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EDITORIAL

Update on mesenchymal stem cell therapies for cartilage disorders

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Abstract

Cartilage disorders, including focal cartilage lesions, are among the most common clinical problems in orthopedic practice. Left untreated, large focal lesions may result in progression to osteoarthritis, with tremendous impact on the quality of life of affected individuals. Current management strategies have shown only a modest degree of success, while several upcoming interventions signify better outcomes in the future. Among these, stem cell therapies have been suggested as a promising new era for cartilage disorders. Certain characteristics of the stem cells, such as their potential to differentiate but also to support healing made them a fruitful candidate for lesions in cartilage, a tissue with poor healing capacity. The aim of this editorial is to provide an update on the recent advancements in the field of stem cell therapy for the management of focal cartilage defects. Our goal is to present recent basic science advances and to present the potential of the use of stem cells in novel clinical interventions towards enhancement of the treatment armamentarium for cartilage lesions. Furthermore, we highlight some thoughts for the future of cartilage regeneration and repair and to explore future perspectives for the next steps in the field.

Key words: Stem cell; Cartilage; Chondral defect; Management; Bone marrow; Mesenchymal stem cells; Adipose

Core tip: An increasing interest in stem cell application for cartilage defect repair is recently expressed, as a consequence of advancements demonstrating the critical function of mesenchymal stem cells as a potential alternative cell source for cartilage repair, as well as of recent clinical data exhibiting the effectiveness of these management strategies. Future research will determine the role of combining stem cells, primary chondrocytes,

and signaling molecules towards cartilage regeneration.

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INTRODUCTION

Cartilage lesions are among the most often recognized pathologies in young adults undergoing arthroscopy. Approximately 60% of the patients treated arthroscopically for any reason had at least one chondral lesion at their knee[1]. Due to the relatively young age of these patients (mean age ranged from 37 to 43 years old) and because the majority of lesions has been graded as Ⅱ or Ⅲ, it was suggested that impending osteoarthritis would be inevitable without treatment in these patients[1].

Effective management of these lesions can be extremely challenging, thus, creating a burden for both patients and physicians. With conservative treatment being unsuccessful, several surgical interventions have been proposed for focal cartilage lesions, including microfracture, autologous chondrocyte implantation [with either periosteum (ACI) or matrix-assisted (MACI)], osteochondral autograft or allograft transplantation, and particulated autologous or allogeneic articular cartilage[2-4]. Despite the plethora of available techniques, the effectiveness of these in terms of preventing or delaying the development of osteoarthritis is questionable.

In the armamentarium against cartilage defects, stem cell-based interventions have gradually taken a more prominent role. As shown in Figure 1, there is an exponential growth in the number of published studies that deal with stem cell use in cartilage disorders (Figure 1). Mesenchymal stem cells (MSCs) are multipotent cells that have been isolated from a variety of tissue types, including bone marrow, synovium, and adipose tissue[5-7]. MSCs have been observed to undergo differentiation down osteogenic, chondrogenic, myogenic, and tenogenic lineages, making them of great importance to the orthopedic and tissue engineering communities.

The regenerative potential of marrow-derived elements was determined in the 1960's, long before the discovery of MSCs, with the observation that superficial chondral defects exhibit limited healing potential, while defects penetrating the subchondral plate result in fibrocartilaginous ingrowth[8]. This observation ultimately led to the development of marrow stimulating techniques for chondral repair such as microfracture[9]. Penetrating the subchondral bone allows bleeding, and formation of a clot containing MSCs and various other bone marrow elements to form. While this technique has been shown to produce improved patient-reported outcomes at short time-points, the repair tissue is fibrocartilaginous in nature, and exhibits poor mechanical properties when compared to native cartilage. At longer time-points, this tissue may become fibrillated and require further management.

The premise behind the use of MSCs for cartilage repair was supported on two characteristics of the stem cells. These multipotent cells, under the appropriate environmental conditions, could differentiate into chondrocytes and repair the chondral defect[10]. Differentiation of both adipose-derived and bone marrow MSCs towards chondrocytes can be enhanced with the use of growth factors[11,12]. Thus, the ideal perspective would be to promote MSC differentiation towards chondrocytes and to utilize the healing response with new chondrocyte-like cells.

Another equally important ability has been revealed for MSCs, *i.e*., their capacity to actively interact with primary cells and extracellular matrix *via* continuous feedback mechanisms[13]. As a consequence, stem cells could act as advocators of the existing chondrocytes *via* their anti-inflammatory and immunomodulatory effect. In addition, this interaction can formulate an appropriate response towards differentiation, proliferation or secretion of supportive molecules that allows stem cells to be actively engaged in the cartilage healing response[14].

MSC transplantation is a technique that offers several potential benefits over other cartilage repair methods. MSCs may be isolated from adipose tissue, which is much less invasive than the harvest of chondrocytes for ACI. MSCs are also phenotypically stable during cell culture expansion, while chondrocytes undergo dedifferentiation. Furthermore, MSCs may be isolated in greater quantities than chondrocytes, allowing for the possibility of single-step procedures, which could decrease economic burden for the patient. Currently, clinical studies involving MSC transplantation are limited.

The aim of this editorial is to summarize the recent work in basic science and clinical interventions in an attempt to provide an update on the recent advances in stem cell treatment options for cartilage disorders. Furthermore, some thoughts for the future of cartilage regeneration and repair *via* stem cell application will be discussed. Due to the plethora of studies in the literature, the main focus of this study would be on clinical interventions for focal cartilage defects.

BONE MARROW DERIVED MSCs

Update on basic science

A better understanding of the pathogenetic phenomena that initiate the process of cartilage degeneration is of paramount importance, as this would allow the formulation of therapeutic approaches that aim to prevent osteoarthritis at its infancy. TGF-beta1 is proven to be a key factor for cartilage homeostasis, and its function is utilized in tissue engineering for chondrocyte proliferation and enhancement of functional properties[15]. Recently, an interesting aspect of the role of transforming growth factor-beta (TGF-beta) in osteoarthritis has been

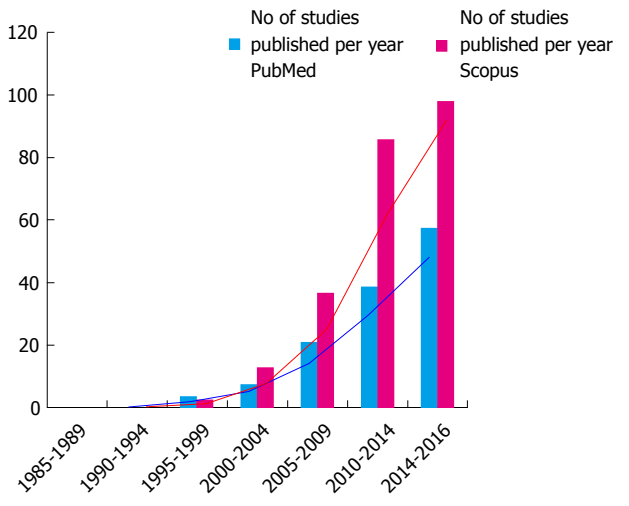

Figure 1 An increasing number of studies about stem cell use in cartilage disorders is published, especially in the last decade.

proposed. Specifically, it was found that mechanical load increases in ACL-deficient knees result in recruitment of additional osteoclasts at the subchondral bone. This leads to activation of TGF-beta1 that assists in recruitment of MSCs that causes atypical subchondral bone formation, a potential initial step in the osteoarthritic pathogenetic cascade[16].

Cell to cell and cell to extracellular matrix interactions are important in the mechanical environment of the joint for suitable response to injury or degeneration. Stem cells appear to play a major role in these interactions with numerous applications in both therapeutic strategies but also in the design of tissue-engineered scaffolds. A recent study demonstrated that interactions of N-cadherin in MSCs could modify the perception of the mechanical properties of the microenvironment, and thus, generate corresponding response of stem cells towards proliferation and differentiation[17]. Furthermore, mechanical stimuli including tension stimulation can result in significant improvement of the functional properties of tissue-engineered human cartilage that could be used for replacing chondral defects[18].

Update on clinical studies

The initial reports for the use of autologous bone marrow-derived MSCs for focal cartilage defects used marrow obtained from the iliac crest and, *via* a subsequent surgery using an open approach, the stem cells were injected into the defect with a periosteal cover sutured on top of the lesion. In the first study, two patients with patellar cartilage defects underwent treatment with MSCs. Significant improvement in pain and functional outcome was maintained for at least 4 years after surgery[19]. In a case report involving a patient with a defect of the medial femoral condyle, autologous transplantation of bone marrow derived MSCs was also associated with improved outcome. Second-look arthroscopy revealed full coverage of the lesion 7 mo after surgery with hyaline-like cartilage as well as significant improvement in clinical symptoms. However, MRI showed irregularities of the repair tissue[20]. The favorable outcome of autologous bone-marrow derived MSCs for cartilage defects at the patellofemoral joint was confirmed by another report of three cases demonstrating clinical improvement in kissing lesions which are usually more challenging to treat[21].

In recent years, as arthroscopic techniques have evolved, all-inside arthroscopic techniques for cartilage repair using MSCs developed with favorable outcome. In a case report, after microfracture, a collagen membrane that was immersed in bone marrow derived MSCs were secured with fibrin glue. MRI imaging at 12 mo demonstrated filling of the cartilage defect, while the patient remained asymptomatic until at least 24 mo[22]. In addition, single stage arthroscopic techniques were also described. In a prospective study, 30 patients with cartilage defects at the knee joint were treated using a combination of microfracture and subsequent application of a mixture gel containing bone marrow aspirated cells, hyaluronic acid (HA), and fibrin. A significant improvement was recorded with an improvement in Lysholm score from 50.8 to 80.1 and subjective IKDC from 39 to 83 preoperatively and postoperatively, respectively[23]. An analogous technique where bone marrow-derived cells were mixed with collagen powder or HA membrane and platelet gel was used for osteochondral defects of the talus[24]. In these patients, a significant improvement in the AOFAS score was recorded with an increase from 64.4 to 91.4, preoperatively to postoperatively, respectively[24]. Furthermore, using bone marrow cells aspirated from the iliac crest, isolated *via* centrifugation and embedded in a HA membrane, 20 patients with chondral defects at their knee experienced significant improvement in pain and function[25]. Both MRI and histological analysis confirmed the presence of regenerated cartilaginous tissue[25]. Nine patients with focal cartilage defects were treated with microfracture supplemented with coverage of a polyglycolic acid/hyaluronan matrix membrane with autologous bone marrow concentrate cells. A significant improvement in IKDC, Lysholm and Tegner scores was reported at 22 mo follow up[26]. The recent advancements in the field have allowed for the successful combination of autologous stem cells with therapeutic interventions already employed in cartilage repair.

When evaluating studies that compared outcomes with or without stem cell augmentation, promising findings are reported. The first attempt to compare clinical outcome between patients treated with autologous chondrocyte implantation and patients treated with autologous bone marrow-derived MSCs, showed that bone marrow MSCs could be equally effective as chondrocytes for focal cartilage lesions. Indeed, both groups demonstrated significant improvement postoperatively with no statistical difference between the groups in Lysholm IKDC and Tegner activity scores[27]. In a comparative study for patellofemoral chondral lesions, 18 patients were treated with bone marrow cells embedded in a biodegradable HA-based scaffold while 19 patients were treated with matrix-

induced autologous chondrocyte implantation (MACI). At 2 year follow up, both groups showed a significant improvement in clinical outcome and pain scores, but bone marrow aspirate concentrate treated patients had significantly better subjective IKDC score[28]. In another study that combined therapeutic approaches, two different techniques using marrow derived MSCs were compared. One combined microfracture with subsequent injection of MSCs with HA. In the other group, MSCs were seeded in a periosteal patch that was sutured over the cartilage defect. Both groups showed improvement postoperatively with a trend towards better outcome for the MSC/HA group[29]. Combination of intra-articular injections of autologous bone marrow-derived MSCs and HA 3 wk after microfracture and medial opening-wedge high tibial osteotomy in 28 patients resulted in approximately 7.6 added improvement for IKDC and Lysholm scores compared to HA injections alone. In this randomized controlled trial an improvement in Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score at 1 year was also seen[30]. Further improvement in the current armamentarium against cartilage defects has leads to technical adaptations that explore the potential use of autologous MSCs instead of primary chondrocytes. The above findings suggest that the use of MSCs result in analogous - if not better - outcomes.

Several carriers have also been successfully used recently for autologous MSCs. In a case series, platelet rich fibrin glue was successfully used as a cell carrier for autologous bone marrow derived MSCs that were subsequently sutured with a periosteal flap. All five patients experienced improvement in clinical scores, while second look arthroscopy performed in two patients demonstrated good integration and healing of the repair area[31]. A type I collagen scaffold was used as a carrier for autologous MSCs in two patients with periosteal graft sutured on top. Both KOOS and IKDC score improved significantly postoperatively at 30 mo follow up[32]. In a pilot clinical study application of a poly-ethylene glycol diacrylate (PEGDA) hydrogel biomaterial after microfracture in 15 patients was compared with the outcome of microfracture alone in three patients. It was suggested that pain was improved in the biomaterial group, however, additional data are necessary before making safe conclusions[33].

Finally, a recent randomized trial used allogeneic MSCs for patients with osteoarthritis. It was suggested that allogeneic bone marrow MScs resulted in improvement in pain, quality of life and cartilage quality as evaluated by MRI compared to HA[34]. Based on these promising data, use of allogeneic bone marrow MSCs may be a viable solution for focal cartilage lesions in some patients.

ADIPOSE AND SYNOVIAL DERIVED STEM CELLS

Update on basic science

Since their identification as a potential source of cartilage matrix molecules, adipose derived MSCs (ADSCs) have become a valuable source in several models for cartilage regeneration[7,35]. A primary advantage of ADSCs is their abundance and the relative ease of obtaining cells from the patient[14,36]. Another advantage of ADSCs is that they have been demonstrated to have a prominent chondro-inductive effect. As shown in an *in vitro* co-culture model, the combination of articular chondrocytes with ADSCs resulted in a two-fold increase in GAG content and increased collagen II gene expression[37].

Expression of pro-chondrogenic genes in ADSCs *via* adenovirus-mediated gene transfer of TGF beta2 could lead to ectopic neocartilage formation, while recently a combined expression of IGF-1 and FGF-2 in ADSCs demonstrated a synergistic effect towards enhanced chondrogenic differentiation[38,39]. Towards this direction, poly lactic-co-glycolic acid) (PLGA) nanoparticles that deliver a specific plasmid of bone morphogenetic protein 4 (BMP-4) into rabbit ADSCs significantly enhanced chondrogenesis and appear to benefit cartilage repair *in vivo*[40].

