime, or alternatively teicoplanin if there was a history of cephalosporin or penicillin allergy. Vancomycin was utilised in select cases where there was a history of Methicillin Resistant Staphylococcus Aureus (MRSA) present. Preoperative antibiotics were administered at induction of anaesthesia, within one hour of skin incision.

All THRs were performed following a uniform technique using anterolateral approach to the joint. Both uncemented and cemented techniques were utilised as determined by the operating surgeon. All TKRs were performed through a medial parapatellar approach to the knee. One gram of TXA was administered parentally at the time of preoperative antibiotic administration in the TXA group. Intraoperative surgical drains were placed routinely in all joints, and removed on the first post-operative day. DVT prophylaxis consisted of thrombo-embolic deterrent stockings worn for 6 wk post-operatively and chemical prophylaxis consisting of

Table 1 Patient demographics

	Control group (n = 100)	TXA group (n = 100)	P value
Male/female	49/51	44/56	0.47
Age in years	62.57 ± 12.14	62.9 ± 12.6	0.86
THR/TKR	60/40	52/48	0.25
Pre-operative Hgb	13.61 ± 1.42	13.77 ± 1.41	0.43
Pre-operative Hct	0.41 ± 0.04	0.41 ± 0.04	0.32
Pre-operative platelets	253.01 ± 55.87	256.85 ± 69.75	0.67

THR: Total hip replacement; TKR: Total knee replacement; Hgb: Haemoglobin; Hct: Haematocrit; TXA: Tranexamic acid.

Table 2 Differences between the groups following surgery

	Control group (n = 100)	TXA group (n = 100)	P value
Post-operative Hgb	10.82 ± 1.55	11.33 ± 1.27	0.01
Post-operative Hct	0.32 ± 0.05	0.34 ± 0.04	0.01
Post-operative platelets	204.32 ± 44.68	212.22 ± 52.49	0.25
Mean length of stay in hospital in days	6.53 ± 5.92	5.47 ± 4.26	0.15

Hgb: Haemoglobin; Hct: Haematocrit; TXA: Tranexamic acid.

subcutaneous low molecular weight heparin for three days while an in-patient on the ward. Oral rivaroxaban was then commenced on the fourth post-operative day and continued until the end of the second week post-operatively for TKR, and the end of the fifth week post-operatively for THR, as per National Institute for Health and Care Excellence guidelines. On the second post-operative day, a full blood count was performed. The hospital transfusion protocol was initiated where a patient's haemoglobin was less than 8 g/dL or the patient was symptomatic with anaemia.

The following variables were ascertained following retrospective review of data: Age, gender, pre-operative and post-operative haemoglobin, pre-operative and post-operative haematocrit, pre-operative and post-operative platelet counts, tranfusions of blood product, length of stay in days and thrombotic complications including DVT or pulmonary embolus.

In consultation with our hospital blood bank and purchasing department, the cost of a vial of 1 g of TXA was determined at €0.75 at our institution. One unit of packed red blood cells cost €201, and a single "bed-day used" (BDU) at our institution was valued at €1081. "Bed-days used" is a measure of hospital activity. A single BDU may be defined as a patient occupying an in-patient bed for all or part of one 24-h period. All figures were correct in respect of 2015.

Descriptive statistics were used to represent the data including proportions, means and standard deviations. Independent sample *t*-tests were used to assess continuous outputs, and two sample tests of proportion were used for binary outcomes. Statistical analysis was performed using Stata statistical software package, version 13 (StataCorp, Texas, United States). A value of $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 200 patients were included in this study. One hundred patients were included in the control group, who did not receive perioperative TXA. One hundred patients were included in the TXA group, who received TXA at the time of surgery. The average age of participants in both groups was 63 ± 13 years. Table 1 displays the baseline characteristics of patients. There were no statistically significant differences between the groups across all variables at baseline. The control group (n = 100) comprised 40 TKR and 60 THR. The TXA group (n = 100) consisted of 48 TKR and 52 THR.

Primary outcome - proportion of patients requiring transfusion

There was a highly significant difference between the groups ($P < 0.001$) in the proportion of patients who required transfusion following surgery (22 patients in the control group *vs* 2 patients in the TXA group). However, the number of units of blood received by those individuals that required transfusion did not differ significantly between the groups (P = 0.34).

Secondary outcomes

Table 2 indicates that there were significant differences in haemoglobin and haematocrit levels between the groups following surgery (P = 0.01). Differences in post-operative platelet counts between the groups were not statistically different (P = 0.25). The mean length of stay in hospital, equivalent to BDUs, for the TXA group was 5.47 ± 4.26 d *vs* 6.53 ± 5.92 d for patients in the control group, although this difference was not statistically significant (P = 0.15).

In the control group, one patient developed multiple pulmonary emboli on the second post-operative day following TKR. In the TXA group, one patient developed a DVT in the peroneal vein one week post-operatively following TKR. Both patients recovered uneventfully.

Two patients in the TXA group required blood transfusion. One patient was a 72-year-old lady who underwent uneventful left TKR. Her pre-operative haemoglobin dropped from 10.4 g/dL to 7.4 g/dL. Although asymptomatic, she activated the transfusion protocol and was transfused two units of blood. The second patient transfused blood was a 78-year-old lady who underwent uneventful right THR. She had a background history of a myelodysplastic syndrome and B12 deficiency. She was transfused perioperatively on the advice of the haematology service.

Cost analysis

This study analyzed the financial benefit of TXA in terms of reduction in transfusion rate and reduction in length of stay in hospital. At a cost of €0.75 per 1 g of TXA, the total cost burden for use of TXA for 100 arthroplasties was calculated at €75. There was a 20% difference in

Table 3 Cost analysis

	Control group (n = 100)	TXA group (n = 100)	Difference
No. of patients transfused	22	2	20
No. of units transfused	55	3	52
Total cost of transfusion	€11055	€603	€10452
BDU	653	547	106
Total cost of BDU	€705893	€591307	€114586

BDU: Bed days used; TXA: Tranexamic acid.

transfusion rate between the control and TXA group, in favour of the latter. A total of 55 units of blood were transfused in the control group, in contrast to 3 units of blood in the TXA group. With a cost of €201 per unit of packed red cells, we therefore estimated the savings in terms of transfusion following TXA administration at €10452. When this figure was offset against the cost of TXA, we estimated overall savings of €10377, equivalent to €103.77 per patient.

On average, the control group remained in hospital for 6.53 d, equivalent to 653 BDUs in total for this cohort. The TXA group averaged 5.47 d, or 547 BDUs in total in hospital. It was therefore calculated that for 100 patients given TXA perioperatively, a total of 106 d were saved, at a cost of €1081 per BDU. On this basis, we estimated savings of €114586, or €1145.86 per patient. Table 3 summarizes our cost analysis.

DISCUSSION

Elective THR and TKR are among the most common surgical procedures that may lead to considerable blood loss requiring transfusion[11,12]. Blood loss following lower limb arthroplasty remains a concern for orthopaedic surgeons, although the rates of significant blood loss have improved over the past quarter of a century[13]. Despite this, blood losses of up to 1500 mL or higher following TKR have been reported[14].

Orthopaedic surgeons have generally tended to minimize the use of allogeneic blood transfusion in THR and TKR on the basis of concerns for potentially serious complications including sepsis[15], increased length of stay in hospital[16], and mortality[17]. Efforts have therefore focused on the use of pharmacological agents and other methods to minimize blood loss. Autologous transfusion[18], cryotherapy[19], hypotensive anaesthesia[20], fibrin tissue adhesive[21] and erythropoietin alpha[22] have been studied in this regard.

The first reported successful use of TXA in knee arthroplasty by Benoni *et al*[23] in 1995 has led to increased interest in the use of antifibrinolytics in lower limb arthroplasty. A number of studies including retrospective and systematic reviews have supported the use of TXA in arthroplasty[8,9,24,25]. This study examined the affect of perioperative intravenous TXA on blood loss in lower limb arthroplasty. A statistically significant difference (P < 0.001) was identified in the number of patients transfused in the control group (n = 22) *vs* the TXA group (n = 2). This has clinical significance for the patient. With a drop in the number of patients transfused from 22% to 2%, patients were at reduced risk of recognized transfusion related complications. These figures are similar to the findings of Tuttle *et al*[10] and Gillette *et al*[26] who have reported transfusion rates post TXA of 17.5% *vs* 5.5% and 21.6% *vs* 8.9%, respectively.

Statistically significant differences were also found between pre-operative and post-operative haemoglobin (P = 0.01) and haematocrit (P = 0.01). Higher post-operative haemoglobin may reduce the number of laboratory tests performed during admission, while also reducing patient fatigue, hypotensive episodes, and length of stay in hospital[26]. This may result in improved savings in overall cost.

Financial savings may also be made in terms of the cost of blood products, the expense of additional blood tests and laboratory labour, and the overall length of stay in hospital. The use of TXA in this series resulted in estimated savings of the cost of blood products of €104.52 per patient. Although the difference in length of stay in hospital between the control and TXA groups only trended towards statistical significance (P = 0.15), in financial terms there was a significant difference. Patients in the TXA group left hospital on average one day earlier than those in the control, with estimated savings of €1145.86 per patient. Larger studies may demonstrate statistical difference in terms of length of stay. Nevertheless, these findings support the growing body of evidence supporting the cost effectiveness of both intravenous and topical formulations of TXA[10,26]. Recent evidence further suggests TXA is also safe in high-risk arthroplasty patients[27].

There are potential limitations to this study. The findings of this study are inherently limited by its retrospective nature. Moreover, patients were not randomized into either the control or TXA groups, and this potentially introduces a selection bias. However, the 200 patients included in this analysis were consecutive, and underwent arthroplasty following a standardized technique, and in a single surgeon series. Additionally, no statistically significant differences in baseline variables between the groups were found.

In conclusion, the addition of perioperative intravenous TXA has been shown to reduce the rate of blood transfusion post-operatively while also generating considerable cost savings.

COMMENTS

Background

Hip and knee arthroplasty can potentially result in large volume blood loss, with the consequent need for transfusion of blood products. This carries increased risk to the patient, while also is a costly intervention. Antifibrinolytic agents such as tranexamic acid (TXA) were originally described in the trauma setting to prevent blood loss.

Research frontiers

There has been increased interest among in the use of TXA as a means of reducing blood loss in lower limb arthroplasty. Concerns remain, however, regarding possible increased risk of thromboembolic disease.

Innovations and breakthroughs

In a large single surgeon series of 200 consecutive lower limb arthroplasties, the perioperative use of TXA resulted in significant financial savings. There was no increased rate of thromboembolic disease following the use of TXA.

Applications

In a time of increasing demand being placed on diminishing health resources, measures that result in cost savings should be encouraged. However, care must be taken to ensure that the use of newer agents is safe to patients. Perioperative TXA appears to provide a favourable cost-benefit profile, while also being safe in lower limb arthroplasty. Further study is required to evaluate the thromboembolic risk of TXA in lower limb arthroplasty.

Terminology

TXA is an abbreviation for tranexamic acid, an antifibrinolytic agent. It stabilizes clot by competitively binding to plasminogen.

Peer-review

This is a good article.

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ORIGINAL ARTICLE

Observational Study

Postural spinal balance defined by net intersegmental moments: Results of a biomechanical approach and experimental errors measurement

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Abstract

AIM: To describe initial results and experimental error measurement of a protocol analyzing Human posture through sagittal intersegmental moments.

METHODS: Postural analysis has been recently improved by development of three-dimensional radiographic imaging systems. However, in various situations such as global sagittal anterior malalignment interpretation of radiographs may not represent the real alignment of the subject. The aim of this study was to present initial results of a 3D biomechanical protocol. This protocol is obtained in a free standing position and characterizes postural balance by measurement of sagittal intersegmental net moments. After elaboration of a specific marker-set, 4 successive recordings were done on two volunteers by three different operators during three sessions in order to evaluate the experimental error measurement. A supplementary acquisition in a "radiographic" posture was also obtained. Once the data acquired, joint center, length, anatomical frame and the center of mass of each body segment was calculated and a mass affected. Sagittal net intersegmental moments were computed in an ascending manner from ground reaction forces at the ankles, knees, hips and the lumbo-sacral and thoraco-lumbar spinal junctions. Cervico-thoracic net intersegmental moment was calculated in a descending manner.

RESULTS: Based on average recordings, clinical interpretation of net intersegmental moments (in N.m) showed a dorsal flexion on the ankles (8.6 N.m), a flexion on the knees (7.5 N.m) and an extension on the hips (8.5 N.m). On the spinal junctions, it was flexion moments: 0.34 N.m on the cervico-thoracic; 6.7 N.m on the thoraco-lumbar and 0.65 N.m on the lumbo-sacral. Evaluation of experimental error measurement showed a small inter-trial error (intrinsic variability), with higher inter-session and inter-therapist errors but without important variation between them. For one volunteer the "radiographic" posture was associated to significant changes compared to the free standing position.

CONCLUSION: These initial results confirm the technical feasibility of the protocol. The low intrinsic error and the small differences between inter-session and inter-therapist errors seem to traduce postural variability over time, more than a failure of the protocol. Characterization of sagittal intersegmental net moments can have clinical applications such as evaluation of an unfused segment after a spinal arthrodesis.

Key words: Posture; Sagittal alignement; Biomechanical evaluation; Intersegmental net moments

Core tip: Postural evaluation is commonly performed using full-spine radiographs. However, a biomechanical approach using a dedicated protocol is possible in order to evaluate sagittal intersegmental net moments. Results from this study confirmed the technical feasibility of the protocol. Furthermore, these results revealed postural variability over time. Such evaluation may have various clinical applications such as evaluation of an unfused segment after a spinal arthrodesis.

Blondel B, Viehweger E, Moal B, Tropiano P, Jouve JL, Lafage V, Dumas R, Fuentes S, Bollini G, Pomero V. Postural spinal balance defined by net intersegmental moments: Results of a biomechanical approach and experimental errors measurement. *World J Orthop* 2015; 6(11): 983-990 Available from: URL: http://www.wjgnet.com/2218-5836/full/v6/i11/983.htm DOI: http://dx.doi.org/10.5312/wjo.v6.i11.983

INTRODUCTION

The clinical relevance of sagittal plane spino-pelvic parameters has continuously been demonstrated since their description by Duval-Beaupère *et al*[1] and Legaye *et al*[2] and multiple outcomes-related studies have reported correlations between sagittal radiographic parameters and Health Related Quality of Life scores pre or postoperatively[3-5]. These reports demonstrated that sagittal vertical axis (SVA, defined by the offset between the C7 plumb-line and the postero-superior corner of S1), Pelvic Tilt (PT, defined as the angle between a line drawn from the center of the femoral heads to the midpoint of the sacrum and the vertical), and more recently Pelvic Incidence minus Lumbar Lordosis (reflecting spino-pelvic harmony) are the 3 most important parameters due to their correlation with clinical outcomes for patients with spinal deformities[6,7]. With the exception of the pelvic incidence, those parameters are not fixed and are affected by the aging process of the spine where an increase of the thoracic kyphosis is usually associated with a pelvic retroversion (increased PT) and a loss of lumbar lordosis acting as compensatory mechanisms to maintain the head over the pelvis; then finally leading to a positive SVA[7]. This chain of correlation is also visible in patients with spinal deformities leading to a progressive anterior malalignment associated with an increased disability[6].

Most of the work accomplished so far in this domain is based on plain radiograph. Despite recent advancements, there are limitations to biplanar radiographic acquisitions and significant differences have been reported between bi-dimensional and three-dimensional postural analyses[8,9]. Furthermore, while posture is a dynamic condition with constant reciprocal interactions in an effort to maintain the head over the pelvis, radiograph only represents a snapshot of posture and therefore can lead to misinterpretation of sagittal alignment[10,11]. This last point is especially important for patients with an anterior malalignment who will adopt an "artificial" posture during radiographic exam in order to "fit" into the cassette footprint. In the context, it appears evident that there is a need for new evaluation tools for postural analysis independent from radiographs.

The aim of this study is to report the experimental error measurement and the impact of the radiographic posture from a protocol characterizing the net intersegmental moments which occurs at the center of musculo-skeletal joints during a free standing posture.

MATERIALS AND METHODS

Study sample

After informed consent, two healthy adult volunteers were recruited for this pilot study. Both volunteers had no previous history of back pain, any known spinal disorder or previous back surgery.

Marker set

The protocol used for this study was based on a set of markers that could be used to calculate the center of mass of pre-defined segments, previously published[12] and summarized hereafter. Based on published reports[13-15], a set of 36 markers was used to divide the body in 10 segments (head, thorax, abdomen, pelvis, thighs, legs and feet): 4 markers were placed on the head, 8 on the thorax, 1 on the abdomen, 3 on the pelvis, 4 on each thigh, 4 on each leg and 3 on each foot. Among these 36 markers, the spine was described using 6 markers allowing a description of thoracic and lumbar curvatures (C7, T6, T8, T12, L3 and S1).

This set of markers was defined in order to be able to localize the centers of mass of each body segment using easily recognizable anatomical landmarks, then using anthropometric tables and the height/weight of the subject, a mass was attributed to each segment according to Dumas *et al*[13].

Data acquisitions

Once equipped, each volunteer was asked to adopt a free standing position (with horizontal gaze) without external constraint or support, with shoulders flexed at 30° and fingers tips on zygomatic processes (*i.e.,* the "radiographic" posture). The location of the markers over time were recorded using a Vicon® (Vicon, Oxford, United Kingdom) optoelectronic system with 6 high resolution infrared cameras and a 100Hz sampling frequency.

Each foot was positioned over a forceplate (AMTI, United States) in order to collect the ground reaction force of the subject. The sagittal net intersegmental moments (ankles, knees, hips, hip-pelvis complex, lumbosacral junction, thoraco-lumbar junction and cervico-thoracic junction) were calculated in an ascending manner (*i.e.,* going upward from the ground reaction forces) between each body segment previously identified except for the cervico-thoracic junction where the sagittal net intersegmental moment was calculated using a descending manner from the center of mass and mass of the head and neck.

Experimental error measurement

In order to estimate experimental errors of this protocol, measurements were repeated according to the experimental design described by Schwartz *et al*[16]. Postural data from the two volunteers were acquired by three trained therapists, during three different sessions with one week interval (Figure 1). During each session, the volunteer was asked to stand 4 times in a free standing position with each foot on a force platform (with a free walk between each trial), without modifications of the markers, and postural data were recorded during several seconds, then "radiographic" posture was recorded one time. Between each therapist evaluation, markers were all removed and the volunteer was equipped again.

Finally, changes in spinal net intersegmental moments were calculated during a trunk flexion/extension for one volunteer.

Analysis of the acquired data was conducted on a one-second record sample, with the less body sway, in order to calculate mean and maximum net reaction moments in the sagittal plane at each joint center, with an evaluation of the intra-subject, the intra-observer (inter-session) and inter-observer (inter-therapist) variability according to Schwartz's methodology[16]. Analysis between free standing and "radiographic" posture was done by comparison of mean spinal net moments for each volunteer and a significant difference was defined as a difference superior to the experimental error measure.

Results of estimated moments were interpreted using the convention as follows: Positives values were associated to extension moments on spinal junctions and knees, to dorsal flexion of the ankles and pelvic retroversion. Negatives values were associated to flexion moments on spinal junctions and knees, to plantar flexion of the ankles and pelvic anteversion.

RESULTS

Study sample

The first volunteer was a 30-year-old male, 180 cm in height and 80 kg in weight. The second volunteer was a 26-year-old female, 158 cm in height and 52 kg in weight.

Results of mean and maximum net intersegmental moments

Results from analysis on the 2 volunteers revealed similar orientation of net sagittal moments on each joint (Table 1). Based on all the recordings acquired from the two volunteers, it was possible to estimate mean net intersegmental moments as follows: (1) A mean dorsal flexion moment of -10.4 N.m on the right ankle and -6.8 N.m on the left; (2) A mean moment of -7.15 N.m on the right knee and -7.95 N.m on the left; (3) A mean moment of 7.26 N.m on the right hip and 9.72 N.m on the left; and (4) On the spinal junctions: a mean moment of -0.65 N.m at the lumbosacral junction, -6.72 N.m at the thoracolumbar junction and -0.34 N.m at the cervicothoracic junction. Detailed results for each volunteer are summarized in Table 1.

According to the convention described in this protocol, the clinical interpretation of the net intersegmental moments applied on the different joints was: ankle dorsal flexion, knee flexion, hip extension (pelvic retroversion) and a flexion at the different spinal junctions. In other words, in order to maintain a free standing posture muscular system will have to generate

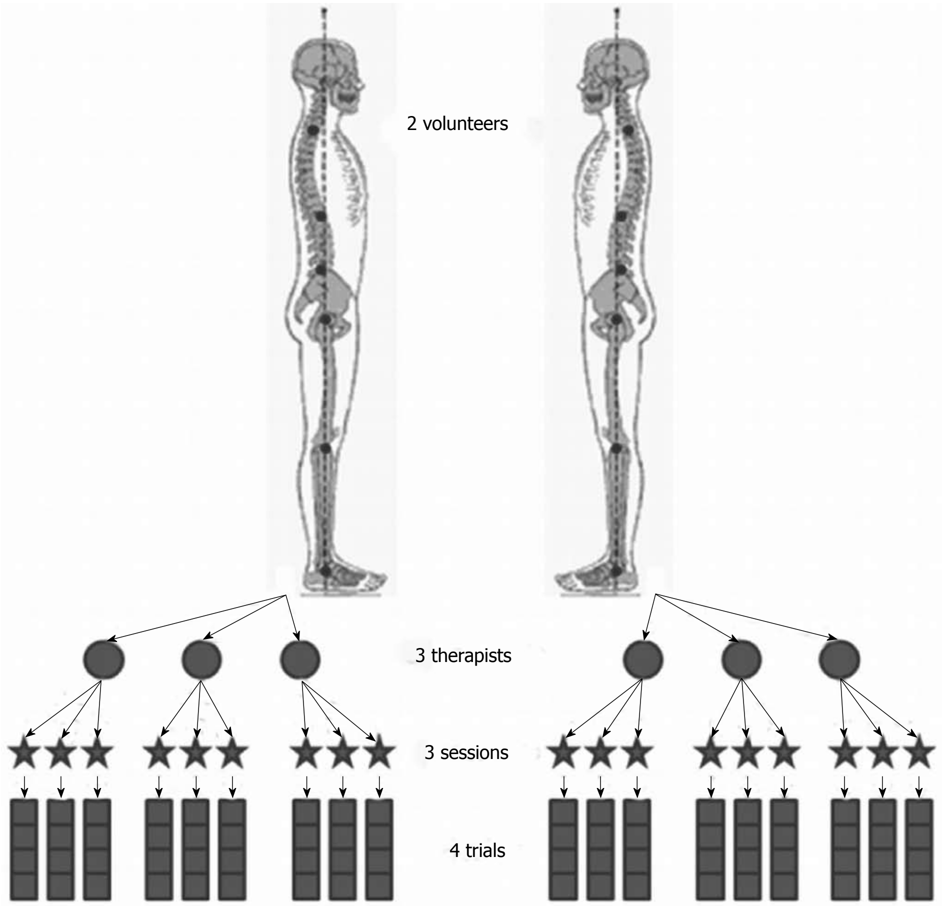

Figure 1 Experimental error measurement based on Schwartz's methodology.

Table 1 Mean net sagittal articular moments and maximum net sagittal articular moments in N.m for each volunteer

		Cervical	Thoracic	Lumbar	Hip right	Hip left	Knee right	Knee left	Ankle right	Ankle left
Mean	Volunteer 1	-0.65	-9.23	-0.45	10.73	14.62	-6.7	-5.81	-13.04	-7.52
moments	Volunteer 2	-0.03	-4.2	-0.86	3.79	4.82	-7.59	-10.09	-7.76	-6.08
Max	Volunteer 1	0.71	10.76	7.71	11.35	15.2	7.6	7.59	14.06	8.59
moments	Volunteer 2	0.43	5.92	3.91	4.27	5.08	8.12	10.44	8.5	6.49

Signs of the moments were consistent between the two subjects. Maximum moments are expressed in absolute values.

Table 2 Results of the experimental error measurement (N.m)

	Cervical	Thoracic	Lumbar	Hip right	Hip left	Knee right	Knee left	Ankle right	Ankle left
Inter-trial error	0.26	1.36	1.08	1.66	1.71	1.55	1.5	2.14	2.03
Inter-session error	0.43	5.27	5.24	3.21	3.78	2.09	2.75	2.46	2.8
Inter-therapist error	0.48	6.68	6.64	4.09	4.5	4.22	4.07	2.6	2.86

an ankle plantar flexion, a knee extension, a pelvic anteversion and a spinal extension.

Measurement of the experimental errors

As per the methodology described by Schwartz, the following experimental errors were calculated: inter-trial errors (intrinsic error corresponding to the intra-subject variability), the inter-session errors (extrinsic error related to intra-observer variability) and the inter-therapist errors (extrinsic error related to inter-observer variability). Results from these analyses are summarized in Table 2.

Free standing posture vs "radiographic" posture

In order to quantify the effect of an imposed posture, the net intersegmental moments at the spinal junctions during the "radiographic posture" were compared to the one obtained during the "free posture". Change was

Table 3 Summary of differences imposed by the "radiographic" posture compared with the free standing

		Cervical	Thoracic	Lumbar
Volunteer 1	Mean Diff FSP *vs* RX (N/m)	1.15	2.79	0.35
	Inter-trial significant diff	Yes	Yes	No
	Inter-session significant diff	Yes	No	No
	Inter-therapist significant diff	Yes	No	No
Volunteer 2	Mean Diff FSP *vs* RX (N/m)	0.11	0.88	0.3
	Inter-trial significant diff	No	No	No
	Inter-session significant diff	No	No	No
	Inter-therapist significant diff	No	No	No

Mean differences are in absolute values. Difference is considered significant when superior to experimental error measure.

considered significant only if the difference was greater than the intrinsic experimental error calculated for each junction. Results from these analyses did not showed significant differences for volunteer 2. Significant variations were observed on volunteer 1 mainly on the intra-subject measurement. Adopting a "radiographic" posture led to the following changes: an extension moment at the cervico-thoracic level, a decrease of the flexion moment at the thoraco-lumbar level and no significant change on the moment at the lumbo-sacral level. Results are summarized in Table 3.

Impact of trunk flexion/extension on spinal junctional moments

From the free standing position to an anterior flexion of the trunk at 45°, recordings demonstrated a progressively increased flexion moment (in absolute values) on the cervico-thoracic (> 3.5 N.m), the thoraco-lumbar (> 35 N.m) and the lumbo-sacral junctions (> 45 N.m).

During trunk extension (around 40°) recordings demonstrated changes towards extension moments on the cervico-thoracic (> 3.5 N.m), the thoraco-lumbar (> 18 N.m) and the lumbo-sacral junctions (> 35 N.m). These results are summarized in Figure 2.