Concerns about the degree of stemness of ADSCs have been raised since ADSCs demonstrate an inferior chondrogenic potential when compared to BMSCs[41]. Indeed, ADSCs may need specific conditions to chondro-differentiate and this process may require a prior step of pre-differentiation[42]. However, the immunosuppressive effect and the chondroprotective role of ADSCs should not be underestimated. In a mice model of osteoarthritis injection of ADSCs resulted in inhibition of cartilage destruction and synovial thickening[43]. Similarly, in a rabbit model, intra-articular injections of ADSCs delayed the progression of osteoarthritis and meniscus damage *via* inhibition of metalloproteinase and TNFa expression[44]. In one study performed in a rat OA model, fluorescein-labeled ADSCs were injected into an arthritic knee joint and were detectable *via* non-invasive bioluminescence imaging for up to 10 wk post-injection. Histological analysis confirmed that injected cells were present and proliferating in synovial, meniscal, and articular cartilage tissues. Furthermore, ADSC-treated rats showed a significantly increased O'Driscoll histological score, suggesting a chondro-protective or regenerative effect from these cells[45]. Additional research is needed to better understand the protective or reparative mechanism of ADSCs. Recently, a similar role in chondroprotection has been demonstrated for synovial derived MSCs[46].

Update on clinical studies

Interest in ADSCs increased considerably after a case series reported that patients that received intra-articular injection of ADSCs had reduced pain and improved knee function[47,48]. In humans, ADSCs have been used in intra-articular injections since 2011. To date, eleven studies have been recorded. ADSCs have been isolated either from the abdominal area, buttocks, or infrapatellar fat pad. In all studies, ADSC injection showed improved clinical outcome in terms of reduced pain and

improvement in functional scores. Data obtained from MRI at 6 mo showed promising data suggesting cartilage regeneration[47]. Also, macroscopic appearance from second-look arthroscopy showed hyaline-like cartilage with smooth surface[47]. Finally, histology in a specimen obtained also confirmed characteristics of hyaline cartilage. Unfortunately, there are some disadvantages in these clinical studies. First, most are case reports without a control group. Another limitation is the fact that in most cases an additional therapeutic intervention was simultaneously performed[49]. High-level of evidence studies are necessary in order to confirm the promising results of the clinical cases described.

In a randomized single blinded study evaluating only 14 patients synovial mesenchymal cells were used in a matrix collagen membrane and were compared with matrix autologous chondrocyte implantation[50]. Functional outcomes were similar between the two groups, while mesenchymal cells were reported to have better outcome in certain outcomes, such as KOOS score[50].

Synovial MSCs, cultured in autologous human serum, arthroscopically implanted in 10 patients with single cartilage defect showed promising results[51]. Specifically, synovial cells were harvested and were cultured in autologous human serum[51]. At 3-year follow up, improved MRI features and Lysholm score were reported, however no benefit was seen in Tegner activity level[51].

Another type of stem cells used in clinical studies is the autologous peripheral blood progenitor cells (PBPCs). Specifically, one week after arthroscopic drilling of a cartilage defect, 8 mL of PBPCs were injected at the knee together with 2 mL of HA[52]. Articular cartilage biopsies in five patients showed the presence of hyaline cartilage[52]. Clinical outcomes from the same group have been reported in a randomized study that compared the outcomes in patients that underwent subchondral drilling and subsequent HA injections with and without PBPCs[53]. It was shown that the presence of PBPCs did not result in better clinical outcome (IKDC scores of 74.8 *vs* 71.1 for PBPC and no PBPC group, respectively). However, PBPC group exhibited better histologic and MRI scores compared to control[53].

OTHER TYPES OF STEM CELLS

Other types of stem cells have been proposed as potential candidates for cartilage repair treatment. In a recent animal model, weekly injections of embryonic MSC-derived exosomes demonstrated restoration of osteochondral defects and presence of hyaline cartilage[54]. Chondrocytes have also been demonstrated to adopt stem cell-like characteristics when cultured under specific biochemical and mechanical conditions[55]. In this study, dedifferentiated chondrocytes were found to be highly proliferative and chondrogenic, making them an attractive source for cartilage repair. Additional research should identify additional progenitor cell populations that may be used in cartilage repair and should focus in further characterizing their properties.

CRITICISM

Autologous MSCs have demonstrated potential in the repair of cartilage defects, and that lead to an increased interest has been expressed for the use of stem cells in cartilage lesions (Figure 1). However, an analysis of these studies in terms of level of evidence shows that less than 10 studies are randomized and approximately 15 studies have a control group. Additional randomized controlled clinical studies are necessary to determine whether isolated MSCs or ADSCs offer any benefits over traditional marrow stimulating techniques such as microfracture. Furthermore, long-term follow-up with MRI or second-look arthroscopy will be critical for determining the durability of repair tissue generated by MSC implantation, particularly before utilizing these techniques in younger, active patients.

The use of MSCs is not without clinical limitations or disadvantages. Cost of stem cell preparation represents an unknown factor that needs to be included in the equation of their application. Detailed cost effectiveness studies are needed to clarify the potential benefit for their use in comparison to the current strategies for cartilage repair. Moreover, the use of autologous MSCs has a certain amount of donor morbidity. Iliac crest marrow aspiration has been associated with chronic pain, dysesthesia, potential wound drainage and scaring[56]. These complications are relatively minor and occur rarely, but it is important to establish a better understanding of the potential problems that are associated with stem cell use, as these techniques become more popular. For adipose and synovial derived MSCs donor morbidity is significantly less, but future studies should focus on potential withdraws for their use as well. Finally, the use of allogeneic MSCs in co-culture systems could offer a potential solution, but again, additional research should determine whether the potential risk of immune response related complications outweighs their benefits[14].

From a basic science perspective, the mechanisms underlying chondrogenic differentiation of MSCs and subsequent matrix production require elucidation. As it stands, the quality of repair tissue generated by marrow stimulation is known to be mechanically inferior to native articular cartilage. It may be the case that disruption to the subchondral plate contributes to this phenomenon, and implantation of autologous MSC or ADSC could circumvent this issue.

FUTURE PERSPECTIVES

The success of autologous MSC implantation is dependent on determining their benefit over simpler techniques such as microfracture. Studies will also be necessary to determine which delivery method is most appropriate. An appealing aspect of MSC implantation

is that it has the potential to be performed in a single surgical procedure. However, MSCs can also be isolated at an earlier time point and pre-differentiated prior to implantation. Studies comparing the efficacy of the multitude of cell delivery techniques are necessary to determine a standard of care.

A lot of interest has been focusing in the filed of lubricin expression from MSCs[57,58]. This potential may indicate that tissue engineering of cartilage from stem cell sources could ensure the presence of lubricin in the superficial cartilage[59].

Finally, effective application of stem cells appears to be linked with the presence of primary cells, and the interactions between primary chondrocytes and MSCs may worth to be examined further. This is an attractive field that may attract a lot of interest since recent work have shown that endogenous stem cells may have the capacity for cartilage repair and regeneration[55,60]. Additional research is also necessary to incorporate the advances in the field of tissue engineering and explore the potential of capitalizing the benefit from combining successful approaches from basic science to clinical practice.

CONCLUSION

Over the recent years, a growing number of studies arise in the field of MSCs use in cartilage repair, building a progressively stronger foundation for their clinical applications. With the assistance of basic science, a better understanding of their exact role in cartilage physiology is established. New studies initiate to demonstrate the critical role of MSCs in the initial steps of cartilage degeneration, opening a new horizon full of possible alternative methods to address the complicated problem of cartilage repair and regeneration. Clinical work has shared valuable data that confirm their effectiveness as an alternative cell source for cartilage repair. More importantly, recent clinical findings revealed the advantages and disadvantages of each type of MSCs signifying the importance of combining chondrocytes with different types of stem cells. The effective combination of different treatment approaches showed that careful selection of the treatment plan should be based on the characteristics of the patient.

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MINIREVIEWS

New insights in the treatment of acromioclavicular separation

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Abstract

A direct force on the superior aspect of the shoulder may cause acromioclavicular (AC) dislocation or separation. Severe dislocations can lead to chronic impairment, especially in the athlete and high-demand manual laborer. The dislocation is classified according to Rockwood. Types Ⅰ and Ⅱ are treated nonoperatively, while types Ⅳ, Ⅴ and Ⅵ are generally treated operatively. Controversy exists regarding the optimal treatment of type Ⅲ dislocations in the high-demand patient. Recent evidence suggests that these should be treated nonoperatively initially. Classic surgical techniques were associated with high complication rates, including recurrent dislocations and hardware breakage. In recent years, many new techniques have been introduced in order to improve the outcomes. Arthroscopic reconstruction or repair techniques have promising short-term results. This article aims to provide a current concepts review on the treatment of AC dislocations with emphasis on recent developments.

Key words: Acromioclavicular dislocation; Rockwood classification; Coracoclavicular ligament reconstruction; Hookplate; Arthroscopically assisted acromioclavicular reconstruction; Weaver and Dunn procedure; Conoid and trapezoid ligaments

Core tip: Current literature suggests that the decision for treatment of type Ⅲ injuries should be made on a case-by-case basis, with an emphasis on initial nonoperative treatment. Early operative treatment for grades Ⅲ-Ⅵ dislocations may result in better functional and radiological outcomes than delayed surgery. There are numerous surgical techniques presented in the literature. The authors prefer an autograft tendon reconstruction of the coracoclavicular joint without bone tunnels in combination with direct suture fixation of the acromioclavicular joint. Arthroscopic techniques are evolving but there is currently

no evidence to support arthroscopic over open surgery.

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INTRODUCTION

The interest in acromioclavicular (AC) joint injuries dates back to the time of Hippocrates (460-377 BC) and Galen (129-199 AD)[1]. These ancestors already noted the difficulties in correctly diagnosing and treating this type of injury. Naturally, many developments have been made since then. New insights have led to the introduction of numerous treatment techniques during the past few decades[2]. However, to date, much controversy still exists, and the optimal treatment is not available yet. Moreover, the best timing of surgery remains a topic of debate. This current concepts review aims to provide an up-to-date and evidence-based overview of relevant treatment options for AC joint dislocations, with special emphasis on most promising recent techniques.

Etiology

AC joint dislocations are common injuries among an athletic population. They account for approximately 12% of injuries of the shoulder girdle. The patient is typically male, < 30 years of age and involved in (contact) sports[3]. The typical trauma mechanism is a force that depresses the shoulder girdle, such as occurs during a fall from a cycle or during a collision in contact sports. The force depresses the scapulohumeral complex (rather than the clavicle being elevated), resulting in tears of the AC ligament and the coracoclavicular (CC) ligaments. Associated shoulder injuries are present in 18% of patients with type Ⅲ to Ⅴ dislocations; superior labral anterior posterior (SLAP) lesions being the most common[4].

Anatomy

The AC joint is a diarthrodial joint, consisting of a thin cartilage surface and an interposed fibrocartilaginous meniscoid disk. The joint capsule or AC ligament (*i.e.*, thickenings in the capsule) and the extracapsular CC ligaments provide static stability. Physiologic forces and the weight of the arm place significant translational forces in the vertical, anteroposterior and axial planes of the AC joint. Based on cadaveric studies, the AC ligaments contribute 20% to 50% of resistance to superior migration and 90% to anterior-posterior translation. The CC ligaments are formed by the conoid medially and the trapezoid laterally. They are the primary restraint to inferior and medial translation of the scapulohumeral complex in relation to the clavicle[5]. The conoid ligament is attached proximally on the posteromedial undersurface of the clavicle, typically 4.5 cm from the AC joint (47.2 mm in men and 42.8 mm in women)[6]. It tensions under loads that force the clavicle superiorly (or the scapula inferiorly). The trapezoid attaches proximally on the anterolateral aspect of the inferior clavicle, approximately 2.5 cm from the joint (25.4 mm in men and 22.9 mm in women)[6]. It tensions under medialization of the scapulohumeral complex, *i.e.*, compression of the AC joint. The delto-trapezial fascia provides dynamic stabilization to the AC joint, especially the anterolateral deltoid insertion.

Symptomatology

Patients commonly present with pain at the AC joint, following a trauma such as a fall on the shoulder. The pain is often accompanied by soft tissue swelling as well as a prominent lateral clavicle. Because of the pain, shoulder motion is reduced and patients are limited in their daily and athletic activities. Chronic instability of the AC joint can lead to tremendous impairment of shoulder function including muscle fatigue, scapular dyskinesia, subjective sensation of heaviness of the injured upper limb, and painful horizontal adduction[7].

DIAGNOSIS

The history and physical examination often provide clues to the diagnosis. The patient frequently reports a fall on the shoulder or a collision and has pain localized at the AC joint and often the trapezius muscle (pars ascendens). The patient may also note a swelling, which can be confirmed on physical examination. The patient is examined while standing or sitting. On inspection, a high lateral clavicle can be seen, compared to the uninjured side. The AC joint is tender on palpation. One should compare with the uninjured side. The shoulder range of motion is usually reduced because of the pain in the acute phase. The examiner should check the stability of the AC joint in the superior-inferior and anterior-posterior directions. For types Ⅲ and Ⅴ, the joint feels unstable when the lateral clavicle is depressed manually ("piano key" phenomena). The shoulder is passively adducted in the horizontal plain to test anterior-posterior stability[8] (Figure 1). Chronopoulos *et al*[8] reported a sensitivity of 77% for the cross body adduction test, 72% for the AC resistance test and 41% for the active compression test; the combination of all 3 tests showed a specificity of 95%.

Standard radiographs of the shoulder are obtained, including a true anterior-posterior view, a scapular Y lateral view, an axillary view (or Velpeau view modification if unable to abduct the arm), and a Zanca view of the AC joint (performed by tilting the X-ray beam 10° to 35° toward the cephalic direction and using only 50% of the standard shoulder anteroposterior penetration strength) (Figure 2). It may be useful to obtain radiographs of the opposite side for comparison. A bilateral Zanca view visualizes the ipsilateral and contralateral AC joints on one

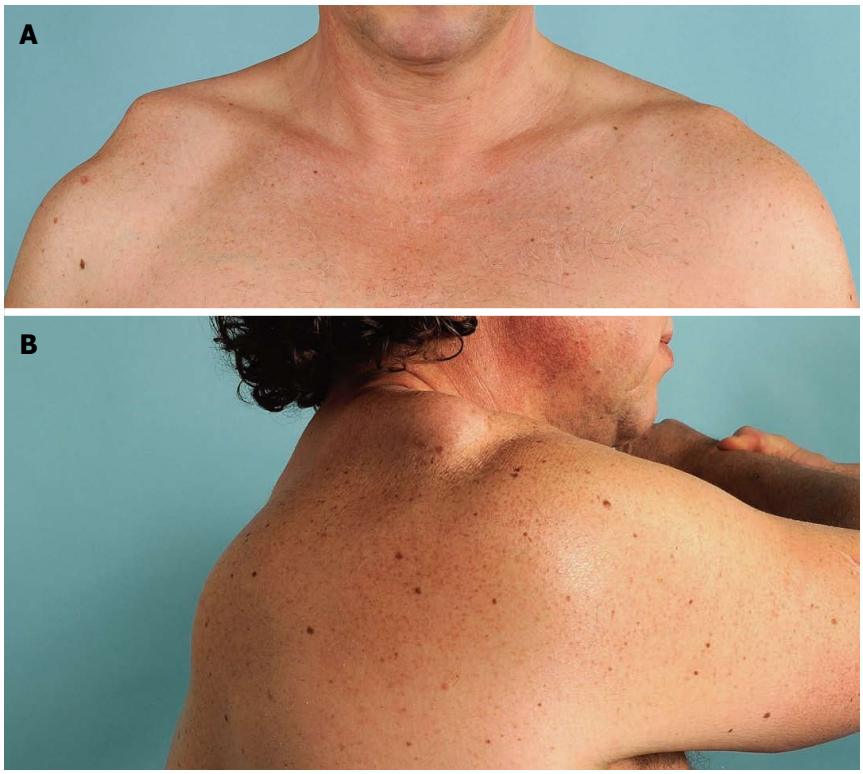

Figure 1 Digital pictures of a patient with a type-V acromioclavicular dislocation. A: Anterior view; B: Lateral view: The shoulder is passively adducted in the horizontal plain to test horizontal stability. Note the horizontal instability in this case.

X-ray cassette, while the same orientation of the beam is maintained[9] (Figure 2). In addition, a cross-body adduction radiograph may differentiate between a stable and unstable AC joint by assessment of the degree to which the clavicle overlaps the acromion[10]. The additional value of stress views with distal traction by weights on the arms is questionable. More precise imaging techniques, such as computed tomography or magnetic resonance imaging, are normally unnecessary, unless associated injuries are suspected.

The radiographic images are assessed on the relation between acromion and clavicle, as well as the CC distance, ideally comparing left and right. Associated injuries of the shoulder girdle must be ruled out.

CLASSIFICATION

Rockwood has made a classification that is used the most widely nowadays (Figure 3)[11,12]. In type Ⅰ, neither AC nor CC ligaments are disrupted. In type Ⅱ, the AC ligament is disrupted and the CC ligament is intact (50% vertical subluxation of the distal clavicle). In type Ⅲ, both ligaments are disrupted. In type Ⅳ, the ligaments are disrupted and the distal end of the clavicle is displaced posteriorly into or through the trapezius muscle. An axillary radiographic view is particularly helpful in identifying type Ⅳ injuries. In type Ⅴ, the ligaments and muscle attachments are disrupted, and the clavicle and acromion are widely separated. In type Ⅵ, the ligaments are disrupted, and the distal clavicle is dislocated inferior to the coracoid process and posterior to the conjoint tendon. Type Ⅵ lesions are extremely rare but do occur[13]. Reproducibility and interobserver reliability of the classification is only moderate and is likely limited by the inability of a classification based on plain radiographs to fully assess a soft tissue injury[14].

In practice, the difference between type Ⅲ and Ⅴ can be subtle and confusing. There is no clear definition or consensus on how to differentiate between these types. A suggested definition is 25% to 100% superior displacement of the distal clavicle in type Ⅲ dislocations and 100% to 300% displacement in type Ⅴ[15,16]. Others describe more than 100% clavicle displacement in type Ⅲ and more than 300% displacement in type Ⅴ[7]. The CC distance can also be used to differentiate between the two types (CC distance 20% or 25% to 100% of contralateral side in type Ⅲ; CC distance more than 100% of the contralateral side in type Ⅴ)[7].

The International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS) Upper Extremity Committee has made a subdivision of type Ⅲ dislocations in order to better identify patients who would benefit from surgery[15]. Type ⅢA is defined as a stable AC joint with normal scapular function and no overriding of the clavicle on the cross-body adduction view. Type ⅢB is defined as unstable with scapular dysfunction and an overriding clavicle on the cross-arm adduction view. However, it is unclear to what extent this subdivision predicts treatment outcomes.

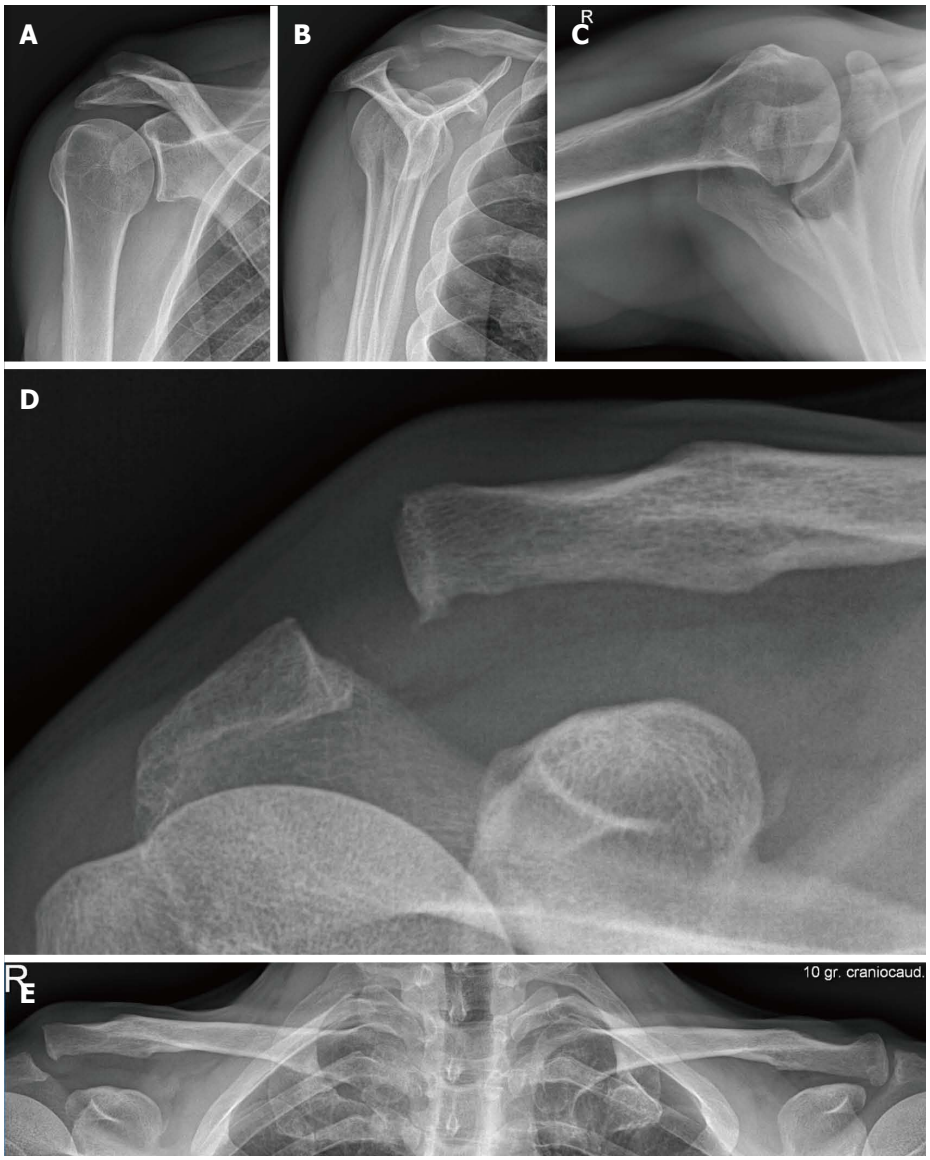

Figure 2 Standard radiographic series of the shoulder. A: A true anterior-posterior view; B: Scapular Y lateral view; C: Axillary view; D: Zanca view; E: In case of acromioclavicular separation, a bilateral Zanca view can be useful.

TREATMENT

There is general agreement that types Ⅰ and Ⅱ injuries should be treated nonoperatively in all cases[2]. Most authors suggest that types Ⅳ, Ⅴ and Ⅵ should be treated operatively[5,7]. In contrast, type Ⅲ separations have caused much debate during the past decades. In the past, many type Ⅲ lesions were treated surgically. However, it has turned out that there is no clear superior outcome after surgical treatment[17,18]. Operative treatment of type Ⅲ is sometimes reserved for high-demand laborers and athletic patients[17]. Most surgeons now generally agree that nonoperative treatment is indicated initially in all patients with type Ⅲ injuries; if unsuccessful, operative reconstruction of the AC and CC ligaments can be provided at a later stage[19,20].

Nonoperative

Nonoperative treatment is indicated for types Ⅰ and Ⅱ dislocations and consists of temporary immobilization with a sling or collar and cuff for 1 to 3 wk. Early range-of-motion exercises are encouraged. Daily and athletic activities are resumed when the pain permits. Heavy lifting and contact sports are usually postponed until 6 wk. Unsatisfactory outcomes in conservative treatment may be explained by persistent instability, especially a horizontal component of instability[21].

Open surgery

Numerous surgical repair or reconstruction techniques have been published. In 2013, the number of different surgical techniques described was 162[2]. These techniques can basically be grouped in four categories: (1) Fixation of the AC and/or CC with hardware including screws and K-wires; (2) hook plates; (3) fixation of the CC with suture buttons; and (4) reconstruction of the CC ligaments with autograft or allograft tendon[16]. Whichever construct is used, it needs to maintain the

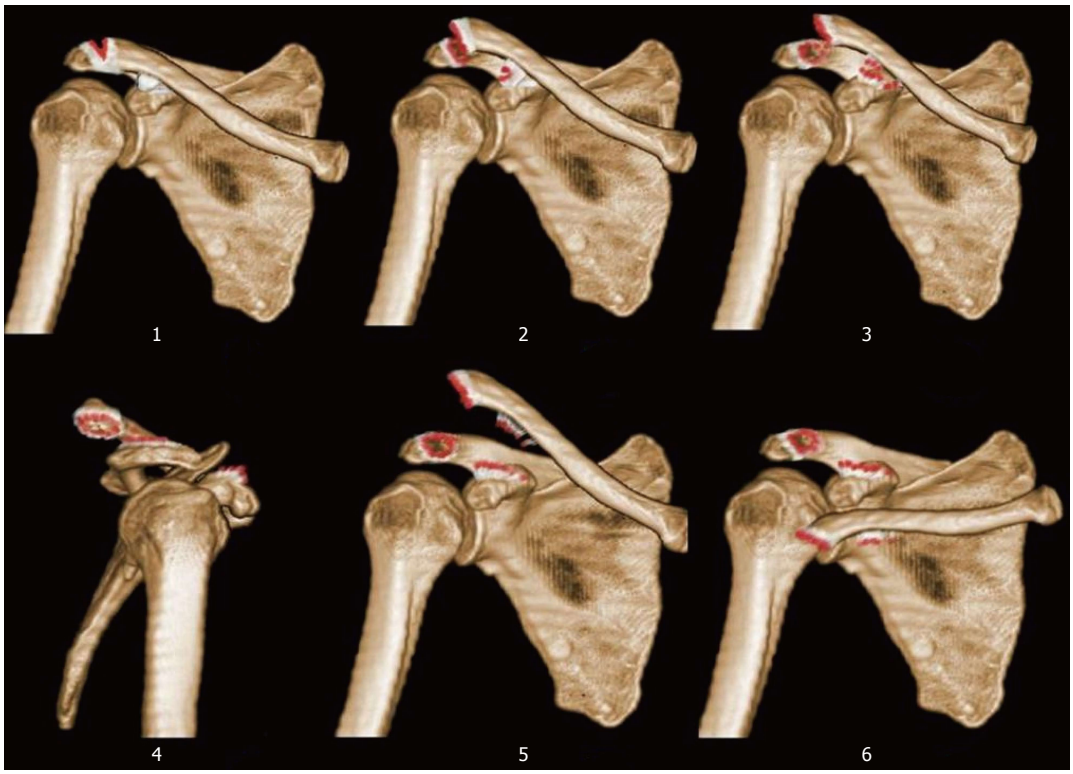

Figure 3 Rockwood classification (Case courtesy of Dr Roberto Schubert, Radiopaedia.org, rID: 19124).

reduction long enough for the biological healing process to be able to take place.

Hardware fixation: Previously, temporary trans-articular K-wire fixation of the AC joint has been used in combination with direct ligament repair. However, this technique has led to unsatisfactory outcomes, including K-wire breakage, migration and loss of reduction[7]. Likewise, CC cerclage or screw fixation such as the Bosworth screw have led to unacceptable risk of screw breakage[10]. Some remove the screw after 6 to 8 wk to avoid this complication. Even with adequate screw positioning, hardware failure and obligatory screw removal have decreased the popularity of this technique.

Hook plate fixation: The hook plate is a metal device that keeps the AC joint in a reduced position by hooking its tip under the acromion and fixing it to the clavicle with screws[18]. It can be used alone or in conjunction with other methods of ligament repair.

The joint separation is either reduced and then the hook plate is positioned, or the hook plate is inserted with the hook under the posterior aspect of the acromion and then pushing the plate segment against the distal end of the shaft of the clavicle, in that way levering the clavicula downwards. Most of the time the 4-hole (shortest) hook plate can be used. Either the hook can be adjusted to the morphology of the acromion or the plate can be adjusted to the morphology of the distal clavicle.

The advantage of this technique is that it provides a strong and stable construct. There are case series that report acceptable results of hook plate fixation[22,23]. A disadvantage is that the plate crowds the subacromial space, causing subacromial impingement, rotator cuff lesions, and even acromial stress fractures due to the hook[24]. The hook makes a pinpoint contact with the undersurface of the acromion, which might explain why complications commonly occur after hook plate fixation[25]. Furthermore, pain or discomfort is experienced because of the hardware[16]. Because of these reasons, removal of the plate is routinely required after 3 to 4 mo, making a second operation necessary[18,22,23]. This in turn can lead to loss of reduction[22,23].