DISCUSSION

Sagittal spino-pelvic parameters have been reported as of primary importance in the management of spinal deformities due to their correlation with clinical and functional outcomes in preoperative and postoperative evaluations[6,7,17,18]. More recently, those findings were revisited in order to define guidelines in realignment objectives[19]. Given the constrain of a radiographic environment (*i.e.*, arms positioning), several authors demonstrated that the "radiographic" posture could lead to postural modifications[10,11] and therefore to subsequent alignment misinterpretation, especially for patients with a marked sagittal anterior malalignment.

Our objective was to propose a new protocol focusing on the calculation of resulting intersegmental moments during a free standing posture (*i.e.*, without constrain of the radiographic environment) and to evaluate the experimental error of the protocol.

Analysis protocol

Results from this study confirm the feasibility of the proposed protocol for postural analysis and provide preliminary values of the resulting net sagittal moments on various articulations during normal stance. In a free standing position, net flexion moments calculated at each spinal junction correspond to the impact of the body weight. Therefore, in order to stand in an upright position, these moments have to be compensated by the action of posterior muscles. Muscular role is crucial in order to maintain a satisfactory posture and Mahaudens *et al*[20], demonstrated, in an energy-cost analysis, the impact of poor muscle efficiency on gait for adolescent with idiopathic scoliosis (AIS). Previous studies have already analyzed spinal alignment and posture using gait analysis but, to our best knowledge, characterization of posture with net sagittal moments has never been reported yet. Chen *et al*[21] reported poor postural stability control in AIS patients, without modifications of gait patterns in comparison with normal subjects. More recently, Engsberg *et al*[22] and Lenke *et al*[23] analyzed posture and trunk range of motion in AIS patients, post-operatively; they found a reduced gait speed, an improved coronal balance, but unchanged sagittal balance and a reduced range of motion in fused and unfused spinal segments. Using the protocol described in this study could provide further steps in the comprehension of the net reaction moment which occurs below or above a fused segment or evaluate an adjacent level degeneration.

Experimental error measurement

Measurement of the experimental error was done according to Schwartz *et al*[16], and as for these authors, in our protocol the inter-trial error was the smallest, with higher inter-session and inter-therapist errors. This increased measurement error can be considered in different ways: it can be related to a lack of reliability of the protocol or can reflect the postural variability. Results from trunk flexion/extension moments showing a linear relation between trunk flexion/extension and moments, as well as the small differences between errors from

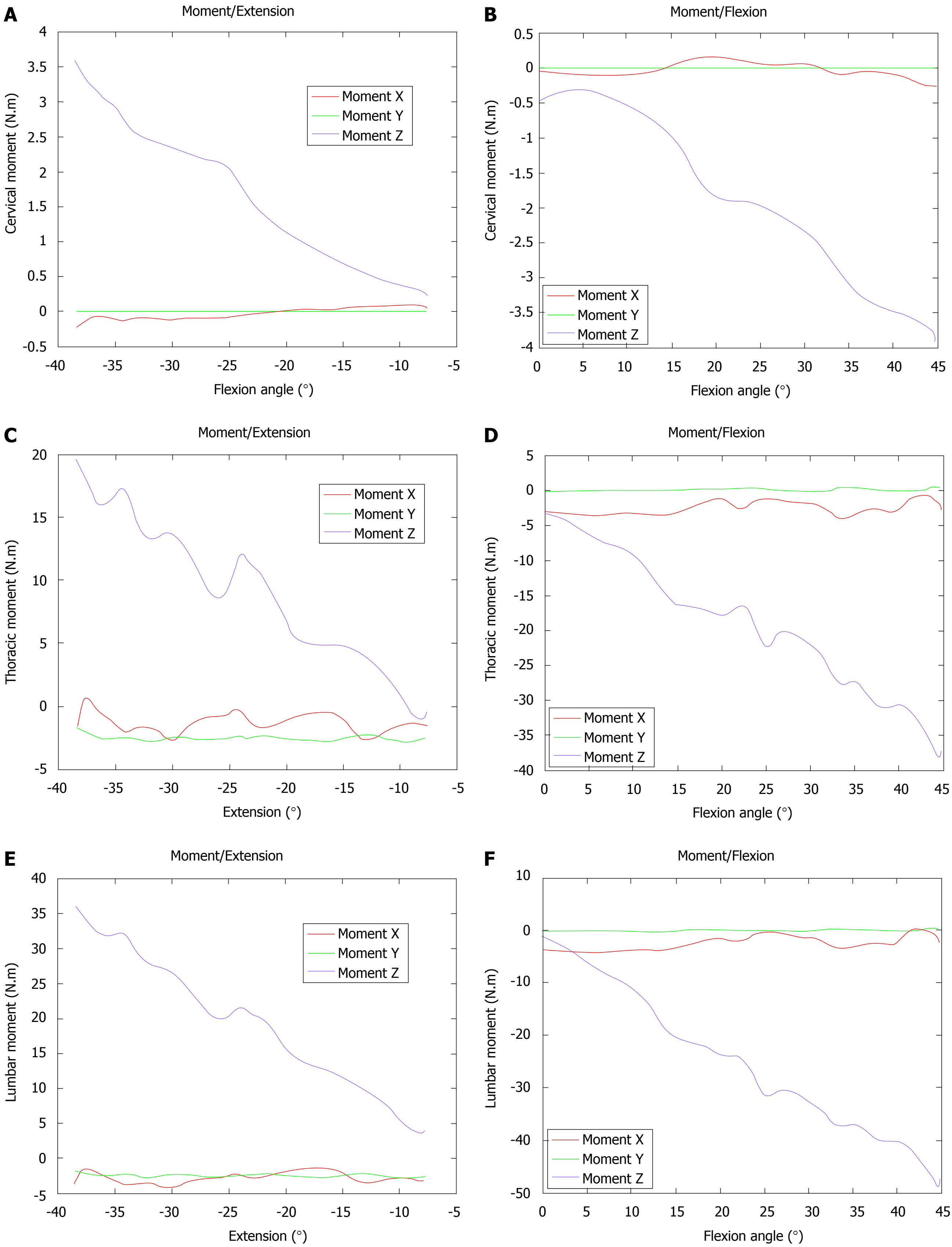

Figure 2 Results of the net sagittal moments (moment Z) on each spinal junction during trunk extension (A, C, E) and flexion (B, D, F).

inter-session and inter-therapist measurements are more likely to reveal changes in posture. Furthermore, differences found between the free-standing posture and the "radiographic" posture provides an additional argument in favor of a postural variability rather than a protocol failure.

Free standing vs "radiographic" posture

Results from the analysis comparing the free standing and the "radiographic" posture revealed differences superior to the intrinsic experimental error for the volunteer 1 and no significant changes were visible for the volunteer 2, underlining the variability of posture with time and among individual. Clinical expressions of these changes were associated with an extension of the upper part of the trunk when the volunteer adopted the "radiographic" posture. These results are in line with previous reports[10,11] where arms positioning could be associated to negative shift of the SVA. Furthermore, this test was conducted in volunteer without sagittal malalignment and these differences may be even much more noticeable in patients with loss of lumbar lordosis and increased thoracic kyphosis.

Results from this study confirm the technical feasibility of the protocol. Using this methodology, it was possible to evaluate net moments applied to spinal junctions. Measurements of experimental errors showed differences between inter-trial, inter-session and inter-therapist recordings traducing variability of posture. Differences were also noted between free standing and "radiographic" posture. Further steps will be needed in order to include a larger sample of volunteers for description of normative values and to determine sagittal parameters from this protocol that can be associated with conventional radiographic parameters. Future development of this protocol can help to evaluate various clinical situations such as adjacent level degeneration or modification of forces applied on unfused segment after spinal surgery.

COMMENTS

Background

In clinical practice, postural analysis is mainly based on radiographs. However, in various situations such as global sagittal anterior malalignment interpretation of radiographs may not represent the real alignment of the subject.

Research frontiers

Biomechanical analysis can currently be applied to postural analysis. Such development will help to understand spinal disorders and impact of surgical procedures on posture.

Innovations and breakthroughs

Results from this study confirm the technical feasibility of the protocol. Using this methodology, it was possible to evaluate net moments applied to spinal junctions. Differences were also noted between free standing and "radiographic" posture. Future development of this protocol can help to evaluate various clinical situations such as adjacent level degeneration or modification of forces applied on unfused segment after spinal surgery.

Applications

Future development of this protocol can help to evaluate various clinical situations such as adjacent level degeneration or modification of forces applied on unfused segment after spinal surgery.

Peer-review

In this biomechanical study the authors describe the initial results and experimental error measurement of a protocol analyzing human posture through sagittal intersegmental moments. After elaboration of a specific marker-set, 4 successive recordings were done on two volunteers by three different operators during three sessions in order to evaluate the experimental error measurement. A supplementary acquisition in a "radiographic" posture was also obtained. And these authors concluded that the first results confirm the technical feasibility of the protocol while the characterization of sagittal intersegmental net moments can have clinical applications such as evaluation of an unfused segment after a spinal arthrodesis.

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ORIGINAL ARTICLE

Prospective Study

Effect of body mass index on functional outcomes following arthroplasty procedures

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Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at safaksayar@gmail.com.

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Abstract

AIM: To evaluate the body mass index (BMI) change in arthroplasty patients and its impact on the patients' functional results.

METHODS: Between October 2010 and May 2013, 606 patients who were operated due to gonarthrosis, coxarthrosis, aseptic loosening of the total knee and hip prosthesis were evaluated prospectively. Patients were operated by three surgeons in three medical centers. Patients who were between 30-90 years of age and who were underwent total knee arthroplasty, total hip arthroplasty, revision knee arthroplasty, or revision hip arthroplasty were included in the study. We excluded the patients who cannot tolerate our standard postoperative rehabilitation program. Additionally, patients who had systemic inflammatory diseases, diabetes mellitus, or endochrinopathies were excluded from the study. The remaining 513 patients comprised our study group. Preoperative functional joint scores, height, weight and BMI of all patients were recorded. We used the Knee Society Score (KSS) for knee and Harris Hip Score (HHS) for hip patients. Postoperative functional scores were measured at 1st, 6th and 12th months and recorded separately at outpatient visits.

RESULTS: The mean age of the patients was 64.7 (range: 30-90) years (207 males/306 females) and the mean follow-up duration was 14.3 (range: 12-26) mo. We found that arthroplasty patients had weight gain and had an increase in BMI at the postoperative 1st, 6th and 12th months. The mean BMI of the patients was 27.7 preoperatively, 27.8 at the postoperative 1st month, 28.1 at the 6th month and 28.6 at the 12th month (P < 0.01). At the last visit, the mean postoperative HHS of the hip arthroplasty patients was 82.2 ± 7.12 (preoperatively, 52.3; 1st month, 78.2; 6th month, 81.1; 12th month, 82.2), and the mean KSS of the knee arthroplasty patients was 79.3 ± 4.31 (preoperatively, 35.8; 1st month, 75.2; 6th month, 79.1; 12th month, 79.3). Worse functional results were noted in the patients who had a BMI increase, however, this correlation was statistically significant only at the postoperative 6th month (P = 0.03).

CONCLUSION: To prevent the negative functional effects of this weight gain during the postoperative period, arthroplasty patients should be advised for weight control and risky patients should consult with a dietician.

Key words: Body mass index; Arthroplasty; Obesity; Functional outcomes; Weight gain

Core tip: Although the patients should be expected to mobilize more easily and loose weight after arthroplasty procedures, we hypothesized that the body mass index (BMI) usually increases in the postoperative period of total joint arthroplasty of the lower extremity. We aimed to evaluate the BMI changes in arthroplasty patients and impact of BMI changes on functional results in total knee arthroplasty and total hip arthroplasty patients. In our study, we determined that lower extremity arthroplasty patients gained weight during the postoperative period and this weight gain deteriorated functional outcomes of the patients. This correlation was statistically significant at the 6th month postoperatively (P = 0.03).

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INTRODUCTION

In the twenty-first century osteoarthritis (OA) is the most common joint disorder in the adult population[1,2]. This degenerative disease mostly affects weight-bearing joints and the number of cases of symptomatic OA is likely to increase worldwide due to the aging of the population and the epidemic of obesity[2]. As a result of restricting functional status due to pain in OA, patients are vulnerable to gain weight. Therefore, most of arthroplasty candidates are overweight[2,3].

In the treatment of OA, the prevalence of arthroplasty procedures has been increasing[3]. Obesity is associated with increased risks of short- and long-term complications and higher costs in arthroplasty procedures[4,5]. In addition, decreased functional results are associated with obesity in arthroplasty procedures[4-7]. In consequence, orthopedic surgeons usually advised patients to loose weight preoperatively and postoperatively in order to maintain better functional results and low complication rates[7-9].

We hypothesized that the body mass index (BMI) usually increases in the postoperative period of total joint arthroplasty in the lower extremity. These postoperatively increased values of BMI may affect the morbidity and functional results of the patients. We aimed to evaluate the BMI changes in arthroplasty patients and impact of BMI changes on functional results in total knee arthroplasty (TKA) and total hip arthroplasty (THA) patients.

MATERIALS AND METHODS

Between October 2010 and May 2013, 606 patients who were operated due to gonarthrosis, coxarthrosis, aseptic loosening of the total knee and hip arthroplasties were evaluated prospectively. These patients were operated by three surgeons in three medical centers. Patients who were between 30-90 years of age and who were underwent TKA, THA, revision knee arthroplasty, or revision hip arthroplasty were included in our study. We excluded the patients who cannot tolerate our standard postoperative rehabilitation program. Additionally, patients who had systemic inflammatory diseases, diabetes mellitus, endochrinopathies, concomitant spinal diseases, and concomitant lower extremity deformities were excluded. Nineteen patients who refused to attend the study, 14 patients who required revision surgery, and 60 patients who discontinued the rehabilitation program due to early postoperative complications (periprosthetic fracture in 11 patients, deep venous thrombosis in 20, pulmonary emboli in 3, dislocation of prostheses in 5, early prosthetic infection in 9, and lost to follow-up in 12) were excluded. The remaining 513 patients comprised our study group.