The Canadian Orthopaedic Trauma Society recently completed a multicenter-randomized clinical trial involving hook plate fixation *vs* nonoperative treatment of 83 AC dislocations[18]. Disability and Constant scores were better in the nonoperative group after 3 mo but the differences disappeared at 1 and 2 years. In contrast, radiographic reduction was better in the operative group at all time points but there were more complications and reoperations in this group[18]. The necessity of implant removal, uncertain superiority over nonoperative management, and the higher incidence of complications are important considerations of hook plate fixation.

Suture button CC fixation: Suture buttons have been introduced as an alternative to simple suture fixation to anatomically repair the CC ligaments. These devices consist of two metal buttons that are connected by thick nonabsorbable sutures. The buttons are locked behind

the clavicle and coracoid drill holes and the sutures function as the CC ligaments[16,26]. Biomechanical studies have shown that suture buttons have comparable biomechanical strength as compared to the native ligaments[26,27].

The technique has the advantage of allowing minimally invasive implantation as well as sustaining some range of motion between clavicle and scapula. However, single CC suture button fixation has appeared to be biomechanically inferior to the native CC ligaments *in vivo*[26]. The single-button technique has resulted in high failure rates due to knot slippage, suture breakage, button migration, fractures[28-30] and large or misdirected drill holes[29] as well as failure to address the AC joint capsule[31-33]. Because of high rates of failure with the use of single buttons, the use of multiple suture buttons is now advocated to restore both the conoid and trapezoid ligaments (improving horizontal and vertical instability) and reduce the failure risk[26]. For example, Struhl and Wolfson[34] used a mini-open technique with a continuous loop double endobutton in combination with a lateral clavicle resection. Recently, these authors have added a figure-of-8 ultratape suture through drill holes in the acromion and clavicle to directly augment AC joint stability[34].

Suture button fixation has several advantages, particularly the ability for minimal soft tissue disruption and generally satisfactory outcomes. However, caution should be used as these constructs have been associated with remaining anterior-posterior instability and a risk of hardware issues[35]. Suture button fixation has higher shoulder function scores and lower postoperative pain when compared to hook plate fixation; however, there are higher complication rates[36].

CC ligament reconstruction: The Weaver and Dunn procedure was first described in 1972 and utilizes the native coracoacromial (CA) ligament in AC joint reconstructions. This technique involves the distal clavicle excision in combination with transfer of the CA ligament from the acromion to the distal clavicle remnant in an attempt to restore AC stability[37]. The procedure has been studied extensively, demonstrating up to a 30% failure rate and only approximately 25% biomechanical strength when compared to intact CC ligaments[16,38]. The modified procedure supplements the ligament transfer with a direct CC fixation or hook plate[38,39]. There are a few studies that reported inferior results of the modified procedure compared to anatomic CC ligament reconstruction technique using autogenous semitendinosus graft[40-43].

The utilization of autograft or allograft for the anatomic reconstruction of the CC and AC ligaments in acute AC joint dislocation has rapidly gained popularity in the past few decades. In 2003, Lee *et al*[42] biomechanically compared the strength and stiffness of the native CC ligament with that of reconstructions with CA ligament or free tendon grafts. They reported that tendon grafts had strengths equivalent to the native CC ligament strength, and were significantly stronger than the CA ligament reconstruction.

There are numerous techniques to reconstruct the CC ligaments. Mazzocca *et al*[38,44] used a semitendinosus autograft to reconstruct the anatomical configurations of the trapezoid and conoid ligaments, as well as the AC ligaments, without use of supplemental CC or AC stabilization. With this technique, the lateral 1 cm of the clavicle is excised. A soft-tissue tunnel is created under the coracoid. Two bony tunnels are drilled in the clavicle; one 4.5 cm from the AC joint (positioned slightly posteriorly to reconstruct the conoid ligament) and one 2.5 cm from the AC joint (positioned slightly anteriorly to reconstruct the trapezoid ligament). The graft is passed through the tunnels in a figure-of-eight fashion, and fixed proximally using interference screws while the AC joint is reduced with upper displacement of the scapulohumeral complex. Finally, the lateral limb of the graft is sutured to the acromion to reconstruct the AC ligament.

We use an autograft tendon reconstruction technique of the CC joint without bone tunnels in combination with direct suture fixation of the AC joint (Figure 4). The semitendinosus tendon is harvested. A Sabelhouw incision is made and the lateral clavicle is resected. A double nonabsorbale suture is passed through small drill holes in the lateral clavicle and the acromion for AC joint repair. The coracoid process is exposed through the deltopectoral interval. The semitendinosus tendon is directed under the coracoid and over the clavicle for CC joint repair (it is passed from the medial aspect of the coracoid to the posterior aspect of the clavicle to mimic the conoid ligament and from the lateral aspect of the coracoid to the anterior aspect of the clavicle to mimic the trapezoid ligament). The AC joint is reduced by elevation of the arm, the AC joint sutures are tightened, and the semitendinosus is secured with interrupted nonabsorbable sutures over the clavicle. Advantages of this technique without bone tunnels or interference screws are low costs, avoidance of iatrogenic fracture risk, no foreign body use (except for sutures), and the same biomechanical strength as anatomic repair with bone tunnels[45]. We have treated 23 patients with Rockwood type 4 or 5 lesions with use of this technique, of whom five were failures from elsewhere. All patients indicated that they would undergo the procedure again and were satisfied with the cosmetic outcome. They were able to participate in work and sports without restrictions. Two complications occurred; one patient had a temporary frozen shoulder and another had a recurrence due to a fall after 6 wk.

Arthroscopic surgery

Minimally invasive AC joint reconstruction and repair techniques have been developed since the introduction of arthroscopic shoulder surgery. Although arthroscopically assisted AC reconstruction should be used by skilled arthroscopists only, it has the possible advantages of the minimally invasive nature, direct visualization of

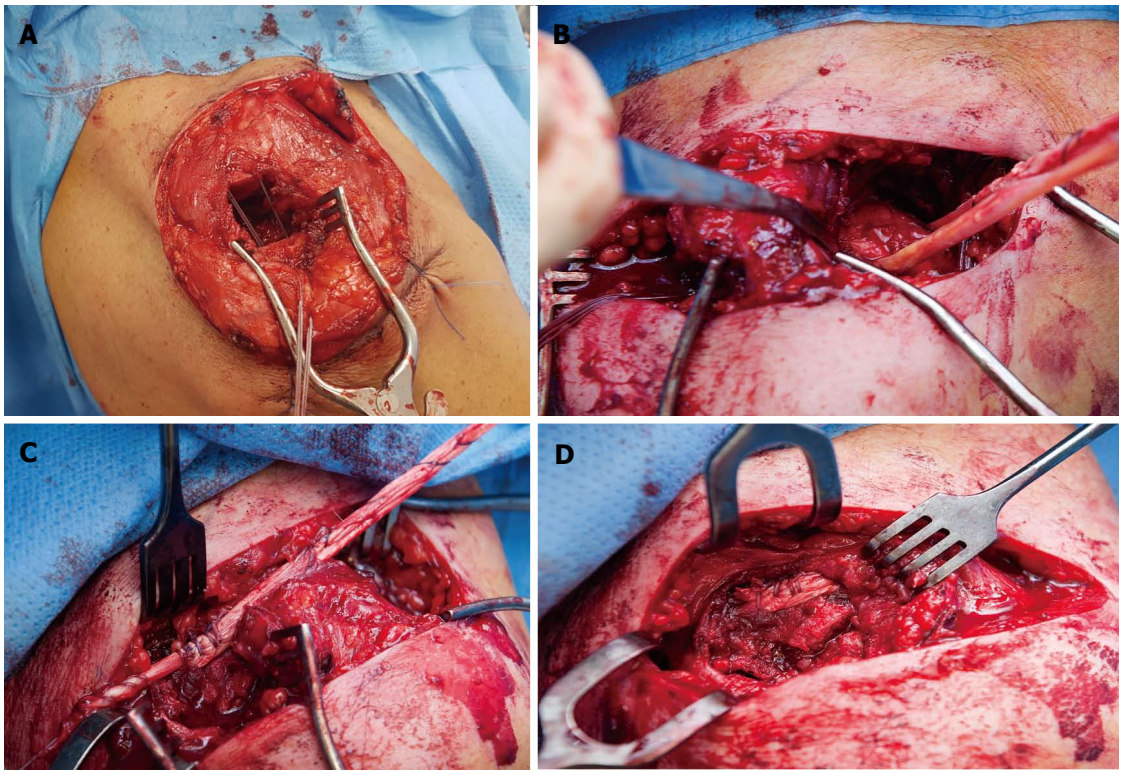

Figure 4 Intra-operative pictures of an autograft tendon reconstruction technique of the coracoclavicular joint without bone tunnels in combination with direct suture fixation of the acromioclavicular joint. A: The lateral clavicle is resected, and a double nonabsorbale suture is used for AC joint repair; B-D: A semitendinosus tendon is passed under the coracoid and over the clavicle for CC joint repair. AC: Acromioclavicular; CC: Coracoclavicular.

the reduction and placement of coracoid fixation, the possibility to address additional pathologies, and the deltotrapezial fascia can remain attached[46,47]. A further advantage of arthroscopic treatment is a diagnostic glenohumeral arthroscopic evaluation. Concomitant injuries are common in AC joint dislocations and may occur in up to 20%-25% of patients[47-49].

Suture button fixation is typically used with arthroscopically assisted AC repair. Initially, one button was used for repair. Murena *et al*[49] described arthroscopic treatment of type Ⅲ-Ⅳ acute AC dislocation with a double flip button. They found excellent clinical results in terms of Constant score (mean 97 points) and patient satisfaction, but a disappointing radiological result with a partial loss of reduction due to distal migration of the flip button within the upper third of the clavicle in one-fourth of the cases, at a mean follow-up of 31 mo. However, because of a high failure risk of one-button repair, either multiple suture buttons or augmentation techniques are used nowadays. An example of a multiple suture button technique is that by Imhoff *et al*[47]: Anatomic CC ligament reconstruction utilizing double Tight Rope (Arthrex Inc., Naples, FL, Italy) suspensory fixation. This dual anatomic technique aims to reproduce the native conoid and trapezoid ligaments. The surgical procedure is begun with a diagnostic shoulder joint arthroscopy, followed by arthroscopic preparation of the coracoid undersurface through the rotator interval. After a guided superior skin incision and AC joint reduction, the conoid and trapezoideal tunnels are drilled with use of a drill guide system. The two TightRope devices are inserted through the tunnels and fixated. The longest follow-up case series of double suture button fixation in 23 patients reported a high satisfaction rate (96%) after 58 mo but eight radiographic failures were noted[47].

An example of augmentation in arthroscopic-assisted reconstruction of AC joint instability is the technique by DeBerardino *et al*[46]: CC ligament reconstruction with an allograft augmented GraftRope (Arthrex Inc., Naples, FL, Italy) system. This technique utilizes an arthroscopically placed fixation with a GraftRope construct augmented with an allograft (or autograft) centrally. After glenohumeral joint arthroscopy, the subacromial bursa is debrided and the AC joint visualized. Joint reduction is checked with fluoroscopy. Following clearance of the coracoid base, the tunnel is drilled with use of a drill guide through a small incision over the clavicle. A semitendinosus or tibialis tendon is passed through the implant system before it is inserted with use of a passing suture. An interference screw is placed between the graft limbs for final construct fixation.

A technique to perform the Weaver-Dunn procedure in an all-arthroscopic way is described by Boileau *et al*[50] This procedure also starts with debridement of the undersurface of the base of the coracoid process through the rotator interval. Then the scope is moved to anterior, where the CA ligament is released from the acromion (with a chip of bone remained attached to the ligament). Thereafter, a lateral clavicle resection is performed, and the medullary canal of the clavicle is enlarged and deepened with a burr. Then, the CC reduction and

fixation is performed with use of a double-button system. Finally, the bone-ligament transfer of the CA ligament is pulled in the created cavity of the lateral clavicle and fixed through a second drill hole on the superior cortex. A mean follow-up of 36 mo is now available for a group of 57 patients[51]. Two patients experienced a recurrent dislocation and 6 patients a partial loss of reduction. The Subjective Shoulder Value ranged from 54% to 85%, and 96% of the patients were satisfied with the procedure and the cosmesis[51]. There are no randomized controlled trials comparing the outcomes of open *vs* arthroscopically assisted or all-arthroscopic techniques. Arthroscopic techniques in case series are relatively safe procedures, with equivalent outcomes to open surgery, but demonstrate a distinct complication profile[39,46,47,52-58]. Arthroscopic suture button techniques generally demonstrate good radiographic outcomes but significant hardware irritation.

Postoperative management

The rehabilitation programs differ between surgical techniques. In general, a sling is provided and progressive range-of-motion exercises up to 90 degrees elevation are begun early after surgery for 6 wk. After this initial period, range-of-motion and strengthening exercises are gradually increased. Non-contact sports can be resumed after 3 mo. Generally, contact athletes are allowed unrestricted sport activities after 6 mo.

TIMING OF SURGERY

Accurate reduction in AC dislocation is considered easier when surgery is performed earlier after injury[59,60]. However, there is no clear definition of early and delayed surgery. Rockwood and Young[12], have noted that acute pain generally disappears 2-3 wk after an AC dislocation. Therefore, approximately 3 wk seems a clinically relevant dividing line.

A recent review of Song *et al*[60] summarized eight studies comparing acute and delayed surgical treatment of AC dislocation. The dividing line between early and delayed surgery was defined as 3, 4 and 6 wk after injury. They concluded that early surgery (< 3 wk) has better reduction and clinical outcomes than delayed surgical treatment (> 3 wk) and no significant difference in the complication rate[60]. The studies included in this review used several different methods of reconstruction and this limits the strength of this conclusion.

Delayed surgery is necessary for patients with AC dislocations that failed conservative treatment or with intolerance for early surgical treatment. Adam *et al*[3] reported higher rates of deformity recurrence and poorer functional outcome in chronic cases. On the other hand, other studies report satisfactory results after surgical treatment of chronic AC dislocations[48,52,59,61].

In conclusion, early surgery for grade Ⅲ-Ⅴ dislocations may result in better functional and radiological outcomes, with a reduced risk of loss of reduction compared with delayed surgery[7,54,60]. However, a nonoperative trial period of 6 mo seems justified for type Ⅲ lesions, based on high satisfaction rates and normal functionality in 80% of patients[62]. For example, Rolf *et al*[63] treated patients early at a mean of 10, or delayed at a mean of 7.7 mo (after failure of conservative treatment).

OUTCOMES

Many shoulder scoring systems are used to determine functional outcomes in the literature. Unfortunately, none of these is specific for AC dislocations. In a review of eight studies, more than 30 shoulder scoring systems were applied[60]. This makes reliable comparison of studies difficult.

A Cochrane review in 2010 reported data from three studies (174 participants) and found no significant difference in movement, strength, or function between surgically and conservatively treated patients[64]. Another review in 2013, which specifically looked at Rockwood type Ⅲ AC dislocations in eight studies (247 participants), showed the objective and subjective shoulder function outcome was better in the operative group (especially in young adults), though the rate of complications and radiographic abnormalities were higher[17]. The rehabilitation time was shorter in the conservative group but the cosmetic outcome was worse.

AC dislocation is a typical sports related injury[65]. Therefore, resumption of sports and work are important outcome aspects. Recently, a retrospective review of Dunphy *et al*[66] showed that most patients (77%) were able to return to work following nonsurgical management of type Ⅴ injuries after six months but had limited functional outcome scores. Patients who are treated nonoperatively for a Rockwood type Ⅲ AC dislocation need roughly half the time to return to work and sport, compared with patients treated operatively[2,7,67]. Manual workers treated surgically returned to work after an average of 11 wk, compared with 4 wk after nonsurgical treatment[67]. Gstettner *et al*[68], however, reported that operative treatment of Rockwood type II AC dislocation resulted in more patients returning to the same level of activity at work (82% *vs* 63%). The level of sports did not differ (67% *vs* 65%). In Rockwood type Ⅴ, overhead athletes require more time to resume their sports activity[69]. In minimally invasive anatomic CC reconstructions of type Ⅲ AC dislocation, 100% return to sports rates has been reported; however, the influence of type of sport was not considered[56,70].

The main concern when comparing outcome data is the lack of long-term outcome studies. We performed a literature search of comparative studies with a minimum of 4 years of follow-up (Table 1). We found five studies and classified the operative techniques in the four categories described above[39,52-59]. There were one randomized controlled trial and four retrospective cohort studies. The studies described early and delayed treatment of type Ⅲ-Ⅴ dislocation, as well as different operative techniques. Generally, few statistically significant differences were found between the groups

Table 1 Characteristics of comparative studies with a minimum 4-yr follow-up

Ref.	Type of study	LE	Rockwood classification (No. of patients)	Operative technique (No. of patients)	Category[1]	FU (yr)	Outcome
Boström Windhamre *et al*[55] 2010	Retrospective case control	Ⅲ	Delayed type Ⅲ-Ⅴ (47)	Weaver-Dunn and PDS suture (23)	3	6.1	Constant score: $P > 0.05$ SPADI: $P \geq 0.05$
				Weaver-Dunn and hookplate (24)	2		QuickDASH: $P > 0.05$ VASa: $P = 0.03$ (in favor of PDS) Subluxation: $P > 0.05$
Kovilazhikathu Sugathan *et al*[56] 2012	Retrospective cohort	Ⅳ	Early type Ⅲ (7) Delayed type Ⅲ (11)	Open reduction and internal fixation + tension band wiring (7)	1	6.3	OSS: $P = 0.05$ Complications: 71% (early), 9% (delayed)
				Modified Weaver-Dunn procedure with PDS suture (11)	3		
Motta *et al*[52] 2012	Retrospective case control	Ⅲ	Early type Ⅲ-Ⅴ (34) Delayed type Ⅲ-Ⅴ (17)	CC reconstruction with LARS (34)	3	5.4	Reduction[a]: $P < 0.05$ (in favor of early reconstruction)
				CC reconstruction with LARS (17)	3		Constant score: $P > 0.05$ SST: $P > 0.05$
Fauci *et al*[59] 2013	RCT	Ⅰ	Delayed type Ⅲ-Ⅴ (40)	Allograft (semitendinosus) (20)	4	4	Constant score[a]: $P = 0.01$
				Synthetic ligament (LARS) (20)	3		Reduction: $P > 0.05$
Jensen *et al*[39] 2014	Retrospective comparative study	Ⅲ	Early type Ⅲ-Ⅴ (56)	Hookplate (30)	2	4	VAS: $P > 0.05$
				Double TR technique (26)	3		SST: $P > 0.05$

[a]Statistically significant difference ($P < 0.05$); [1]Four categories: (1) fixation of the AC and/or CC with hardware including screws and K-wires; (2) hook plates; (3) fixation of the CC with sutures or suture buttons; and (4) reconstruction of the CC ligaments with autograft or allograft tendon. LE: Level of evidence; FU: Follow-up; SPADI: Shoulder pain and disability index; QuickDASH: Disabilities of the arm, shoulder and hand score; VAS: Visual analogue scale; OSS: Oxford shoulder score; LARS: Ligament augmentation and reconstruction system; RCT: Randomised controlled trial; SST: Simple Shoulder Test; TR: Tight rope.

(Table 1). The main differences included more pain experienced by patients treated with a hookplate *vs* PDS sutures, a better reduction and less complications after early reconstruction *vs* late reconstruction, and better Constant scores in allograft *vs* artificial ligament reconstruction[39,52,55,56]. Literature showed no conclusive evidence for outcome of conservatively or operatively treatment of Rockwood type Ⅲ-Ⅴ AC dislocations. Overall, physically active young adults seem to have a slight advantage in outcome when treated operatively. Randomized controlled trials that compare long-term outcomes of nonoperative treatment with different surgical techniques are needed in order to draw firm conclusions.

COMPLICATIONS

Patients with complications have significantly lower clinical scores, suggesting that the presence of complications appears to be the only predictor of poorer clinical outcomes[13,14,35,71]. Complications after surgical treatment range from 27% to 44%[13,28]; the main being infection (4% to 8%), hardware complications (4%) and further surgery (13%)[68]. In a recent review of four studies, 12 (13%) complications were found in 96 patients after early surgery and 14 (18%) complications are occurred in 79 patients after delayed surgery[60].

Hookplate fixation has an overall complication rate of 11%[23] and an infection rate of 5%[7]. Long-term retention of the plate may lead to acromial osteolysis or fracture, which implies that a second surgery is required to remove the plate after 3 mo, when the ligaments have healed[52,55,57].

Clavert *et al*[35] prospectively reported a complication rate of 27% in 116 primary anatomic button fixations. There were 16 cases of hardware failure resulting in symptoms or loss of reduction. Forty-eight patients also had persistent dislocation of > 150%. Singh[72] reported secondary progressive loss of reduction in 7 out of 9 patients after a mean of 3.1 mo. Three patients underwent revision.

Millet *et al*[73] presented a review of 12 studies that reported complications following anatomic CC ligament reconstruction with biologic grafts and described an overall complication rate of 40%. The most serious complications were graft failure, hardware complications, and distal clavicle and/or coracoid fractures as a result of the bone tunnels. Coracoid/clavicle fractures remain a significant complication that occur predominately in techniques utilizing bone tunnels[74].

The rate of surgical complications in the literature following arthroscopic reconstruction of the CC ligaments varies from 13% to 27% and can reach 40% if postoperative loss of reduction is taken into account[27]. The five most commonly documented complications of arthroscopic fixation are superficial infection (4%), shoulder pain (27%), CC calcification (32%), fracture (5%), and loss of reduction (27%)[74].

Thus, many studies have reported postoperative loss of reduction (17% to 80%) after open anatomic

reconstruction with autogenous tendon graft or arthroscopic assisted fixation with suture buttons[13,14,28,35,75]. However, a partial loss of reduction does not appear to influence the overall functional results[22,63].

Nowadays, the cosmetic outcome is becoming more and more important for patients. However, the surgeon should consider the preference of a better cosmetic outcome against the higher complication rate in surgically treated patients.

RECENT DEVELOPMENTS

There has been an exponential increase in the number of publications on surgical AC joint reconstruction and repair over the past few years[2]. Recent studies have concentrated on minimally invasive or arthroscopic anatomical reconstruction of the CC ligaments[2,7,13,58,76]. Although many improvements have been made, some questions still remain: How many drill holes are needed in the coracoid and clavicle? Which type of graft should be used? And, should only the CC ligaments be reconstructed or both the CC and AC?

Bone tunnels are commonly used for anatomic reconstruction of the CC ligaments. Because the conoid and trapezoid ligaments attach in different areas of the clavicle and the coracoid, making two holes in both bones looks appealing. However, the use of multiple tunnels is technically demanding and increases fracture risk[27,74]. Jerosch *et al*[77] in a biomechanical study evaluated eight different AC reconstruction techniques. They found the best restoration of anatomy with suture anchor fixation in the base of the coracoid process.

The historical choice of material for stabilization of de CC ligament mainly depends on the clinical setting and timing of surgery, with synthetic material (sutures or tape) in the acute and tendon graft in the chronic injury[75]. Today, most surgeons agree that a biological augmentation is required in chronic cases to enhance the healing potential of the torn structures[5,59,63]. Laboratory studies have shown that anatomic reconstruction with double graft tendons have native-like biomechanical properties[19] and clinical data are promising[52].

Since horizontal instability of the AC joint may result in chronic pain and functional shoulder impairment[78], there is a raising focus on the relevance of specific techniques to improve horizontal stability. Schneibel *et al*[78] described persistent horizontal instability in 41% of cases after isolated CC double ligament stabilization, and developed an all-arthroscopic, radiographically assisted technique that uses a triangular AC cerclage in conjunction with the CC reconstruction to provide better horizontal stability[51,78]. Saier *et al*[79] showed biomechanically that only combined AC and CC reconstruction can adequately restore physiological horizontal AC joint stability. In addition, a recently published study showed that triple-bundle reconstruction including AC graft augmentation yielded superior clinical and radiological outcome than single-bundle CC reconstruction[52].

CONCLUSION

The aim of the current review was to provide an up-to-date and evidence-based overview of relevant treatment options for AC joint dislocations.

The recently published literature has significant limitations, namely a paucity of high quality trials and long-term follow-up. Most of the studies include heterogeneous populations with varying severities and chronicity of injury. Also, the existence of many different surgical techniques prevents the drawing of firm evidence-based conclusions.

The available evidence does provide some important clues. Operative treatment of Rockwood Ⅲ AC joint dislocations results in better cosmetic and radiological results and similar function but longer time off work and increased complication rates compared with conservative treatment[7,17,61]. Current literature suggests that the decision for treatment of type Ⅲ injuries should be made on a case-by-case basis, with an emphasis on initial nonoperative treatment[2]. Early operative treatment for grades Ⅲ-Ⅴ dislocations may result in better functional and radiological outcomes, with a reduced risk of infection and loss of reduction compared with delayed surgery.

Various operative techniques have been described. However, most techniques do not anatomically restore the complex articulation of the AC joint. Anatomical CC ligament reconstruction may result in optimal functional and radiological outcomes. The conoid and trapezoid ligaments have unique anatomic alignments and different functions. Each ligament should be considered during operative treatment[39,43].

Arthroscopically assisted AC reconstruction has the possible advantages of the minimally invasive nature, better visualization of the coracoid and the possibility to detect associated glenohumeral lesions, but demonstrates a distinct complication profile in the less experienced arthroscopist. There is currently no evidence to support arthroscopic rather than open surgery, as comparative studies are not available.

Further studies are needed especially in terms of randomized controlled trials and long-term outcomes to confirm stability of the AC joint and optimal functional results.

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MINIREVIEWS

Transforaminal Percutaneous Endoscopic Discectomy using Transforaminal Endoscopic Spine System technique: Pitfalls that a beginner should avoid

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Abstract

Transforaminal Percutaneous Endoscopic Discectomy (TPED) is a minimally invasive technique mainly used for the treatment of lumbar disc herniation from a lateral approach. Performed under local anesthesia, TPED has been proven to be a safe and effective technique which has been also associated with shorter rehabilitation period, reduced blood loss, trauma, and scar tissue compared to conventional procedures. However, the procedure should be performed by a spine surgeon experienced in the specific technique and capable of recognizing or avoiding various challenging conditions. In this review, pitfalls that a novice surgeon has to be mindful of, are reported and analyzed.

Key words: Transforaminal Percutaneous Endoscopic Discectomy; Transforaminal Endoscopic Spine System; Lumbar disk herniation; Pitfalls; Spine surgery

Core tip: Transforaminal Percutaneous Endoscopic Discectomy (TPED) is an evolving minimally invasive technique that has been proven to be safe and effective in treating symptomatic lumbar disc herniation (LDH). However, this relatively new therapeutic approach requires special training and expertise so as to evade complications that may endanger the safety of the patient. In this review, current concepts regarding challenging indications

and contraindications of this novel technique are analyzed focusing on several conditions and pitfalls that a beginner spine surgeon should avoid when treating LDH using TPED with Transforaminal Endoscopic Spine System technique, so as to eliminate possible risks and thus improve outcomes.

Kapetanakis S, Gkasdaris G, Angoules AG, Givissis P. Transforaminal Percutaneous Endoscopic Discectomy using Transforaminal Endoscopic Spine System technique: Pitfalls that a beginner should avoid. *World J Orthop* 2017; 8(12): 874-880 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/874.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.874

INTRODUCTION

Symptomatic lumbar disc herniation (LDH) is a common etiology for spine surgery. Although microdiscectomy is considered to be the gold standard method, the need for minimally invasive techniques and the improvements in the use of optics and surgical instruments have led to the utilization of Transforaminal Percutaneous Endoscopic Discectomy (TPED) using the Transforaminal Endoscopic Spine System (TESSYS) technique[1-3].

TPED has several advantages such as direct visualization of the pathology, reduced soft tissue trauma, reduced blood loss, quicker recovery and preservation of the adjacent anatomy. It can be an effective and safe method in the hands of an experienced spine surgeon if specific steps are followed[1]. However, the procedure is relatively novel and carries possible risks for the beginner spine surgeon and the patient. Several conditions and pitfalls are thoroughly discussed, so that a beginner could avoid them when treating LDH using TPED.