Two hundred and thirty-five cases of primary hip prosthesis, 252 cases of primary knee prosthesis, 15 cases of hip revision prosthesis and 11 cases of knee revision prosthesis comprised the study group. Hip arthroplasty surgeries were performed *via* direct lateral approach (Hardinge) with cementless hip prostheses. In primary cases, a double wedge metaphyseal filling

1/3 proximal porous coated femoral stem was used (Synergy, Smith and Nephew) and in revision cases a cylindrical fully coated femoral stem (Echelon, Smith and Nephew) was used. A cementless porous coated acetabuler shell was used for acetabuler fixation (Reflection interfit, Smith and Nephew) and ultrahigh molecular weight polyethylene in combination with cobalt-chrome or ceramic head was used for bearing surfaces. Knee arthroplasties were performed *via* anterior midline skin incision and medial parapatellar incision with fixed bearing cemented posterior cruciate ligament retaining knee prosthesis in primary cases. In revision cases, fixed bearing PCL substituting knee prosthesis was used (Genesis II, Smith and Nephew).

A standard knee and hip physical therapy protocol was applied by three physiotherapists to all patients. According to this protocol all arthroplasty patients performed isometric quadriceps and range of motion exercises after the first day of operation. The day after surgery all patients were mobilized with full weight bearing *via* two crutches. All patients were allowed to walk without crutches after 6 wk. We did not give any rehabilitation program 6 wk after the operation. Patients had control visits at the 1st month, 6th month, and 12th month postoperatively. Their functional status was evaluated with Harris Hip Score (HHS) for hip and Knee Society Score (KSS) for knee arthroplasties by three physiotherapists' recordings. BMI values of the subjects were recorded at the operative day, postoperative 1st month, 6th month, and 12th month.

Detailed information on surgical interventions was provided to all patients. An informed consent form concerning the operative technique to be performed was signed by all patients. The patients were enlightened about the rehabilitation program to be instituted. We did not recommend any dietary modification to any patient.

Statistical analysis

Statistical Package Social Sciences for Windows 12.0 was used for statistical analyses. In quantitative comparisons, data were assessed by Student's *t*-test and paired samples *t*-test. In qualitative comparisons, data were assessed by χ^2 and Fisher exact χ^2 tests. Preoperative and postoperative BMI of the patients were analyzed by repeated measures analysis of variance (ANOVA). Benferroni test and Pearson correlation were used to analyze the change in BMI and related functional outcomes. Statistical significance was accepted as $P < 0.05$.

RESULTS

The mean age of the patients was 64.7 years (range: 30-90 years; 207 males/306 females) and the mean follow-up duration was 14.3 (range: 12-26) mo. At the last control, the mean postoperative HHS of the hip arthroplasty patients was 82.2 ± 7.12, and the mean KSS of the knee arthroplasty patients was 79.3 ± 4.31.

According to the results of our study, we observed that our patients had gained weight throughout the postoperative period due to decreased mobilization. The mean BMI of the patients was 27.7 preoperatively, 27.8 at the postoperative 1st month, 28.1 at the 6th month and 28.6 at the 12th month. Preoperative and postoperative BMI values of the patients were analyzed by repeated measures ANOVA. According to this analysis, the mean BMI change was statistically significant ($P < 0.001$).

The mean HSS of the hip arthroplasty patients was 52.3 preoperatively, 78.2 at the postoperative 1st month, 81.1 at the 6th month, and 82.2 at the 12th month. The mean KSS of the knee arthroplasty patients was 35.8 preoperatively, 75.2 at the 1st month, 79.1 at the 6th month, and 79.3 at the 12th month. There were statistically better postoperative results in comparison to the preoperative values ($P = 0.0002$). In the correlation analysis of functional parameters with postoperative BMI values, there was no correlation between BMI increase and bad functional outcomes ($P > 0.05$). However, in the correlation analysis of functional outcomes and BMI increase at the 6th month postoperatively, there was a correlation between BMI increase and bad functional outcomes ($P = 0.03$).

The patients were analyzed separately by Bonferroni test and this also revealed the statistically significant BMI change between preoperative values and values at the 1st, 6th and 12th months ($P < 0.001$). Also a subgroup analysis was done; one group was the patients who had a BMI increase and the other was the patients who had no BMI increase. In the functional assessment and comparison of these two subgroups, there was no statistical difference ($P = 0.152$).

DISCUSSION

OA mostly affects weight bearing joints and the number of cases of symptomatic OA is likely to increase worldwide due to the aging of the population and the epidemic of obesity[2,3]. Arthroplasty is the final option for these patients with high satisfaction. However, obesity (BMI > 30 kg/m^2) related bad functional outcomes had been reported by many authors[2,5,8]. We evaluated the change in BMI of patients after arthroplasty operations and its correlation with functional outcomes.

BMI is a frequently used tool for measurement of obesity in epidemiological studies[2]. According to the World Health Organization, the optimal BMI for good health is 20-25 kg/m^2[2].

The effect of obesity on the clinical and functional status of the artroplasty patients is controversial[6,10-13]. Ibrahim *et al*[11] made a comparative study on hip arthroplasty patients and reported that in the short term a BMI > 30 plays no role in an increase in complications or re-operation. In another study, 78 THA patients were evaluated for BMI and functional outcome at 2 years. The authors concluded that the majority of patients undergoing primary THA had an increase in their BMI. Also, they reported that pre-operative BMI or BMI change postoperatively is not a predictor of complications or mid-term outcome of THA[12]. However, in a cohort study that evaluated 5357 hip arthroplasties, the authors reported that with a minimum 1-year follow-up the outcome and early revision were statistically and clinically poorer for obese patients[6]. Similarly, Kremers *et al*[13] found that obesity was associated with high treatment costs and long hospital stay in a large cohort of patients who underwent TKA. Their cohort study was performed with 8129 patients in 2000-2008 years and at the end of the study the effect of obesity on costs was independent of obesity-related complications[13]. In our study, we did not find any difference in the functional evaluation of the patients who had a BMI increase and those who had no BMI increase at the last follow-up ($P > 0.05$). However, there was a correlation between bad functional outcomes and BMI increase at the 6th month ($P = 0.03$).

In a study with 78 women who underwent elective primary TKA, it was found that obesity had a negative impact on functional recovery and mobility[10]. In that study, all the patients were overweight. However, in our study we evaluated BMI changes and our main finding was the weight gain of the patients independent from other factors like comorbidities. Although we detected a significant increase in BMI in patients, there was no correlation between BMI changes and functional outcomes.

In the literature there are few studies noticing that arthroplasty patients have weight gain independent from other factors[14,15]. In a study the authors noticed that obese patients could not achieve weight loss after THA operation although their mobilization problems had resolved[14]. Zeni *et al*[15] reported that 66% of their TKA patients had weight gain at the end of the two-year follow-up. We also determined that our patients also gained weight independent from other comorbidities and confirmed this BMI increment in THA patients with functional assessment.

Although dissenting opinions have been proposed by some authors[11], there were many studies that reported higher complication rates and bad functional outcomes[4,8,9,14]. In one of the largest studies that examined the relationship between obesity and complications after TKA and hip arthroplasty, 35817 THR patients and 32485 TKR patients were included in the study and postoperative complications during the 6 mo following total hip and knee replacement surgery were recorded. The study revealed that obesity increased the risk of wound infection and DVT[16]. In our study, we did not see any difference in complications due to BMI increase.

According to the results of our study, we observed that our patients had gained weight throughout the postoperative period. This may be due to decreased mobilization and change in eating habits. Although we treated these patients for their functional recovery, postoperative weight gain can result in bad functional outcomes, higher rates of postoperative complications, and higher risk of hypertension, diabetes mellitus and cardiovascular diseases.

Main limitation of our study is the absence of a control group with a given dietary program. Additionally, physiotherapy effect has not been evaluated. Besides immobilization, other factors (genetic, nutritional type, and other diseases) that could cause patients to gain weight were not considered. The sample size was limited to 513 patients including 207 men and 306 women. It is possible to reach statistical results closer to reality by increasing the sample size. Multivariate analyses were also examined with consideration of age, sex and genetic factors. Follow-up time shows differences within the population and the mean follow-up period was 14.3 mo (range: 12-26). The main strength of our study is the absence of any data investigating the functional outcomes regarding the BMI changes in the literature. References were limited to compare the results of our research due to the scarcity of research which compared preoperative and postoperative BMI in patients undergoing total knee and hip arthroplasty. In contrast, there were pretty many sources investigating the effect of BMI on the results of TKA and THA.

In conclusion, by taking into consideration of the statistical analysis of data related to our study, it is possible to mention that our patients had an increase in their body weight. However, this BMI increase does not affect the functional outcomes of the patients. This BMI increase may be due to decreased mobilization and change in their eating habits. To prevent the negative functional effects of this weight gain during postoperative period, arthroplasty patients should be advised for weight control and risky patients should consult with a dietician.

COMMENTS

Background

The main objective of this study was to assess the body mass index (BMI) change in arthroplasty patients independent from the other factors like comorbidities and effect of BMI change on the functional outcomes.

Research frontiers

In addition to the effects on musculoskeletal system, especially on weight bearing joints like knee and hip, BMI or obesity effects general health of the patients like cardiovascular diseases. Most of the arthroplasty candidates are overweight people due to decreased mobilization and problems in their daily living activities. There are some studies that analyzed the effect of high BMI or obesity on the functional recovery of the arthroplasty patients and related complications. However, there is no study that evaluated the patients prospectively for BMI change independent from other factors.

Innovations and breakthroughs

Nowadays, most of the patients need and request faster recovery from the surgery. Due to this, in the orthopedic literature there are many studies that analyzed the functional outcomes and the effect of other factors on these outcomes like obesity and postoperative rehabilitation, especially for arthroplasty procedures. In order to get better functional results, the surgeons should take care of other factors apart from surgical procedure like daily activities or eating habits after surgery.

Applications

BMI increase may cause other problems for patients and if most of the arthroplasty patients gain weight after these surgical procedures, patients should be warned for this problem or may consult with a dietician.

Peer-review

This paper aimed to study the effect of BMI on functional outcomes following arthroplasty procedures.

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SYSTEMATIC REVIEWS

Perioperative outcomes in minimally invasive lumbar spine surgery: A systematic review

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Abstract

AIM: To compare minimally invasive (MIS) and open techniques for MIS lumbar laminectomy, direct lateral and transforaminal lumbar interbody fusion (TLIF) surgeries with respect to length of surgery, estimated blood loss (EBL), neurologic complications, perioperative transfusion, postoperative pain, postoperative narcotic use, and length of stay (LOS).

METHODS: A systematic review of previously published studies accessible through PubMed was performed. Only articles in English journals or published with English language translations were included. Level of evidence of the selected articles was assessed. Statistical data was calculated with analysis of variance with $P < 0.05$ considered statistically significant.

RESULTS: A total of 11 pertinent laminectomy studies, 20 direct lateral studies, and 27 TLIF studies were found. For laminectomy, MIS techniques resulted in a significantly longer length of surgery (177.5 min *vs* 129.0 min, $P = 0.04$), shorter LOS (4.3 d *vs* 5.3 d, $P = 0.01$) and less perioperative pain (visual analog scale: 16 ± 17 *vs* 34 ± 31, $P = 0.04$). There is evidence of decreased narcotic use for MIS patients (postoperative intravenous morphine use: 9.3 mg *vs* 42.8 mg), however this difference is of unknown significance. Direct lateral approaches have insufficient comparative data to establish relative perioperative outcomes. MIS TLIF had superior EBL (352 mL *vs* 580 mL, $P < 0.0001$) and LOS (7.7 d *vs* 10.4 d, $P < 0.0001$) and limited data to suggest lower perioperative pain.

CONCLUSION: Based on perioperative outcomes data, MIS approach is superior to open approach for TLIF. For laminectomy, MIS and open approaches can be chosen based on surgeon preference. For lateral approaches, there is insufficient evidence to find non-inferior perioperative outcomes at this time.

Key words: Minimally invasive; Spine surgery; Lumbar

spine; Perioperative outcomes; Estimated blood loss; Neurologic complications; Transfusion; Postoperative pain; Narcotic use; Length of stay; Length of surgery

Core tip: Perioperative outcomes in minimally invasive (MIS) approaches to the lumbar spine have not been specifically examined in systematic reviews of MIS lumbar laminectomy, direct lateral and transforaminal lumbar interbody fusion (TLIF) surgeries. Based on perioperative outcomes data, MIS approach is superior to open approach for TLIF. For laminectomy, MIS and open approaches can be chosen based on surgeon preference. For lateral approaches, there is insufficient evidence to find non-inferior perioperative outcomes at this time.

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INTRODUCTION

Minimally invasive surgical (MIS) approaches to lumbar spinal surgery have been an area of increasing clinical interest for over 50 years. Percutaneous approaches to lumbar disk herniation began with chemonucleolysis treatment for sciatica by Smith[1] in 1964. In 1997, Smith[1] and Foley *et al*[2] introduced the tubular distraction system for a microendoscopic approach to microdiscectomy. This system allowed direct visualization of the surgical field while minimizing dissection and distraction of the paraspinal muscles and thoracolumbar fascia. By reducing the size of the operative field and reducing the number of damaged blood vessels, muscles and fascial structures, blood loss and post-operative pain would be reduced, leading to a shorter hospital stay, faster time to mobilization, and reduced post-operative analgesia needs.