Indications

Generally, the indication for TPED, in compliance with clinical findings, is usually found to be persistent sciatica caused by LDH. There are several inclusion criteria such as radiculopathy, positive nerve root tension sign, sensory or motor neurological lesion on clinical examination, cauda equine syndrome, hernia confirmed by magnetic resonance imaging (MRI) of the lumbar spine. Failure of 12-wk conservative treatment is also a strong indication[2,3].

Challenging conditions

Various conditions have been reported as contraindications for TPED including: Recurrent herniated disc, migrated LDH, sequestration of the disc, central or lateral recess spinal stenosis, or previous surgery at the affected level, segmental instability or spondylolisthesis, spinal tumor or infection and vertebral fracture[1,4-6]. The following conditions should draw the maximum attention in the hands of an inexperienced spine surgeon.

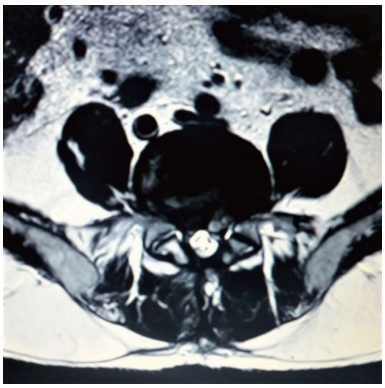

Figure 1 Case of recurrent disc herniation after open discectomy.

SURGICAL TECHNIQUE-RELATED CONDITIONS

Recurrent disc herniation

The gold standard treatment for recurrent LDH is considered to be open discectomy (Figure 1). However, in the hands of an experienced spine surgeon, TPED for recurrent LDH is a feasible and effective alternative to conventional repeated discectomy, while reducing tissue damage, scar tissue formation and instability[7].

Scar tissue formation

Conventional microdiscectomy is an open surgery with high risk of scar tissue formation contrary to endoscopic discectomy. In case of recurrent LDH and repetitive procedures scar tissue formation is almost inevitable. These cases can be difficult to manage with TPED. The altered anatomy of the region, the possible nerve tension and the difficult visualization of the anatomic structures are major obstacles for a beginner spine surgeon. Recently, percutaneous endoscopic interlaminar lumbar discectomy with dissection of the scar tissue from the medial facet joint rather than from the neural tissue has been proposed as an effective alternative surgical method on the background of recurrent disc herniation[8]. Also, less systemic cytokine response in patients following microendoscopic *vs* open lumbar discectomy has been found to exist, indicating the minimally invasive character of the first one[9]. Additionally, microendoscopic discectomy has been associated with lower risks for surgical site infection and major complications contrary to open discectomy[10].

Migrated or extruded LDH

TPED is usually appropriate for normal or caudal LDHs. Pediculectomy or translaminar approach may be required to remove an upward- or downward-migrated LDH[11,12] (Figures 2 and 3). Dorsal LDH located behind the dural sac is not treated with TPED. Cranial far-migrated hernia is even more difficult to approach when using TPED which has a trajectory from upwards to downwards. Open surgery is also proposed for far-migrated disc

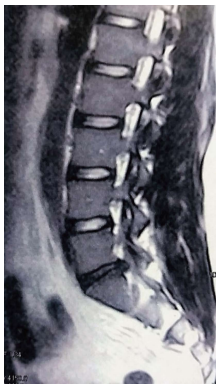

Figure 2 T2 weighted sagittal magnetic resonance imaging demonstrating a disc herniation located at the L5/S1 level.

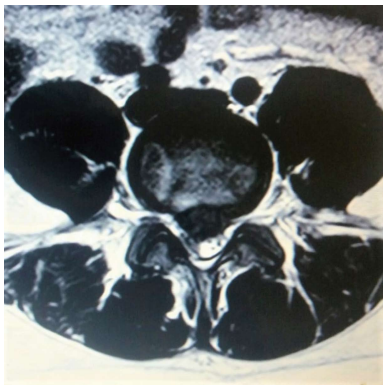

Figure 3 Case of a migrated central hernia.

herniations[12]. Even for extruded disc fragments endoscopic transforaminal discectomy has been proposed as a safe and effective alternative[13].

PATIENT-RELATED CONDITIONS

Intracanal LDH at the L5/S1 level with a high and steep iliac crest

High iliac crests refer usually to men contrary to women[14] (Figure 4). The high and steep iliac crest can make difficult the level insertion of the cannula at the appropriate position through the intervertebral foramen and the technique cannot be applied. In high iliac crest cases where the iliac crest is above the mid L5 pedicle, foraminoplasty may be considered for transforaminal access of L5-S1 disc herniation[15]. Lee *et al*[16] also proposed the foraminoplastic approach in order to facilitate the insertion of the cannula. Tezuka *et al*[17] indicated that treatment for the central type of LDH at the L5-S1 disc level is more difficult than at the L4-L5 due to the iliac crest. This can be solved by using a more perpendicular approach with the possible addition of a foraminoplasty[17]. Interlaminar approach can escape the blockade of crista iliaca, and offer several advantages including a faster puncture orientation, a shorter operation time, and less intraoperative radiation exposure[18]. Application of transiliac approach to

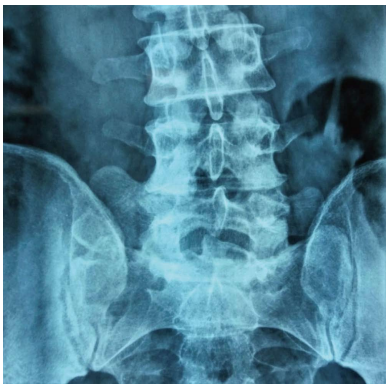

Figure 4 Case of high and steep iliac crests.

intervertebral endoscopic discectomy in L5/S1 LDH has also been suggested[19]. Additionally, it is reported that compared with the L5/S1 level, the L4/5 level might be easier to master after short-term professional training[20]. It is true that some propose the percutaneous endoscopic discectomy as the treatment of choice for foraminal and extraforaminal disc herniations at the L5-S1 level on appropriately selected patients[21]. Since this is considered the most difficult level, we can forecast that TPED might be established as a treatment for all lumbar levels.

Scoliosis

Scoliosis is a form of deformity which results in misalignment of the spine. Idiopathic scoliosis (Cobb angle $\geqslant$ 10) is more common in children aged 10-15 years old and has a prevalence estimated at 0.5%[22]. Degenerative scoliosis is observed in more than 30% of elderly patients with no history of spinal abnormalities and is typically diagnosed in patients older than 40 years[23]. The prevalence of 10°, 10°-20° and > 20° curves is 64%, 44% and 24%, respectively[24]. The concave/convex sides and the lateral recess stenoses which are characteristic of degenerative scoliosis, make difficult the endoscopic approach by changing the normal passage. Basically, the Kambin's triangle is altered making difficult the safe passage of the endoscopic instruments[4]. In coronal projection, the deformation of the lumbar spine affects the form of the meninge something which makes its traumatization more possible. Nevertheless, the use of TPED for LDH on the background of lumbar scoliosis has been recently attempted[25,26].

Spondylolysis-spondylolisthesis

Spondylolysis is a unilateral or bilateral stress fracture of the pars interarticularis and is usually combined with spondylolisthesis. In spondylolistheses, alteration of the normal anatomy of the lumbar intervertebral foramen and its dimensions resulting in foraminal narrowing and disc bulging is observed[27]. The measurement of spondylolisthesis is based on the widely recognized method proposed by Meyerding[28] in 1932 (Figure 5). Meyerding defined the slippage on plain X-ray imaging in accordance to the vertebra below. The caudal

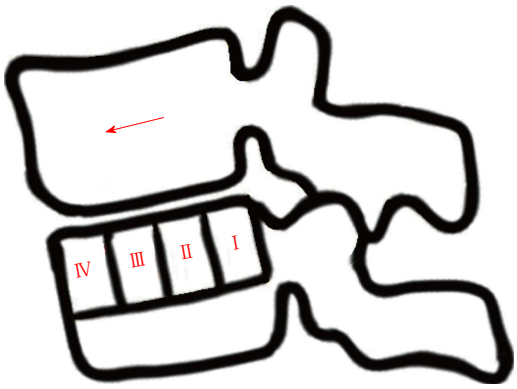

Figure 5 Meyerding's grading of spondylolisthesis regarding cranial anterior vertebral slippage in accordance with the vertebra below.

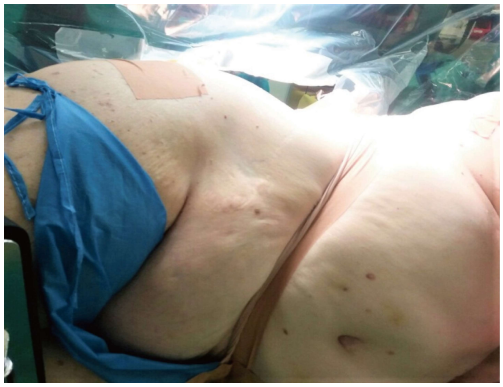

Figure 6 Case of an obese patient to be treated with Transforaminal Percutaneous Endoscopic Discectomy for lumbar disc herniation.

vertebra is divided into four parts. Grade Ⅰ means a translation of the cranial vertebra of up to 25%, Grade Ⅱ of up to 50%, Grade Ⅲ of up to 75%, and Grade Ⅳ up to 100%[28]. Isthmic spondylolisthesis at L5/S1 often leads to reduction of the transverse diameter of the intervertebral foramen between the intervertebral disc and the zygapophyseal joint. The normal shape of the intervertebral foramen is altered, while spinal nerves and roots, sinuvertebral nerves, spinal arteries, and intervertebral veins are compressed between transforaminal and extraforaminal ligaments[29]. The radicular symptoms are usually caused by compression of the exiting L5 nerve root and its adjacent vessels in the L5-S1 foramen. In these cases the only surgical options have been lumbar laminectomy and lumbar fusion, however TPED with foraminoplasty appears as an effective upcoming treatment[30,31]. We believe that beginners should avoid TPED when dealing with spondylolistheses of 2nd grade and greater[32]. Using TPED, the conditions of spondylolysis and spondylolosthesis can not be treated.

Obese patients

In obese patients, a beginner spine surgeon will have to deal with technical considerations due to increased fat tissue, such as bad fluoroscopic verification and difficult transforaminal approach. TPED for LDH in obese patients has shown satisfactory early results, however more studies are needed to confirm its efficacy[33,34] (Figure 6).

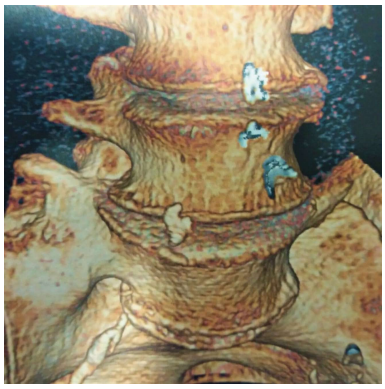

Figure 7 Case of Bertolotti's syndrome.

Muoskeletal malformations

Several variations of the lumbar spine can be an obstacle for the realization of TPED with Bertolotti's syndrome being a common etiology of low back pain, especially for young people[35]. Lumbosacral transitional vertebrae are increasingly recognized as a common anatomical variant associated with altered patterns of degenerative spine changes. Bertolotti's syndrome refers to the association between lumbosacral transitional vertebrae and low back pain[36] (Figure 7). On the co-existence with LDH, Bertolotti's syndrome makes difficult the transforaminal passage through the Kambin's triangle during TPED[27].

High LDH levels in conjunction with abnormal location/ variations of adjacent anatomic formations

Kidneys are important retroperitoneal organs adjacent to the lumbar spine. They are normally located between the transverse processes of T12-L3 vertebrae, with the left kidney typically more superior in position than the right[14] (Figure 8). Treating high level LDHs, especially T12-L1, L1-L2 and L2-L3, using TPED in accordance with abnormal location and possible variations of adjacent organs such as kidneys may result in their traumatization during the passage of the reamers and the cannula.

SURGICAL PROCEDURE

TPED using the efficacy of TESSYS technique is performed under local anesthesia and mild sedation[1,3]. Patients are initially placed at the lateral decubitus position, lying down on the opposite side (Figure 9). Lesion is thus confronted upwards. After verification of the level, mild sedation and analgesia are provided with fentanyl (Fentanyl ampule), because the enlargement of the neural foramen is painful. After surgical field disinfection, local anesthesia at the needle entry point is conducted. This point is anatomically about 11 cm away from midline defined. Transforaminal promotion of the

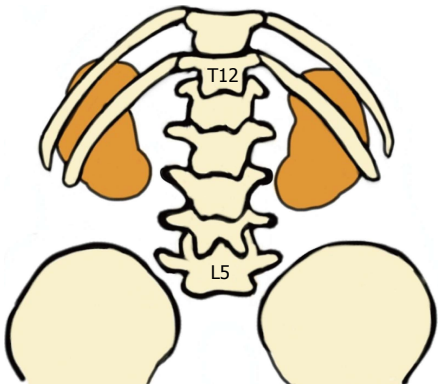

Figure 8 Posterior schematic illustration of the location of kidneys in accordance with lumbar spine levels.

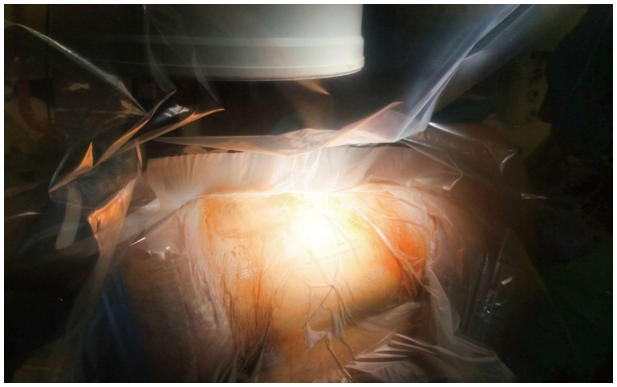

Figure 9 Placement of the patient at the lateral decubitus position and disinfection of the surgical field.