After the development of the microendoscopic microdiscectomy, there were a series of rapid advances, applying the technology to other surgeries. In 1998, McAfee *et al*[3] described the direct lateral interbody fusion (DLIF) as an alternative to anterior lumbar interbody fusion (ALIF). Foley *et al*[4] described the MIS transforaminal lumbar interbody fusion (TLIF) in 2003, followed by Mummaneni *et al*[5] detailing the Mini-Open TLIF. In 2006, Ozgur *et al*[6] described the extreme lateral interbody fusion (XLIF) as another minimally invasive alternative to the ALIF. In 2010, a new, purely percutaneous approach for laminotomy and decompression, the Minimally Invasive Lumbar Decompression (mild®), was described by Chopko *et al*[7].

The initial hope that MIS approaches to the lumbar spine would lead to long-term reductions in patient-reported pain relative to open approaches has not yet been substantiated. Most studies of long-term results have reported similar outcomes between MIS and traditional open surgeries[8-10]. This leaves short-term measures, specifically perioperative outcomes, as the main possible distinguishing clinical feature between MIS lumbar spinal surgery and open surgical technique. There have not been any systematic reviews specifically focusing on perioperative outcomes across minimally invasive lumbar spinal surgical modalities, nor have there been systematic reviews of either minimally invasive laminectomy or far lateral fusion approaches.

This systematic review examines perioperative outcomes in minimally invasive lumbar spinal surgeries across several surgery types for adult degenerative spine disease: (1) MIS laminectomy *vs* open laminectomy; (2) MIS TLIF *vs* open TLIF; and (3) MIS XLIF and DLIF *vs* ALIF.

MATERIALS AND METHODS

A series of searches using the PubMed-National Library of Medicine/National Institutes of health (www.ncbi.nlm.nih.gov) database were performed. Only articles in English journals or published with English abstracts were included. Level of evidence of the selected articles was assessed. Search keywords included: "minimally invasive", "spine surgery", "laminectomy", "TLIF", "DLIF", "XLIF", and "ALIF". Abstracts were reviewed for clinical studies that reported perioperative outcomes in relevant surgical intervention categories (Figure 1).

Laminectomy

Studies were only included if they categorically used "laminectomy" for all subjects. Kinoshita *et al*[11] performed laminotomies for single level decompression, and sometimes performed laminectomies for multiple level decompression. It can be argued that laminotomy *vs* laminectomy is a distinction without a difference, but including laminotomies would then bring a number of microdiscectomy techniques into the range of covered studies. As this would introduce significant heterogeneity into the category, only studies describing laminectomy as part of the decompression surgery were included in the laminectomy category.

TLIF

TLIF studies were included regardless of whether bilateral or unilateral instrumentation was used. Only studies with both an open TLIF and an MIS TLIF arm were included. Studies that compared MIS TLIF with posterior lumbar interbody fusion (PLIF) or did not report TLIF and PLIF results separately were excluded.

DLIF/XLIF

Axial lumbar interbody fusion (AxiaLIF) studies were

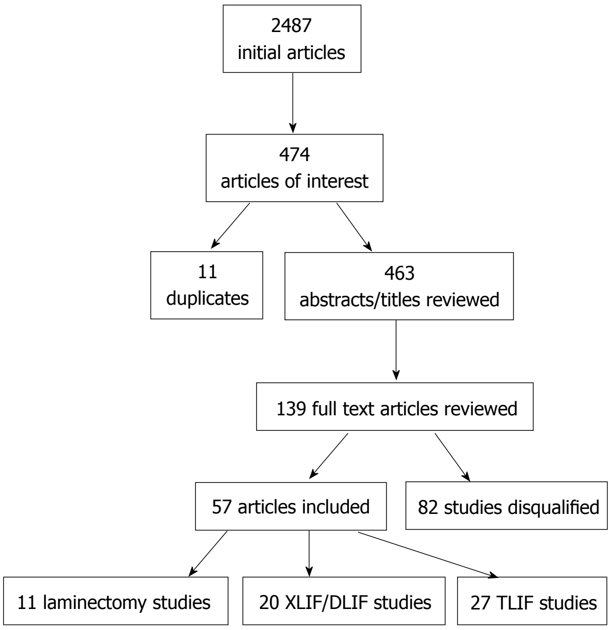

Figure 1 Identified pertinent studies from the literature search. TLIF: Transforaminal lumbar interbody fusion; DLIF: Direct lateral interbody fusion; XLIF: Extreme lateral interbody fusion.

not included. Studies with large portions of the study population receiving dual fixation (XLIF plus PLIF) were excluded.

Perioperative outcomes of interest examined in this systematic review include the following: (1) Length of surgery; (2) Estimated blood loss (EBL); (3) Neurologic complications; (4) Perioperative transfusion; (5) Postoperative pain; (6) Postoperative narcotic use; and (7) Length of stay (LOS).

Results were tabulated by intervention, indication for intervention, data by study arm, and relevant qualifications (bias, observer status, *etc.*) gathered. Multiple reports of the data from the same patient population were disregarded. Data from similar studies was pooled and calculated with analysis of variance (ANOVA). Numerical data that was reported stratified into subgroups other than MIS/non-MIS, were re-pooled and calculated with ANOVA. Numerical data only reported in graph form were incorporated using graphical methods. Durotomy and cerebrospinal fluid leak were included as reportable neurologic complications. Incorporation of isolated additional neurologic complications resulted in some study groups having complication rates above 100%. In order to summarize data across studies, joint statistics were calculated using ANOVA. The statistical review of this study was performed by a biomedical statistician.

RESULTS

Overall results

No studies found used independent observers for EBL or neurologic complications. At least two studies reported change in hemoglobin, presumably independently measured, but did not separately report patient fluid balance[12,13]. No studies used defined criteria for or an independent or blinded observer to decide the following study parameters: (1) Hospital discharge eligibility (*i.e.*, LOS); (2) Opiate prescription or availability; and (3) Need for perioperative transfusion.

Laminectomy

Identified pertinent studies are shown in Table 1, including three randomized controlled trials (RCTs) (Cho *et al*[14], Usman *et al*[15] and Watanabe *et al*[16]), one incompletely randomized trial (Mobbs *et al*[17]; randomized by consecutive, odd/even patient order[18]), and one cohort comparison study[12]. In Table 2, results for length of surgery, EBL, rate of neurologic complications, and LOS are shown. Pooling across RCTs/incomplete-RCTs with published standard deviations, length of surgery was significantly longer for MIS surgeries than open surgeries (177.5 min *vs* 129.0 min, *P* = 0.004), EBL was non-significantly less in MIS surgeries (115.0 mL *vs* 102.1 mL, *P* = 0.580), and LOS was significantly shorter following MIS surgeries than open surgeries (4.3 d *vs* 5.3 d, *P* = 0.010). Pooled rates of neurological complications in the two RCTs specifically reporting complications by group showed non-significantly higher rates of complications in open procedures (2.0% MIS *vs* 4.3% open, *P* = 0.52).

Three studies specifically examined rates of post-operative pain in these patient groups. Watanabe *et al*[16] examined the visual analog scale (VAS) score for post-operative wound pain on post-operative day 7 and found a VAS of 16 (± 17) for MIS patients and a VAS of 34 (± 31) for open laminectomies, a statistically significant difference (*P* = 0.04). Mobbs *et al*[17] examined post-operative narcotic use during hospital stay and found an intravenous morphine equivalent of 9.3 mg in MIS patients and 42.8 mg in open patients, a difference of unknown statistical significance (*P* value not stated). Komp *et al*[21] reported that "no operation-related pain medication was required" in their MIS case series.

No studies reported a need for transfusions following either MIS or open laminectomy.

DLIF/XLIF

No randomized trials using an ALIF control arm were identified in the literature search. One RCT had XLIF as part of the intervention in both the study arm and control arm groups[25]. Two studies mixed traumatic and/or post-infectious patients in the study population; as these indications were in the minority in each of these studies, the studies were included[13,26].

Identified pertinent studies are shown in Table 3, including four cohort control studies and 15 case series. In Table 4, results for length of surgery, EBL, rate of neurologic complications, and LOS are shown. In the authors' opinion, the current non-randomized data does not justify pooling or a meta-analysis due to heterogeneity and potential bias. Only one study (Huang

Table 1 Studies evaluating minimally invasive laminectomy

Ref.	Year	Surgery	Population	MIS patients	Open patients
RCTs/IRCTs					
Cho *et al*[14]	2007	Split process laminectomy: Marmot operation	LSS	40	30
Usman *et al*[15]	2013	Unilateral laminectomy	LSS, no spondylolisthesis	30	30
Mobbs *et al*[17]	2014	Laminectomy: Unilateral laminectomy for bilateral decompression	LSS, max 2 levels, no spondylolisthesis	27	27
Watanabe *et al*[16]	2011	Lumbar spinous process-splitting laminectomy	Neurogenic claudication	22	19
Clinical case series					
Rahman *et al*[18]	2008	Laminectomy	LSS, no discectomy	38	88
Nomura *et al*[19]	2014	Laminectomy: Spinous process-splitting laminectomy	Spondylolisthesis, LSS due to herniation	124	-
Parikh *et al*[20]	2008	Laminectomy	Degenerative disease	75	-
Komp *et al*[21]	2011	Laminectomy: Unilateral laminectomy for bilateral decompression	LSS, no spondylolisthesis > 1	74	-
Nomura *et al*[22]	2012	Laminectomy: Unilateral laminectomy for bilateral decompression: Paramedian approach	LSS, no discectomy	70	-
Tomasino *et al*[23]	2009	Laminectomy: Unilateral laminectomy for bilateral decompression	LSS, herniation in obese	28	-
Wada *et al*[24]	2010	Laminectomy	LSS, elderly patients	15	-

RCT: Randomized controlled trial; IRCT: Incomplete randomized controlled trial; LSS: Lumbar spinal stenosis; MIS: Minimally invasive.

Table 2 Studies comparing perioperative outcomes of minimally invasive laminectomy *vs* open laminectomy

	Length of surgery (min) ± SD		Estimated blood loss (cc) ± SD		Neurologic complications		Length of stay (d) ± SD	
	MIS	Open	MIS	Open	MIS	Open	MIS	Open
RCTs/IRCTs								
Cho *et al*[14]	259 ± 122	193 ± 68	154 ± 135	132 ± 128	-	-	4.0 ± 2.9	7.2 ± 1.6
Usman *et al*[15]	69 ± 0.1	65 ± 0.1	-	-	-	-	4.7 ± 0.5	3.5 ± 0.5
Mobbs *et al*[17]	-	-	40	110	4%	7%	2.3	4.2
Watanabe *et al*[16]	69 ± 29	82 ± 36	44 ± 75	55 ± 48	0%	0%	-	-
Clinical case series								
Rahman *et al*[18]	110 ± 10	157 ± 7	52 ± 14	246 ± 32	5%	8%	2.1 ± 0.7	4.1 ± 0.4
Nomura *et al*[19]	187 ± 68	-	90 ± 94	-	2%	-	-	-
Parikh *et al*[20]	118 ± 40	-	41 ± 90	-	11%	-	1.2	1.3
Komp *et al*[21]	44	-	0[1]	-	14%	-	-	-
Nomura *et al*[22]	77[2]	-	15.0[2]	-	0%	-	-	-
Tomasino *et al*[23]	102 ± 44	-	35 ± 76	-	11%	-	2.1	2.2
Wada *et al*[24]	144	-	60	-	7%	-	-	-

[1]No measurable blood loss; [2]Per level. SD: Standard deviation; RCT: Randomized controlled trial; IRCT: Incomplete randomized controlled trial; MIS: Minimally invasive.

et al[29]) was a prospectively designed and enrolled study; and, it used an approach (minimal access ALIF) that has not been repeated in any other study.

Within the reported data for MIS anterior fusion approaches, average length of surgery varied from 27 min to 295 min, average EBL from "not measureable" to 572 mL, and neurologic complication rates varied from 0% to 130%.

Two studies reported on perioperative transfusion use in this patient population. Hrabalek *et al*[27] reported a 0% transfusion use in the MIS XLIF and open ALIF cohorts. Rodgers's 2010 study, focusing on patients 80 years of age and older, reported no use of perioperative transfusion in MIS XLIF patients, but a 70% rate of transfusion in PLIF patients[12]. Regarding non-controlled studies, Rodgers *et al*[13] reported a 0.2% rate of transfusion in XLIF patients, while Berjano *et al*[34] reported a 1% transfusion rate.

Three non-controlled studies reported on peri-operative pain and narcotic use in patients treated with lateral interbody fusion. Ruetten *et al*[30] reported a mean VAS back of 4 (out of 100) and a VAS leg of 14 (out of 100) on post-operative day 1, stating that no post-operative pain medication was required in their 463 patient series. Marchi *et al*[35] reported mean VAS back of 45 and VAS leg of 31 one week following surgery, while Pimenta *et al*[40] reported a combined VAS Back/Leg value of 50 at the same time point.

Virtually all of the data gathered involved application of the XLIF (NuVasive, San Diego, California, United States) system; there is at this point limited data on other systems.

TLIF

Identified pertinent studies are shown in Table 5, including 1 RCT (Wang *et al*[43]) and 2 incompletely randomized controlled trials (Shunwu *et al*[44]: Randomized by admission date; Wang *et al*[45]: randomized by conse-

Table 3 Studies on minimally invasive lateral approaches to the lumbar spine

Ref.	Year	Surgery	Type of study	Population	MIS patients	Open patients
Cohort studies						
Hrabalek *et al*[27]	2014	XLIF	Retrospective cohort, XLIF *vs* ALIF	DDD, FBSS, spondylolisthesis	88	120
Smith *et al*[28]	2012	XLIF	Retrospective cohort, XLIF *vs* ALIF	DDD, LSS, FBSS, spondylolisthesis, herniation	115	87
[1]Rodgers *et al*[12]	2010	XLIF	Retrospective cohort, XLIF *vs* PLIF	> 80 yr, LSS, FBSS spondylolisthesis, scoliosis, fracture	40	20
Huang *et al*[29]	2010	MIS-ALIF[2]	Prospective cohort, MIS-ALIF *vs* ALIF	Not defined	10	13
Case series						
[3]Rodgers *et al*[13]	2011	XLIF	PCS	LSS, DDD, FBSS, spondylolisthesis, scoliosis	600	-
Ruetten *et al*[30]	2005	XLIF	RCS	Lumbar disc prolapse	463	-
Lykissas *et al*[31]	2014	XLIF	RCS	Degenerative spinal conditions	144	-
Grimm *et al*[32]	2014	XLIF	RCS	DDD, LSS, FBSS, scoliosis, spondylolisthesis, herniation	108	-
Tohmeh *et al*[33]	2011	XLIF	PCS	LSS, DDD, spondylolisthesis, spondylosis, scoliosis, recurrent herniation, ASD	102	-
Berjano *et al*[34]	2012	XLIF	RCS	DDD, LSS, spondylolisthesis	97	-
Lee *et al*[26]	2014	DLIF	RCS	LSS, spondylolisthesis, scoliosis, post-infectious	90	-
Marchi *et al*[35]	2012	XLIF	PCS	Spondylolisthesis	52	-
Sharma *et al*[36]	2011	XLIF	RCS	Spondylosis ± listhesis, scoliosis	43	-
Pimenta *et al*[25]	2011	XLIF	PCS	DDD	36	-
Ahmadian *et al*[37]	2013	XLIF	RCS	L4/L5 spondylolisthesis	31	-
Caputo *et al*[38]	2012	XLIF	PCS	Scoliosis	30	-
Malham *et al*[39]	2012	XLIF	PCS	DDD, spondylolisthesis, scoliosis	30	-
[4]Pimenta *et al*[40]	2013	XLIF	RCT	L4/L5 DDD	30	-
Elowitz *et al*[41]	2011	XLIF	PCS	LSS	25	-
Oliveira *et al*[42]	2010	XLIF	PCS	Degenerative spinal conditions	21	-

[1]Author financial conflict, different time period for cohort; [2]Minimally invasive flank incision; [3]Reported data likely includes data separately reported in Rodgers *et al*[13]; [4]This randomized control trial did not have an open surgery arm. DDD: Degenerative disc disease; FBSS: Failed back surgery syndrome; LSS: Lumbar spinal stenosis; ASD: Adjacent segment disease; MIS: Minimally invasive; RCT: Randomized controlled trial; XLIF: Extreme lateral interbody fusion; ALIF: Axial lumbar interbody fusion; PCS: Prospective cohort study; RCS: Retrospective cohort study; PLIF: Posterior lumbar interbody fusion; DLIF: Direct lateral interbody fusion.

Table 4 Studies comparing perioperative outcomes of minimally invasive lateral *vs* open anterior approaches to the lumbar spine

Ref.	Length of surgery (min) ± SD		Estimated blood loss (cc) ± SD		Neurologic complications		Length of stay (d) ± SD	
	MIS	Open	MIS	Open	MIS	Open	MIS	Open
Cohort studies								
Hrabalek *et al*[27]	-	-	-	-	28%	24%	-	-
Smith *et al*[28]	112 ± 31	173 ± 31	90 ± 74	311 ± 370	3%	6%	1.7 ± 1.3	3.6 ± 0.9
Rodgers *et al*[12]	-	-	1.4 g Hb	2.7 g Hb	-	-	1.3	5.3
Huang *et al*[29]	176 ± 8	202 ± 15	572 ± 93	970 ± 209	-	-	11.6 ± 1.3	12.5 ± 1.3
Case series								
Rodgers *et al*[13]	-	-	1.38 g Hb	-	1%	-	1.2	-
Ruetten *et al*[30]	27	-	0[1]	-	0%	-	-	-
Lykissas *et al*[31]	295 ± 180	-	-	-	135%	-	-	-
Grimm *et al*[32]	122	-	181	-	20%	-	3.0	-
Tohmeh *et al*[33]	-	-	-	-	48%	-	-	-
Berjano *et al*[34]	-	-	-	-	16%	-	-	-
Lee *et al*[26]	52 ± 19	-	0[1]	-	19%	-	-	-
Marchi *et al*[35]	73 ± 31	-	< 50	-	29%	-	-	-
Sharma *et al*[36]	-	-	-	-	70%	-	-	-
Pimenta *et al*[25]	130	-	-	-	28%	-	1.4	-
Ahmadian *et al*[37]	-	-	94	-	-	-	3.5	-
Caputo *et al*[38]	-	-	-	-	[2]	-	-	-
Malham *et al*[39]	84	-	70	-	20%	-	-	-
Pimenta *et al*[40]	69 ± 11	-	< 50	-	13%	-	-	-
Elowitz *et al*[41]	-	-	-	-	20%[3]	-	-	-
Oliveira *et al*[42]	86	-	44	-	14%	-	1.2	-

[1]"Non-measurable" blood loss; [2]Anterior thigh numbness in "substantial percentage" of patients which resolved in all patients at 4 wk; [3]Anterior thigh numbness for more than 3 wk. Hb: Hemoglobin; SD: Standard deviation; MIS: Minimally invasive.

Table 5 Studies on minimally invasive transforaminal lumbar interbody fusion

Ref.	Year	Surgery	Population	MIS patients	Open patients
RCTs/IRCTs					
Wang *et al*[43]	2011	TLIF	LSS, herniation, spondylolisthesis	41	38
Shunwu *et al*[44]	2010	TLIF	Degenerative lumbar disease	32	30
Wang *et al*[45]	2011	TLIF	Failed discectomy and decompression	25	27
Cohort studies					
Wong *et al*[46]	2014	TLIF	FBSS, DDD, spondylolisthesis	144	54
Zhang *et al*[47]	2013	TLIF	DDD	82	76
Villavicencio *et al*[48]	2010	TLIF	LSS, DDD ± herniation, spondylolisthesis	76	63
Lee *et al*[49]	2012	TLIF	LSS, DDD, herniation, spondylolisthesis	72	72
Terman *et al*[50]	2014	TLIF	DDD, LSS, spondylolisthesis, herniation	53	21
Cheng *et al*[51]	2013	TLIF	Spondylosis/listhesis, foraminal stenosis	50	25
Liang *et al*[52]	2011	TLIF	Degenerative lumbar instability	45	42
Yang *et al*[53]	2013	TLIF	Lumbar degenerative diseases	43	104
Gu *et al*[54]	2014	TLIF	Degenerative conditions	43	38
Wang *et al*[55]	2010	TLIF	Spondylisthesis	42	43
Zairi *et al*[56]	2013	Mini open TLIF	DDD, spondylolisthesis	40	60
Seng *et al*[57]	2013	TLIF	DDD, spondylolisthesis	40	40
Pelton *et al*[58]	2012	TLIF	DDD, spondylolisthesis	33	33
Singh *et al*[59]	2014	TLIF	DDD, spondylolisthesis	33	33
Brodano *et al*[60]	2013	Mini open TLIF	DDD, spondylolisthesis	30	34
Zou *et al*[61]	2013	TLIF	LSS, spondylolisthesis, herniation	30	30
[1]Peng *et al*[62]	2009	TLIF	DDD, spondylolisthesis	29	29
Archavlis *et al*[63]	2013	TLIF	SDS and severe FJO	24	25
Dhall *et al*[64]	2008	Mini open TLIF	DDD, spondylolisthesis	21	21
Schizas *et al*[65]	2009	TLIF	DDD, spondylolisthesis	18	18
Adogwa *et al*[66]	2011	TLIF	Grade Ⅰ spondylolithesis	15	15
Niesche *et al*[67]	2014	TLIF	Recurrent lumbar disc herniation	14	19
Lau *et al*[68]	2011	TLIF	Spondylosis/listhesis/lysis	10	12

[1]Differences in indications for study and control groups. LSS: Lumbar spinal stenosis; FBSS: Failed back surgery syndrome; DDD: Degenerative disc disease; SDS: Severe degenerative stenosis; FJO: Facet joint arthropathy; MIS: Minimally invasive; TLIF: Transforaminal lumbar interbody fusion; RCT: Randomized controlled trial; IRCT: Incomplete randomized controlled trial.

cutive, odd/even patient order). In Table 6, results for length of surgery, EBL, rate of neurologic complications, and LOS are shown. Pooling across RCTs and incompletely-RCTs with published standard deviations, length of surgery was non-significantly longer for MIS surgeries than open surgeries (150 min *vs* 143 min, P = 0.09), EBL was significantly less in MIS surgeries (352 mL *vs* 580.9 mL, P < 0.0001), and LOS was significantly shorter following MIS surgeries than open surgeries (7.7 d *vs* 10.4 d, P < 0.0001). Pooled rates of neurological complications in the two RCTs specifically reporting complications by group showed non-significantly higher rates of complications in open procedures (4.1% MIS *vs* 5.3% open, P = 0.697).

Regarding post-operative pain, Wang *et al*[45] polled patients on post-operative day 2, finding a VAS back of 2.2 ± 0.6 in MIS patients and 4.3 ± 0.5, a statistically significant difference (P < 0.05). Investigating the need for perioperative blood transfusions, Shunwu *et al*[44] found that 0 of 32 of the MIS patients needed transfusion, while the 30 open patients needed an average of 0.40 units of blood (SD: 0.97), a significant difference (P = 0.017).

DISCUSSION

The current growing trends in the use of MIS approaches in lumbar spine surgery have led to a concerted effort to compare outcomes between MIS and open techniques. Previous studies on long-term outcomes between MIS and open approaches in lumbar spine surgery have not revealed a significant difference between the two approaches[8-10]. This is the first systematic review of perioperative outcomes in lumbar MIS lumbar spine surgery aiming to reveal differences between MIS and open techniques in terms of lengths of surgery, EBL, neurologic complications, perioperative transfusion, postoperative pain, postoperative narcotic use and LOS.

To facilitate the interpretation of the currently existing data, lumbar spine procedures were divided into different types including decompressive laminectomy and interbody fusions. Interbody fusions were further subdivided into TLIF and lateral *vs* anterior interbody fusions.

In decompressive laminectomy, this study found the muscle-sparing MIS approach to result in significantly longer operative times compared to the open approach (177.5 min *vs* 129.0 min, P = 0.004). Although decompressive lumbar laminectomy is a relatively straightforward spinal operation, there exists a steep learning curve associated with microscope-assisted tubular spinal surgery[68], which could be one important factor accounting for the differences in operative times between the two techniques. With the growing popularity of minimally invasive approaches and the growing number of younger surgeons performing minimally

Table 6 Studies comparing perioperative outcomes of minimally invasive *vs* open transforaminal lumbar interbody fusion

Ref.	Length of surgery (min) ± SD		Estimated blood loss (cc) ± SD		Neurologic complications		Length of stay (d) ± SD	
	MIS	Open	MIS	Open	MIS	Open	MIS	Open
RCTs/IRCTs								
Wang *et al*[43]	168.7 ± 36.4	145.0 ± 26.8	207.7 ± 57.6	258.9 ± 122.2	2%	0%	6.4 ± 2.5	8.7 ± 2.1
Shunwu *et al*[44]	159.2 ± 21.7	142.8 ± 22.5	399.8 ± 125.8	517.0 ± 147.8	0%	0%	9.3 ± 2.6	12.5 ± 1.8
Wang *et al*[45]	139.0 ± 27.0	143.0 ± 35.0	291.0 ± 86.0	652.0 ± 150.0	12%	19%	-	-
Cohort studies								
Wong *et al*[46]	173	309	115	485	12%	13%	2.8	4.4
Zhang *et al*[47]	120 ± 35	115 ± 28	250 ± 75	650 ± 150	0%	3%	-	-
Villavicencio *et al*[48]	223 ± 68	215 ± 60	163 ± 131	367 ± 298	11%	13%	3.0 ± 2.3	4.2 ± 3.5
Lee *et al*[49]	166 ± 52	182 ± 45	161 ± 51	447 ± 519	1%	0%	3.2 ± 2.9	6.8 ± 3.4
Terman *et al*[50]	-	-	100	450	-	-	2.0	3.0
Cheng *et al*[51]	245 ± 73	279 ± 15	393 ± 284	536 ± 324	0%	12%	4.8 ± 1.8	6.1 ± 1.8
Liang *et al*[52]	127 ± 60	96 ± 46	194 ± 86	357 ± 116	-	-	-	-
Yang *et al*[53]	175 ± 35	177 ± 30	362 ± 177	720 ± 171	7%	2%	4.0 ± 1.3	7.1 ± 1.0
Gu *et al*[54]	196 ± 28	187 ± 23	248 ± 94	576 ± 176	5%	3%	9.3 ± 3.7	12.1 ± 3.6
Wang *et al*[55]	145 ± 27	156 ± 32	264 ± 89	673 ± 145	10%	7%	10.6 ± 2.5	14.6 ± 3.8
Zairi *et al*[56]	170	186	148	486	3%	3%	4.5	5.5
Seng *et al*[57]	185 ± 9	166 ± 7	127 ± 46	405 ± 80	-	-	-	-
Pelton *et al*[58]	112 ± 33	185 ± 34	125 ± 76	275 ± 99	-	-	2.0 ± 0.7	3.0 ± 1.1
Singh *et al*[59]	116 ± 28	186 ± 31	124 ± 92	380 ± 191	-	-	2.3 ± 1.2	2.9 ± 1.1
Brodano *et al*[60]	144	102	230	620	3%	9%	4.1	7.4
Zou *et al*[61]	150 ± 41	175 ± 37	131 ± 74	318 ± 177	0%	0%	7.5 ± 2.7	9.3 ± 4.2
Peng *et al*[62]	216	171	150	681	-	-	4.0	6.7
Archavlis *et al*[63]	220 ± 48	190 ± 65	185 ± 140	255 ± 468	13%	4%	7.0	11.0
Dhall *et al*[64]	199	237	194	505	0%	5%	3.0	5.5
Schizas *et al*[65]	-	-	456	961	17%	6%	6.1	8.2
Adogwa *et al*[66]	300	210	200	295	0%	0%	3.0	5.0
Niesche *et al*[67]	140	130	150	380	0%	11%	5.0	10.0
Lau *et al*[68]	390	365	467	566	0%	0%	5.0	6.2

RCT: Randomized controlled trial; IRCT: Incomplete randomized controlled trial; SD: Standard deviation; MIS: Minimally invasive.

invasive approaches, over time, as younger surgeons become more proficient with MIS techniques, operative times will likely decrease and we could see a decrease in the difference in operative times between MIS and open lumbar decompressions.