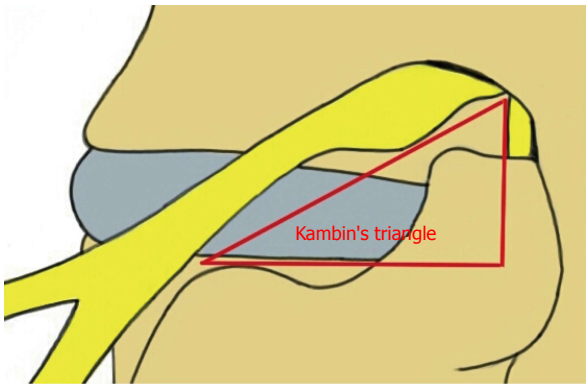

Figure 10 Kambin's triangle. The hypotenuse is parallel to the exiting nerve root, the base is according to the superior border of the transverse process of the caudal vertebra, and the height represents the trajectory of the traversing nerve root.

needle through the anatomic triangle of Kambin (safe zone) is subsequently performed[4] (Figures 10 and 11). Sequential transforaminal passage of three different size reamers (5.5, 6.5, 7.5 mm, joimax GmbH) constitute the next step (Figure 12). The cannula and endoscope are afterwards carefully inserted, in order to ensure nerve root preservation (Figure 13). Removal of herniated disc material is finally accomplished with

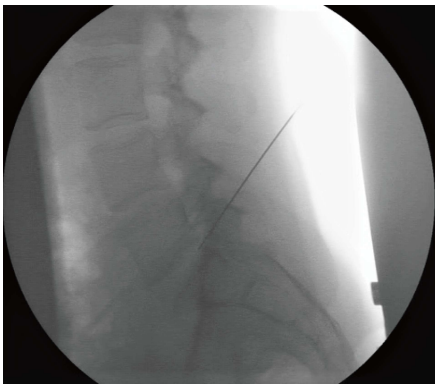

Figure 11 Fluoroscopic verification of the operated level and insertion of the needle.

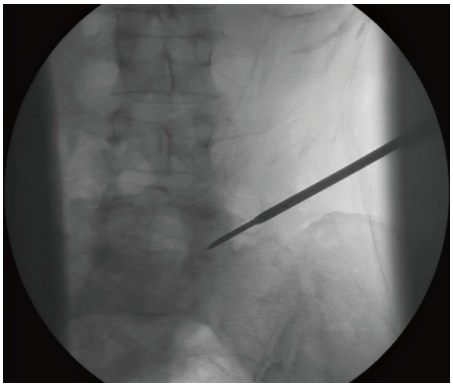

Figure 12 Sequential transforaminal passage of different size reamers.

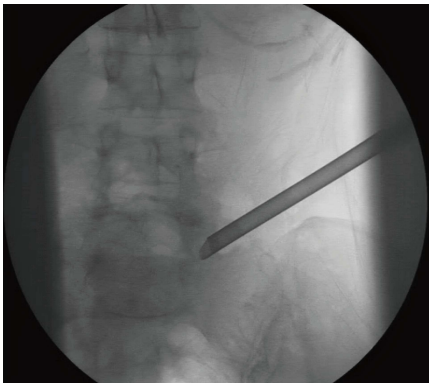

Figure 13 Insertion of the cannula and the endoscope afterwards.

graspers (Figure 14). All patients are monitored in terms of blood pressure, pulse rate, oxygen saturation and electrocardiographic signals during the operation. Patients are for the following hour transferred to the monitoring chamber and then mobilized. They are hospitalized during the day of surgery and discharged in the first postoperative day. Possible complications could be: Nerve root damage, postoperative dysesthesia, dural tears, post-operative hematoma, wood infection and visceral injury[5,37,38]. Patients are usually scheduled to have a check-up 6 wk after the surgery

Table 1 Summary of the indications, contraindications, advantages and disadvantages of the technique

Indications	Contraindications (for the beginners)
Radiculopathy	Surgical technique-related conditions
Positive nerve root tension sign	Recurrent disc herniation
Sensory or motor neurologic lesion on clinical examination	Scar tissue formation
Cauda equine syndrome	Migrated or extruded LDH
Hernia confirmed by MRI of the lumbar spine in compliance with clinical findings	Patient-related conditions
Failure of 12-wk conservative treatment	Intracanal LDH at the L5/S1 level with a high and steep iliac crest
	Scoliosis
	Spondylolysis-Spondylolisthesis
	Obese patients
	Muoskeletal malformations
	High LDH levels in conjunction with abnormal location/ variations of adjacent anatomic formations
Advantages	Disadvantages
Safe and effective technique	Careful selection of patients is needed
Direct visualization of the pathology	Limited space for surgical maneuvering
Less blood loss	Long learning curve
Less trauma and scar tissue	
Faster rehabilitation	
Preservation of the spine stability and the adjacent anatomy	

LDH: Lumbar disc herniation; MRI: Magnetic resonance imaging.

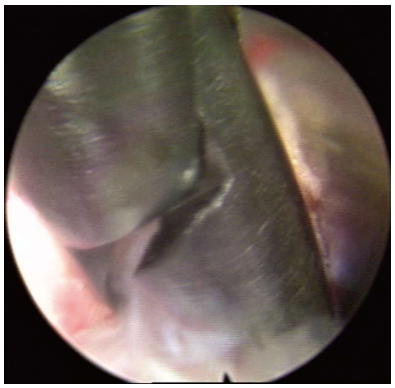

Figure 14 Removal of herniated disc material with a grasper.

at the outpatient clinic. Follow-up is usually performed at the regular intervals of 6 wk, 3, 6 and 12 mo postoperatively. The indications, contraindications, advantages and disadvantages of the procedure are summarized in Table 1.

CONCLUSION

TPED is an evolving minimally invasive technique which requires training and expertise. Every condition which alters the normal architecture of the spine and makes the access to the LDH difficult tests the abilities of the spine surgeon and sets a question mark on the feasibility and limits of TPED. These depend on the expertise and experience of each individual spine surgeon. It should be kept in mind that TPED is a combination of two interventional approaches involving the percutaneous and the endoscopic aspect; both of them indicate its demanding character. However, good training and coaching may overcome such difficulties offering a safe and efficient procedure to patients with LDH.

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ORIGINAL ARTICLE

Basic Study

Role of fast-setting cements in arthroplasty: A comparative analysis of characteristics

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Abstract

AIM

To evaluate the behaviour of two fast-setting polymethylmethacrylate (PMMA) cements CMW® 2G and Palacos® fast R + G, as reference: Standard-setting Palacos® R + G.

METHODS

The fast-setting cements CMW® 2G and Palacos® fast R + G were studied, using standard-setting high viscosity Palacos® R + G as a reference. Eleven units (of two batch numbers) of each cement were tested. All cements were mixed as specified by the manufacturer and analysed on the following parameters: Handling properties (mixing, waiting, working and hardening phase) according to Kuehn, Mechanical properties according to ISO 5833 and DIN 53435, Fatigue strength according to ISO 16402, Benzoyl Peroxide (BPO) - Content by titration, powder/liquid-ratio by weighing, antibiotic elution profile by High Performance Liquid Chromatography. All tests were done in an acclimatised laboratory with temperatures set at 23.5 ℃ ± 0.5 ℃ and a humidity of > 40%.

RESULTS

Palacos® fast R + G showed slightly shorter handling

properties (doughing, hardening phase, n = 12) than CMW® 2G, allowing to reduce operative time and to optimise cemented cup implantation. Data of the quasistatic properties of ISO 5833 and DIN 53435 of both cements tested was comparable. The ISO compressive strength (MPa) of Palacos® fast R + G was significantly higher than CMW® 2G, resulting in ANOVA (P < 0.01) and two sample t-test (P < 0.01) at 0.05 level of significance (n = 20). Palacos® fast R + G showed a higher fatigue strength of about 18% mean (ISO 16402) of 15.3 MPa instead of 13.0 MPa for CMW® 2G (n = 5 × 10^6 cycles). Palacos® fast R + G and CMW® 2G differed only by 0.11% (n = 6) with the former having the higher content. The BPO-content of both cements were therefore comparable. CMW® 2G had a powder/liquid ratio of 2:1, Palacos® fast R + G of 2.550:1 due to a higher powder content. Despite its higher gentamicin content, CMW® 2G showed a significantly lower antibiotic elution over time than Palacos® fast R + G (n = 3).

CONCLUSION

Both cements are compliant with international standards and are highly suitable for their specified surgical indications, affording a time-saving measure without detriment to the mechanical properties.

Key words: Polymethylmethacrylate; Elution; Fast-setting; Viscosity; Antibiotic; Fatigue; Arthroplasty

Core tip: Polymethylmethacrylate (PMMA) cements provide reliable fixation of the implants in joint arthroplasty. Fast-setting high viscosity PMMA cements exist that have altered setting characteristics compared to standard setting cements. These potentially offer benefits to surgeons based upon their handling properties. Such cements have gained popularity in arthroplasty surgery as described in the United Kingdom and Australian National Joint Registries. The use of fast-setting cements has various beneficial as well as economic effects, such as time-saving and better antibiotic elution.

Caraan NA, Windhager R, Webb J, Zentgraf N, Kuehn KD. Role of fast-setting cements in arthroplasty: A comparative analysis of characteristics. *World J Orthop* 2017; 8(12): 881-890 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/881.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.881

INTRODUCTION

Polymethylmethacrylate (PMMA) cements provide reliable fixation of the implants in joint arthroplasty[1,2]. The chemical composition of each bone cement accounts for its mechanical and handling properties. The polymerization reaction of PMMA is divided in to four phases: Mixing, waiting, working and setting. Bone cements are classified based upon the amount of time they spend in each of these phases. The most popular cements are high viscosity varieties which have the best results in registry figures but also offer the surgeon short waiting and extra-long working phases[3]. However, high viscosity cements can take up to 13 min to set[4].

Fast-setting high viscosity cements exist that have altered setting characteristics compared to standard setting cements. These potentially offer benefits to surgeons based upon their handling properties. Such cements have gained popularity in arthroplasty surgery as described in the United Kingdom and Australian National Joint Registries[2,5].

Fast-setting high viscosity cements are characterised by a short mixing, moderate working and very short hardening phase in comparison to standard-setting high viscosity PMMA cements[6,7]. They potentially offer benefits to both surgeon and patient based on their handling properties. These benefits might include: (1) Reduced operative time. Fast setting cements are homogenised quickly and demonstrate very short mixing and waiting phases, allowing them to be applied rapidly[8,9]. Usually, fast setting cements are setting at the same time that a standard high viscosity cement is reaching the end of their working properties. By reducing the operative time, they may offer an economic advantage[10-12]. Of more importance, as longer operative time is correlated with increased risk of prosthetic joint infection, they may also offer an advantage in reducing infection[13,14]; (2) cemented cup implantation. The short waiting phase of fast setting cements might have the advantage of minimising the risk of bottoming out of the socket during insertion[15]. A high viscosity, fast setting cement flows away less readily during pressurisation and thus, once the correct cup position is achieved, it can be kept under pressure during the working phase with less progressive movement[16]; (3) cemented knee arthroplasty. Some authors have advocated the use of a sequential mixing technique to ensure even cement mantles in total knee arthroplasty[6]. Fast setting cements are central to this technique in order to avoid excessive operative time. In addition, others state that high viscosity fast setting cements tend to penetrate the cancellous bone less deeply. This reduces the peak temperature at the interface and facilitates cement removal at revision arthroplasty[17]; (4) cement spacer and bead production: The handling properties of fast setting cements allows manipulation of the dough more rapidly, facilitating the production of hand-made spacers and beads[18]; and (5) augmentation surgery. The short waiting phase of fast setting high viscosity cements leads to the dough sticking less to surgeon's gloves. These favourable handling properties will be of benefit when filling bone defects or augmenting the fixation of screws in osteoporotic bone[19].

There is extensive published data on the mechanical properties of standard-setting high viscosity cements.

Table 1 Testing material

Product	Powder (g)	Liquid (mL)	Batch number	Viscosity
DePuy CMW® 2G	40	20	#3620322	Very high-viscosity
			#3572255	Very high-viscosity
Palacos® fast R + G	51	20	#7743	Very high-viscosity
			FZ52#050214	Very high-viscosity
Reference: Palacos® R + G	40.8	20	#7735	Standard high viscosity
			#7753	Standard high viscosity

However, the varied possible clinical applications, described above, for the use of fast-setting cements demands a similar detailed knowledge of their properties. There is therefore a need to describe the clinically relevant cement properties of these newer cements including, handling behaviour, antibiotic elution, quasistatic and dynamic mechanical properties.

The aim of this research is to study the behaviour of two fast-setting cements and compare these against the "gold-standard" clinically proven standard-setting high viscosity cement, Palacos® R + G. The design was an *in vitro* non-interventional, experimental and prospective comparative study.

MATERIALS AND METHODS

Materials

The fast-setting cements CMW® 2G and Palacos® fast R + G were studied, using standard-setting high viscosity Palacos® R + G as a reference[20-22]. Eleven units (of two batch numbers) of each cement were tested (Table 1).

Methods

All cements were mixed manually as specified by the manufacturer, in porcelain crucibles with metal spatulas by our team, consisting of experienced laboratory technicians of Heraeus Holding GmbH and me, after intense training for several weeks with different cements.

All cements were analysed on the following parameters: (1) Handling properties (mixing, waiting, working and hardening phase) according to Kuehn[7]; (2) Mechanical properties according to ISO 5833[23] and DIN 53435[24]; (3) Fatigue strength according to ISO 16402[25]; (4) Benzoyl Peroxide (BPO) - content by titration, powder/liquid-ratio by weighing; and (5) Antibiotic elution profile by High Performance Liquid Chromatography (HPLC)[26] (Table 2). All tests were done in an acclimatised laboratory with temperatures set at 23.5 ℃ ± 0.5 ℃ and a humidity of > 40%.

Fatigue testing: Fatigue was tested according to ISO 16402[25]. The run follows the four-point bending test method described in ISO 5833[24]. The dynamic testing is executed with a pulsating sinusoidal loading under force control. The tests are continued until failure occurs or the specimen reaches a predetermined maximum number of cycles ($n = 5 \times 10^6$). The specimens had the dimensions 3.3 mm × 10 mm × 70 mm[27].

Gentamicin elution: Cylindrical cement specimens (d = 25 mm, h = 10 mm) with a surface of approximately 3.1 cm^2 were used. For the dissolution the PMMA cement samples were stored at 37 ℃ in dissolution medium (0.1 M phosphate buffer, pH 7.4). Aliquots were taken and the dissolution medium was renewed at day 1, 3, 7, 14, and 21. An appropriate amount of dissolution medium was added to ensure that the samples were completely covered. The dissolution medium samples were stored at -20 ℃ until analysis. Sample preparation and the determination of concentrations were done at AZB (Analytisches Zentrum Biopharm GmbH Berlin).