This study also found that patients undergoing MIS decompression were found to have less postoperative pain, lower perioperative transfusion rates and decreased LOS compared to those who underwent open decompression. These findings are not surprising given that the MIS technique results in significantly smaller surgical incisions, is muscle sparing and bypasses the need for extensive paraspinal and soft tissue stripping.

In terms of perioperative outcomes following lumbar decompressive laminectomy, there is a state of equipoise between MIS and open approaches, with neither technique clearly superior. At this time, individual patient and surgeon preferences are appropriate to guide decision making until further evidence becomes available.

Lumbar interbody fusion has become a popular surgical tool in the treatment of a wide variety of lumbar pathology including degenerative disc disease, recurrent lumbar herniation, spondylolisthesis and complex lumbar stenosis[69]. Currently popular approaches for achieving lumbar interbody fusion include the open anterior (ALIF) and MIS lateral (DLIF and XLIF) retroperitoneal approaches and the open and MIS posterior transforaminal (TLIF) approaches. While each one of these approaches utilizes a different anatomic corridor, they all have a common end goal of achieving interbody fusion. However, approach specific limitations and direct and indirect complications make each one of these approaches unique and worthy of comparison.

There are currently no randomized trials comparing ALIF and DLIF/XLIF in the literature. There is a wide variation in the reported outcomes data between MIS and open approaches for ALIF and DLIF/XLIF and this heterogeneity does not allow for meta-analysis of the current literature due to the high risk of potential bias. Furthermore, all of the currently available literature on lateral approaches involves the use of a single commercial system (XLIF, NuVasive, San Diego, California, United States) while there are currently many different commercial systems in use across the country.

There is currently a dearth of high quality literature on MIS alternatives (DLIF, XLIF) to ALIF. Although there appears to be no evidence of inferiority, these approaches should be considered investigational by surgeons and patients until better quality studies justify evidence-based statements of non-inferiority.

There have been several high quality studies in the literature comparing MIS TLIF and open TLIF surgeries. In terms of EBL, LOS, transfusion need and perioperative pain, the current data all favor MIS TLIF.

Although EBL differences across randomized studies did not reach clinically meaningful levels of ⩾ 750 mL, one of the randomized studies did find a significantly reduced transfusion need between MIS and open TLIF[44].

LOS was found to be significantly reduced in MIS TLIF by almost three days, however all of the studies originated from Chinese hospitals. LOS effect estimates, however, may not be applicable across countries, as different health systems use different discharge qualifications and have appreciably different LOS for similar procedures.

There are no outcome categories reported that identify MIS approaches to be significantly worse. Based on current data for perioperative outcomes, it appears that MIS approaches are superior to open approaches in TLIF.

Currently, there exists a wide variation in reported perioperative outcomes in both open and MIS lumbar spine surgery in the literature. Although multiple different outcomes are being reported there exists a lack of defined criteria for many of the reported outcomes such as hospital LOS, postoperative narcotic utilization and need for perioperative transfusion. Furthermore, none of the currently published literature used independent observers when reporting outcomes such as EBL and neurologic complication, leading to the risk of complication under-reporting due to the self-reporting nature of the outcomes data collection.

The current evidence does not clearly support superior perioperative outcomes for patients receiving minimally invasive spine surgery across all modalities. Based on perioperative outcomes data, we recommend a MIS approach to TLIF surgeries. MIS and open approaches can be chosen based on patient and surgeon preference when performing a laminectomy. Regarding lateral approach surgeries, there is insufficient evidence to find non-inferior perioperative outcomes at this time.

COMMENTS

Background

The advents of the surgical microscope and advances in technology have led to an increase in popularity in minimally invasive spine surgery. While prior studies have compared minimally invasive spine surgery to the traditional open spine surgery in terms of long-term outcomes, no study has compared the two techniques in terms of perioperative outcomes.

Research frontiers

Outcomes research in spine surgery has become a very important and highly prioritized area of research with the primary focus of minimizing cost while maximizing outcome.

Innovations and breakthroughs

This is the first study evaluating perioperative outcomes, comparing minimally invasive approaches and techniques *vs* open surgery in the treatment of degenerative lumbar spine disease.

Applications

While minimally invasive spine surgery has shown to have similar long-term outcomes to open spine surgery, it is important to evaluate perioperative outcomes of minimally invasive techniques to the standard open surgery in order to fully determine the advantages or disadvantages of the new technology compared to the gold standard.

Peer-review

The authors present us a comprehensive systematic review regarding short term outcomes following minimally invasive lumbar spine surgery. This topic is of interest and of novelty.

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SYSTEMATIC REVIEWS

Use of chondral fragments for one stage cartilage repair: A systematic review

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Abstract

AIM: To investigate the state of the art regarding Cartilage Autograft Implantation System (CAIS) or Particulated Juvenile Allograft Cartilage (PJAC).

METHODS: The authors searched the English literature regarding CAIS and PJAC. The search strategy was: (particulated cartilage) OR autologous cartilage fragments. All basic science articles were included. Clinical articles with less than 10 patients treated and less than 6 mo of follow-up were excluded. With these criteria, a total of 17 articles were available for the present review.

RESULTS: PJAC and CAIS are relatively novel techniques for cartilage repair. Good basic science evidence was described to support the concept. Although the preliminary clinical reports show encouraging results, clinical data are still limited, especially for CAIS. The indications for both techniques need to be precisely defined (age of the patients, size of the lesion, and involvement of the subchondral bone), together with other debated issues.

CONCLUSION: In conclusion, the authors can state that encouraging preliminary results are available for both techniques. However, further studies are necessary to precisely determine the indications, surgical techniques, and long term outcomes for PJAC and CAIS.

Key words: Cartilage; Juvenile; Chondral fragments; Adult; Particulated cartilage

Core tip: In this systematic review regarding Cartilage Autograft Implantation System (CAIS) and Particulated Juvenile Allograft Cartilage (PJAC), basic science and clinical articles with more than 10 patients treated and more than 6 mo of follow-up were included. A total of 17 articles were available for the present review. Good basic science evidence *in vitro* and *in vivo* was described to support the concept of CAIS. Only one level Ⅱ paper reported the clinical results of the CAIS technique. On the other hand, little basic science evidence and 4

preliminary clinical trials are available regarding the PJAC technique. CAIS and PJAC represent promising single step solutions for cartilage restoration with hyaline-like repair. However, many controversies still exist regarding both techniques, including the indications (age of the patients, size of the lesion, and involvement of the subchondral bone).

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INTRODUCTION

Chondral and osteochondral lesions are common in orthopedics, and their treatment still remains a challenge for the orthopedic surgeon. The overall prevalence of full-thickness focal chondral defects of the knee in athletes has been estimated around 36% (2.4%-75% between all studies)[1]. Depending on the characteristics of the patient and the lesion (symptoms, previous surgeries, involvement of subchondral bone, size, and chronicity of the defect), different options are available for the treatment of focal chondral defects, and these include: Bone marrow stimulation techniques (*i.e.*, microfractures), osteochondral auto/allograft transplantation, and autologous chondrocyte implantation (ACI). All of these techniques have advantages and disadvantages. Although ACI showed to result in hyaline-like repair and better outcomes than simple microfractures[2,3], two surgeries and an expensive laboratory cell expansion are necessary. In order to solve these drawbacks, new single-step solutions were described. Recently, the use of cartilage fragments has been introduced, as a single step chondral repair technique. These can be freshly harvested autologous cartilage chips held in the defect by a scaffold [Cartilage Autograft Implantation System (CAIS)] or Particulated Juvenile Allograft Cartilage (PJAC). The goal of this study is to present the state of the art regarding these two techniques, including basic science and clinical results.

MATERIALS AND METHODS

The authors performed a search in the literature to identify basic science and clinical articles (Level Ⅰ to Ⅳ) that would include the CAIS and PJAC techniques.

The authors searched the PubMed database for English literature regarding this topic in May 2015. The search strategy was as follows: (particulated cartilage) OR autologous cartilage fragments. The search produced 62 articles and 39 articles were excluded by title, leaving 23 papers for the present review. Clinical articles with less than 10 patients treated and less than 6 mo of follow-up were excluded. With these criteria, 10 articles were excluded by abstract, leaving 13 articles for the present review. No articles were excluded after reading the full text version. In addition, relevant references not identified by the database search, but cited by the downloaded articles and matching the inclusion criteria, were included. In this way 4 more papers were included, for a total of 17 articles for the present review[4-20].

RESULTS

CAIS

Basic science (*in vitro*): Six *in vitro* basic science studies reported the results of CAIS technique[4-9].

In 2011, Bonasia *et al*[4] co-cultured adult and juvenile cells (part 1) as well as adult and juvenile cartilage fragments (part 2).

Cartilage donors were 3 adult and 3 juvenile patients. In part 1, juvenile and adult chondrocytes were co-cultured with 5 different proportions: 100%, 50%, 25%, 12.5%, and 0%. The cells were cultured three-dimensionally with low-melt agarose. Isolated juvenile cultures showed better biochemical and histologic scores than mixed and adult cultures. No significant differences were described between co-cultures (1:1) and adult cultures. In part 2, chondral fragments were used (< 1 mm): adult, juvenile, and adult-juvenile co-cultures (1:1). Mixed cartilage fragment showed better proteoglycans/DNA ratio (P = 0.014), percentage of safranin O-positive cells (P = 0.012), Bern score (P = 0.001), and collagen type Ⅱ than adult cultures. No significant differences were noted between juvenile and mixed groups[4].

In 2012, Marmotti *et al*[5] evaluated cultures of rabbit cartilage fragments on Petri dishes, a paste scaffold with injectable hyaluronic acid (HA), and a membrane scaffold with an HA-derivative felt. At 60 d, a time-dependent cell outgrowth from cartilage fragments was observed with both types of scaffolds. Chondrocyte migration was less with Petri dishes than with scaffolds. At 2 mo, neo-matrix was evident and the migrated chondrocytes showed a roundish shape. Newly formed tissue was positive for collagen type Ⅱ immunostaining. A marked reduction in volume was observed in the paste scaffold at 1 and 2 mo, with approximately a 50% of shrinkage from the initial volume after 2 mo[5].

In another study published in 2013, Marmotti *et al*[6] compared *in vitro* the cell outgrowth from human cartilage fragments of adult and young donors using two different types of scaffolds (HA-derivative injectable paste scaffold and HA-derivative membrane scaffold) and evaluated the influence of transforming-growth-factor-β1 (TGF-β1) and granulocyte colony-stimulating factor (G-CSF) on chondrocyte behavior. The histological analysis showed age-dependent and time-dependent chondrocyte migration. A significant difference (P < 0.05) was observed between young and older donors. No difference was detected between the two types of scaffolds. After 1 mo, the number of migrating cells/area significantly increased due to exposure to TGF-β1 and/or G-CSF (P < 0.05). Immunofluorescence revealed that outgrowing cells from unstimulated scaffold sections were positive for SOX9, CD151, CD49c and G-CSF receptor. Immunofluorescence of cells from construct cultures showed an increase in β-catenin in all stimulated groups and an increased Proliferating Cell Nuclear Antigen expression in G-CSF-exposed cultures (P < 0.05)[6].

In 2013, Marmotti *et al*[7] studied the use of cartilage fragments seeded on a HA scaffold + platelet-rich fibrin matrix (PRFM) and fibrin glue (FG). Chondrocyte migration on the scaffolds was evident at 15, 30, and 60 d. At 30 d, high cellularity and intense extracellular matrix (ECM) production were described. At 60 d, ECM was positive for collagen type Ⅱ[7].

In 2014, Wang *et al*[8] tested the effect of knee-joint-specific bioreactor-induced dynamic compression and shear on minced bovine cartilage fragments cultures. The authors noticed that this method of culture was feasible under *in vitro* free-swelling and dynamic loading conditions, simulating *in vivo* post-transplantation. Mechanical stimulation significantly provoked cellular outgrowth and long-term chondrogenic maturation at the mRNA level, whereas histology depicted immature neotissue (weaker collagen type Ⅱ and aggrecan expression with an increased collagen type Ⅰ expression) where typical cartilage matrix was expected[8].

In 2015, Bonasia *et al*[9] evaluated *in vitro* if the degree of chondral fragmentation affected ECM production, in cartilage fragment autograft implantation. The cartilage was taken from five donors undergoing total hip replacement and minced in order to obtain 4 groups with different fragment sizes: (1) "fish scale" (diameter 8 mm, thickness 0.3 mm); (2) cubes with 2 mm side; (3) cubes with 1 mm side; and (4) cartilage paste (< 0.3 mm). The authors observed that ECM production was significantly affected by the degree of chondral fragmentation. At biochemical evaluation (Proteoglycans/DNA ratio), group 4 performed significantly better than group 1 (P < 0.001) and 3 (P = 0.02), while group 2 performed better than group 1 (P = 0.03). At histological evaluation (Bern score), group 4 performed significantly better than group 1 (P = 0.02), 2 (P = 0.04), and 3 (P = 0.03). One of the limitations of this study were the use of arthritic cartilage[9].

Basic science (*in vivo*): Six basic science studies reported the *in vivo* results of CAIS technique[5,7,10-13].

The use of autologous cartilage fragments for the repair of chondral defects was first described by Albrecht *et al*[10] in a rabbit model. The authors compared two groups: defects left untreated (23) and treated with autologous cartilage fragments and FG (52). Untreated defects showed no hyaline-like repair tissue. On the other hand, chondrocyte proliferation, hyaline-like repair, and alcian blue-positive ECM were evident in the cartilage fragment group[10].

In 2006 Lu *et al*[11] studied the CAIS technique in a goat model. Eight skeletally mature goats were used. Two full thickness 7-mm-diameter chondral defects on each side of the trochlear ridge were created through a mini-arthrotomy. The defects were either left untreated (empty) or treated with scaffolds loaded with cartilage fragments or with the scaffold alone. The scaffolds were fixed with a single PDS/PGA staple (DePuy Mitek, Norwood, MA). The technique produced hyaline-like repair tissue at 6 mo[11].

In 2008, Lind *et al*[12] investigated the cartilage repair of autologous cartilage chips or ACI with a collagen membrane in a goat model. Sixteen full-thickness cartilage defects (diameter 6 mm) were created in the femoral condyles of 8 adult goats. At 4 mo, no difference was found in O'Driscoll and Pineda histology scores, tissue filling (35%), or repair tissue stiffness between the two groups[12].

In a similar study, Frisbie *et al*[13] compared empty defects, CAIS technique and ACI in a horse model (10 skeletally mature horses). Arthroscopic, histologic, and immunohistochemistry results showed superiority of both implantation techniques (ACI and CAIS) compared with control groups, with CAIS achieving the highest score[13].

In 2012, Marmotti *et al*[5] compared the repair tissue of 5 different groups of treatment in a rabbit model (50 adult rabbits): cartilage fragments loaded onto HA scaffolds with FG (group 1) or without FG (group 2); scaffolds alone with FG (group 3) or without FG (group 4); empty defects (group 5). At 6 mo, cartilage fragment-loaded scaffolds induced significantly better repair tissue (in terms of histological modified ICRS score and a modified O'Driscoll scale) than the scaffold alone groups. Repair in group 2 was superior compared with the control groups (P < 0.05)[5].

In 2013, Marmotti *et al*[7] studied in a goat model a culture-free approach to osteochondral repair with minced autologous cartilage fragments loaded onto a scaffold composed of a HA-derived membrane, PRFM and FG. Two unilateral osteochondral defects were created in 15 adult goats. The defects were assigned to 3 different treatments: (1) cartilage fragments + HA scaffold + PRFM + FG; (2) HA scaffold + PRFM + FG; and (3) left untreated. Hyaline-like repair tissue was evident in group 1, in terms of morphological, mechanical and histological assessments[7].

Surgical technique: According to the original technique for CAIS described by Cole *et al*[14], hyaline cartilage is arthroscopically harvested (through standard anteromedial and anterolateral portals) from a low load-bearing surface (*e.g.*, lateral wall of the intercondylar notch or trochlear ridge with an amount similar to ACI, roughly 200 mg), using a specifically designed device that minces the cartilage into 1- to 2-mm pieces. After harvest, the device (DePuy Mitek, Raynham, Massachusetts) uniformly disperses the minced cartilage onto the biodegradable scaffold. The scaffold consists of an absorbable copolymer foam of 35% polycaprolactone and 65% PGA, reinforced with a PDO mesh (Advanced Technologies and Regenerative Medicine). The fragments are secured to the scaffold using FG. The joint is approached through a small arthrotomy, the defect is debrided to the level of the subchondral bone, and vertical walls of normal cartilage are created. A template of the defect is then obtained, using a sterile paper. The scaffold is trimmed according to the template and implanted on the defect with the chondral fragments in contact with the subchondral bone. Fixation can be achieved with bioabsorbable staples[14].

Clinical results: Only one paper (level Ⅱ) reported the clinical results of the CAIS technique[14]. Cole *et al*[14], in a randomized controlled trial, compared autologous cartilage fragment repair (CAIS technique) with microfractures, in 29 patients with 2-years of follow-up.

General outcome measures (*e.g.*, physical component score of the SF-36) indicated an overall improvement in both groups, and no differences in the number of adverse events were noted between the groups. At 24 mo, the authors described significantly higher International Knee Documentation Committee (IKDC) score and Knee injury and Osteoarthritis Outcome Score (KOOS) for the CAIS group, compared to the microfracture group. No differences were noted between the groups in terms of MRI qualitative analysis. However, the microfracture group showed a higher risk of developing intralesional osteophytes. The authors concluded that the new technique is a safe, feasible, and effective method for the treatment of focal chondral defects[14].

PJAC

Basic science (*in vitro*): Only one paper described the *in vitro* behaviour of juvenile cartilage fragments cultures[4]. In 2011, Bonasia *et al*[4] compared *in vitro* cultures of isolated adult, isolated juvenile and mixed juvenile/adult chondrocytes (part 1) and chondral fragments (part 2). The results of this study were previously described in the basic science (*in vitro*) section for the CAIS technique[4].

Basic science (*in vivo*): Only one paper described the results *in vivo* (small animal model) of the PJAC technique[4]. In 2015, Bonasia *et al*[4] evaluated the repair of chondral lesions treated with combined autologous adult/allogenic juvenile cartilage fragments, compared with isolated adult and isolated juvenile cartilage fragments in a rabbit model. Fifty-eight adult and 5 juvenile rabbits (cartilage donors) were used. A large osteochondral defect was created in the center of the femoral trochlea of adult rabbits. Four treatment groups were created: Group 1 = untreated defects (controls); Group 2 = adult cartilage fragments; Group 3 = juvenile cartilage fragments; and Group 4 = adult + juvenile cartilage fragments. The defects were evaluated with ICRS macroscopic score, modified O'Driscoll score, and Collagen type Ⅱ immunostaining. At 6 mo, group 4 showed higher modified O'Driscoll score (P = 0.003) and Collagen type Ⅱ immunostaining score ($P < 0.001$) than group 1. Histologically, also group 3 performed better than group 1 (P = 0.03), and group 4 performed better than group 2 (P = 0.004)[15].

Surgical technique: After arthroscopic evaluation through standard anteromedial and anterolateral portals, a limited medial or lateral arthrotomy is performed to fully visualize the lesion.

The defect is outlined with a scalpel to create vertical peripheral walls and the damaged cartilage debrided to the subchondral bone. A sterile foil is used to create a three-dimensional template of the defect. One package of DeNovo NT graft (DeNovo NT® Natural Tissue Graft, Zimmer Inc, Warsaw, Indiana, United States) can cover defects of about 2.5 cm^2. The preservation medium is removed and the chondral fragments positioned in the template 1 to 2 mm apart. The template is then filled with FG to within 1 mm of its full depth. Once the FG is solid, the fragment/glue construct is separated from the foil. The construct is fixed to the bed of the defect with FG. Alternatively, the particulated cartilage can be directly applied into the defect and glued *in situ*[16].

Clinical results: Four papers describing the clinical results of PJAC and matching the inclusion criteria were found[17-20].

In 2013, Coetzee *et al*[17] described the clinical outcomes of patients treated with PJAC for symptomatic osteochondral lesions in the ankle. Twenty-four ankles were included (average age of the patients at surgery 35 years, average lesion size 125 mm^2, mean follow-up 16.2 mo). At final follow-up, the average American Orthopaedic Foot and Ankle Society Ankle-Hindfoot Scale was 85, with 18 (78%) ankles reporting good to excellent scores. Good results were also obtained in terms of Short-Form 12 Health Survey (SF12) physical composite score, SF12 mental health composite score, Foot and Ankle Ability Measure activities of daily living and Sports, as well as visual analog scale for pain[17].

In 2013, Tompkins *et al*[18] evaluated the outcomes and MRI findings after PJAC for the treatment of focal Outerbridge grade 4 articular cartilage defects of the patella. Fifteen knees (13 patients) were enrolled, with a mean age at surgery of 26.4 years, and a mean follow-up of 28.8 mo. The mean International Cartilage Repair Society cartilage repair assessment score on MRI was 8.0 ± 2.8, a nearly normal assessment. Of 15 knees, 11 (73%) were found to have normal or nearly normal cartilage repair. The mean fill of the defect was 89% ± 19.6%, with 12 of 15 knees (80%) showing at least 90% defect coverage. The mean IKDC score was 73.3. The median score for the Kujala survey was 79. The median score on the Tegner activity scale was 5 (range, 3 to 9), and the mean score on the visual analog scale for pain was 1.9[18].

In 2014, Farr *et al*[19] described the results of PJAC in patients with symptomatic articular cartilage lesions on the femoral condyles or trochlear groove of the knee, in a 2-year follow-up prospective study.

Twenty-five patients with a mean age of 37 years were included. At 2 years, some patients underwent voluntary knee arthroscopy and cartilage biopsy. Histological analysis included safranin O staining for proteoglycans and immunostaining for type Ⅰ and Ⅱ collagen. At 2 years, the IKDC and KOOS (for pain, symptoms, activities, and sports) scores significantly improved. The MRI evaluation reported results similar to normal hyaline cartilage. Eight patients underwent arthroscopic biopsy and the repair tissue was considered a mixture of hyaline and fibrocartilage, positive for type Ⅱ collagen, and integrated with the surrounding cartilage[19].

In 2014, Buckwalter *et al*[20] retrospectively evaluated 13 cases of chondral lesion of the patella, treated with PJAC. The mean age was 22.5 years and the mean follow-up was 8.2 mo. Tibial tubercle anteromedialization was performed in 6 patients. The overall KOOS score significantly improved from a mean of 58.4 to 69.2 (P = 0.04)[20].

DISCUSSION

PJAC and CAIS are relatively novel techniques for cartilage repair. Good basic science evidence was described to support the concept. Although the preliminary clinical reports show encouraging results, clinical data are still limited, especially for CAIS. The indications for both techniques need to be precisely defined (age of the patients, size of the lesion, and involvement of the subchondral bone), together with other debated issues.

The controversies regarding these techniques include: (1) No data are available regarding the optimal degree of cartilage fragmentation, related to increased matrix production. Some recent research suggested that fragmentation to pieces smaller than 1 mm (basically to a cartilage paste) is related to increased ECM production. However this *in vitro* study was conducted on arthritic cartilage and these data need to be confirmed on juvenile fragments and non arthritic patients[9]; (2) No data are available regarding the use of CAIS and PJAC associated with scaffolds. If the theory that fragmentation to smaller pieces results in increased matrix production is confirmed, the use of scaffolds might become necessary to keep the cartilage paste in place; and (3) Some basic science studies suggested that mixing allogeneic juvenile and autologous adult cartilage fragments, increased ECM production. These data need to be confirmed in large animal models and in clinical trials[4,15].

In conclusion, the authors can state that encouraging preliminary results are available for both techniques. However, further studies are necessary to precisely determine the indications, surgical techniques, and long term outcomes for PJAC and CAIS.

COMMENTS

Background

Chondral and osteochondral lesions are common in orthopedics, and their treatment still remains a challenge for the orthopedic surgeon. Different options are available for the treatment of focal chondral defects: bone marrow stimulation techniques, osteochondral auto/allograft transplantation, and autologous chondrocyte implantation. All of these techniques have disadvantages (*i.e.*, non-hyaline like repair or two-staged procedures).

Research frontiers

To overcome these limitations, tissue engineering is prospecting new single-step solutions, including the use of cartilage fragments. These can be freshly harvested autologous cartilage chips held in the defect by a scaffold [Cartilage Autograft Implantation System (CAIS)] or Particulated Juvenile Allograft Cartilage (PJAC). The goal of this study is to present the state of the art regarding these two techniques, including basic science and clinical results.

Innovations and breakthroughs

This is the first systematic review regarding CAIS and PJAC. A total of 17 articles were available for the present review. Good basic science evidence *in vitro* and *in vivo* was described to support the concept of CAIS. Only one level II paper reported the clinical results of the CAIS technique. On the other hand, little basic science evidence and 4 preliminary clinical trials are available regarding the PJAC.

Applications

CAIS and PJAC represent promising single step solutions for cartilage repair. However, many controversies still exist regarding both techniques, including the indications (age of the patients, size of the lesion, and involvement of the subchondral bone).

Terminology

CAIS: Cartilage Autograft Implantation System; PJAC: Particulated Juvenile Allograft Cartilage.

Peer-review

The manuscript is interesting.

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