Sample preparation: For the preparation of calibration standards 7.646 mg gentamicin sulphate (equivalent to 5.0 mg gentamicin) were dissolved in 25 mL water to achieve a 200 μg/mL gentamicin stock solution. Working solutions were prepared at 100, 250, 500, 750, 1000, 2500, 5000 and 7500 ng/mL by serial dilutions with water. Tobramycin was used as an internal standard. The internal standard working solution was prepared at a concentration of 25 μg/mL in water.

Up to eight calibration standards from 100-7500 ng/mL were prepared by spiking 200 μL of gentamicin working solutions with 18 μL internal standard working solution. The study samples were diluted by a factor of 20 with water and prepared according to the calibration standards by adding internal standard working solution[26].

Determination of concentrations: Concerning the liquid chromatography (LC) mass spectroscopy (MS) conditions, chromatographic separation was performed on a modular HPLC 1200 Series (Agilent Technologies, Waldbronn, Germany) using a Luna C18 (II) column, 150 mm × 2 mm, with two C18, 4 mm × 2 mm, guard columns (Phenomenex, Aschaffenburg, Germany) thermostated at 25 ℃ (gentamicin), respectively.

For gentamicin the mobile phase A was 0.11 mol/L trifluoroacetic acid/methanol (50:50) and mobile phase B was acetonitrile. An isocratic separation was achieved with an A:B ratio of 95:5 at a flow rate of 0.25 mL/min. The run time was 2.5 min and the total cycle time was less than 3 min. Injection volume was 2 μL. Under the described conditions the four gentamicin components C1, C2, C2a and C1a co-eluted. The HPLC method was previously used by Heller *et al*[26] to determine gentamicin in biopsy samples. The detection of the co-eluted gentamicin components was carried out using an API 4000 QTrap (Applied Biosystems, Darmstadt, Germany). Ionisation was carried out with an electrospray interface (positive polarity) using the mass selective detector in the multiple reaction monitoring

Table 2 Test parameters

Parameter	Characteristics	More details	Sample size	Scale of measure - Ratio scale	Descript. + analyt. statistics
Handling properties *in vitro*	Mixing, doughing and waiting phase	Elapsed time	12	Duration	Median, quartile, boxplot
	Working phase	Elapsed time	12	Duration	
	Hardening phase	Elapsed time	12	Duration	
Quasistatic mechanical properties	ISO bending strength	In MPa	12	Metric	Median, quartile, boxplot, arithmetic mean, ANOVA, independent two-sample *t*-test
	ISO flexural modulus	In MPa	12	Metric	
	ISO compressive strength	In MPa	20-24	Metric	
	Dynstat notched impact strength	In kJ/m^2	16	Metric	
	Dynstat bending strength	In MPa	16	Metric	
Dynamic mechanical properties		In MPa	5	Metric	Chart, bar graph and standard deviation
BPO-content		In %	6	Metric	Arithmetic mean, standard deviation, bar graph
Powder/liquid-ratio		g:mL		Ratio	Bar graph
Elution profile	Gentamicin release per mould body	In µg/FK	3	Metric	Table, S/N-curve

mode (MRM). The extracted ion chromatograms of the following ion transitions were stored and calculated: 478.4 → 322.3 m/z (gentamicin C1), 464.4 → 322.3 m/z (gentamicin C2 and C2a), 450.3 → 322.3 m/z (gentamicin C1a.) and 468.4 → 163.1 m/z (internal standard). The three ion transitions of gentamicin components were summed with Analyst (Applied Biosystems, Darmstadt, Germany) and concentrations were calculated with Excel (Microsoft, Unterschleißheim, Germany).

Statistical analysis

The differences of the middle level (= mean) were analyzed by univariate ANOVA (analysis of variance) with repeated measures for more than two paired samples compared with *post-hoc* Tukey test. The method *P* values, adjusted according to the Tukey-method were compared with the significance level $\alpha = 0.05$, and a comparison was considered statistically significant if $P < \alpha$. In addition, the average group differences and the associated 95%CIs were estimated from this model.

The metric ISO variable mechanism and handling properties were tested descriptively by median, quartile, box plot and span and presented summarized in tabular form for all ISO and DIN mechanical results and as a bar chart for all tested handling results.

By calculating the mean values including the standard deviation and a bar chart, the metric parameters of the (di) benzoyl peroxide content (BPO-content) was descriptively displayed three times for each batch of fast-setting cements. The ratio of polymer powder to monomer liquid was presented with metric parameters as a bar graph. The metric data for all antibiotic elution data were tabulated after the 1st, 3rd and 5th day and presented with its standard deviation as a curve diagram.

Metric data of all fatigue strength data were shown as follows: The quasi-static ISO flexible strength in MPa were indicated by mean and its standard deviation, the fatigue strength in MPa at 5×10^6 cycles and the consequent percentage share of the quasi-static bending strength as a table. It was prepared as SN curve (= S/N curve) in a 95%CI[27].

RESULTS

Handling properties under in vitro condition

For CMW® 2G the polymer powder is filled into the vessel before the monomer liquid. This is contrary to the Palacos® fast R + G and Palacos® R + G process, which both require the filling of the monomer liquid first followed by the polymer powder. The latter technique seems to allow better initial mixing of the liquid and powder moieties. The handling properties of both tested fast setting cements are similar ($n = 12$), but the differences are as follows. CMW® 2G reached the end of the doughing phase according to ISO 5833 at 50 s, approximately 20 s later than Palacos® fast R + G (Figure 1). Palacos® fast R + G was workable at 35 s, immediately after mixing because the dough was no longer sticky and an additional waiting phase is not necessary. CMW® 2G showed a small waiting phase (when still sticky to touch) of approximately 15-20 s after the end of mixing and thus could not be applied until approximately 60 s. Both fast setting cements tested had a similar end of working phase at 3 min after start of mixing. Palacos® fast R + G showed a slightly shorter setting time than CMW® 2G.

Quasistatic mechanical properties

Both fast setting cements tested fulfilled the quasistatic properties of ISO 5833 and DIN 53435[23,25]. Data of ISO bending strength (MPa) of both cements were similar with no statistical difference due to the one-way analysis of variance (ANOVA) ($P = 0.06$) and independent two sample *t*-test ($P = 0.058$) at 0.05 level of significance ($n = 12$). ISO flexural modulus (MPa) of both cements was also similar, resulting in: ANOVA ($P = 0.869$) and independent two sample *t*-test ($P = 0.868$) (for both α

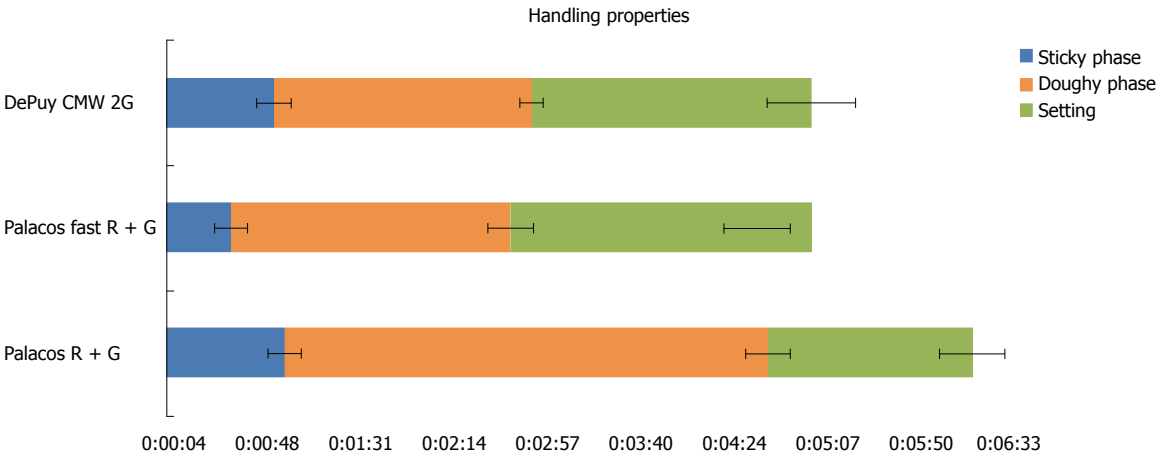

Figure 1 Graphical presentation of handling properties (sticky phase, doughy phase and setting) of tested fast setting cements and the reference material. Data is presented as mean ± SD.

Table 3 ISO mechanical properties of all tested cements

	ISO 5833:2002					
	Bending strength (MPa)		Flexural modulus (MPa)		Compressive strength (MPa)	
Limit	> 50		> 1800		> 70	
DePuy CMW® 2G	75.39	67.3 (-8.09) 81.8 (+6.41)	3002.75	2775 (-227.75) 3159 (+156.25)	91.53	80.94 (-10.59) 99.11 (+7.58)
Palacos® R + G	65.79	61.7 (-4.09) 68.7 (+2.91)	2552	2383 (-169) 2659 (+107)	87.46	81.92 (-5.54) 93.13 (+5.67)
Palacos® fast R + G	72.17	69.3 (-2.87) 76.2 (+4.03)	2995.18	2784 (-211.18) 3118 (+122.82)	106.25	100.26 (-5.99) 110.51 (+4.26)

Table 4 DIN mechanical properties of all tested cements

	DIN 53435			
	Bending strength (MPa)		Notched impact strength (kJ/m^2)	
Limit				
DePuy CMW® 2G	73.1	63.88 (-9.22) 82.81 (+9.71)	2.94	2.01 (-0.93) 3.98 (+1.04)
Palacos® R + G	71.21	65.06 (-7.15) 79.09 (+7.85)	3.2	2.39 (-0.81) 4.50 (+1.3)
Palacos® fast R + G	76.35	65.91 (-10.44) 88.3 (+11.95)	3.19	2.39 (-0.8) 3.98 (+0.79)

= 0.05, n = 12). The ISO compressive strength (MPa) of Palacos® fast R + G was significantly higher than CMW® 2G, ANOVA (P < 0.01) and t-test (P < 0.01) at 0.05 level of significance (n = 20). Dynstat bending strength (MPa) was comparable [ANOVA (P = 0.15) and t-test (P = 0.15) (n = 16)], as was the Dynstat notched impact strength (kJ/m^2) [ANOVA (P = 0.196) and t-test (P = 0.200) (n = 16)] of both fast-setting cements (Tables 3 and 4).

Dynamic mechanical strength (fatigue)

CMW® 2G had a higher initial quasistatic ISO bending strength (62.3 ± 7.2 MPa) for fatigue according to ISO 16402 than Palacos® fast R + G (55.3 ± 1.1 MPa). Subsequently Palacos® fast R + G showed a higher fatigue strength of about 18% mean (ISO 16402) of 15.3 MPa instead of 13.0 MPa for CMW® 2G (n = 5 × 10^6 cycles). All dynamic mechanical testing results showed no statistical significance (Figure 2).

BPO-content

Palacos® fast R + G and CMW® 2G differed only by 0.11% with the former having the higher content (Figure 3, mean values of all batches tested). The BPO-content of both cements were therefore comparable.

Powder/liquid-ratio

CMW® 2G had a powder/liquid ratio of 2:1, Palacos® fast R + G of 2.550:1 due to a higher powder content (Figure 4).

Elution profile

CMW® 2G contains 2.5% gentamicin sulphate in the powder, Palacos® fast R + G only 1.25% gentamicin. Both cements showed a typical biphasic antibiotic elution profile with high initial release of gentamicin within the first 24 h. Despite its higher gentamicin content, CMW® 2G however released only approximately half the amount gentamicin as compared to Palacos® fast R + G after the first 24 h. Further CMW® 2G showed a much lower antibiotic elution over time than Palacos® fast R + G. Additionally, after day 3, CMW® 2G had a significantly lower gentamicin release than Palacos® fast R + G (Figure 5).

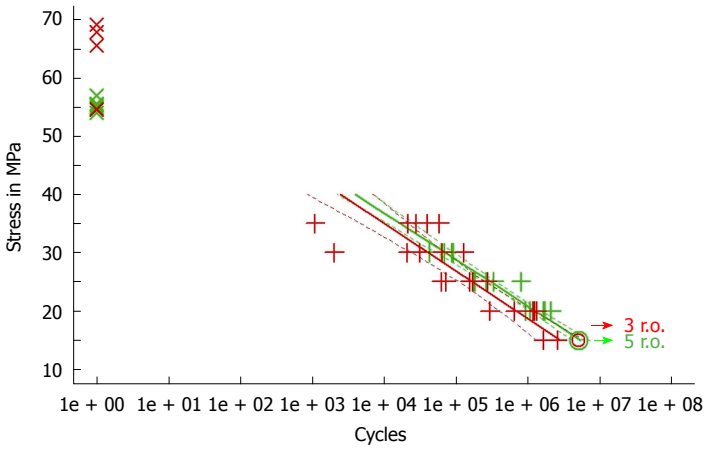

Figure 2 Fatigue strength (n = 5 × 10^6 cycles) of both tested fast setting cements, CMW® 2G (in red) and Palacos® fast R + G (in green). Data is presented in a S/N curve. Lines: Result of the linear regression and the "narrow" confidence band at the 95% level; x: Quasi-static values; +: Failed under fatigue load; o: Run-outs, regression with + and o.

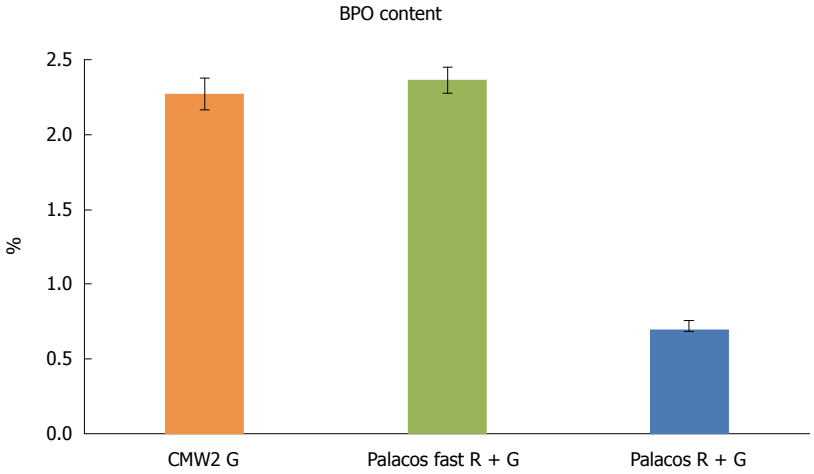

Figure 3 Graphical presentation of Benzoyl Peroxide-content of all tested cements. Data is presented as mean ± SD. BPO: Benzoyl peroxide.

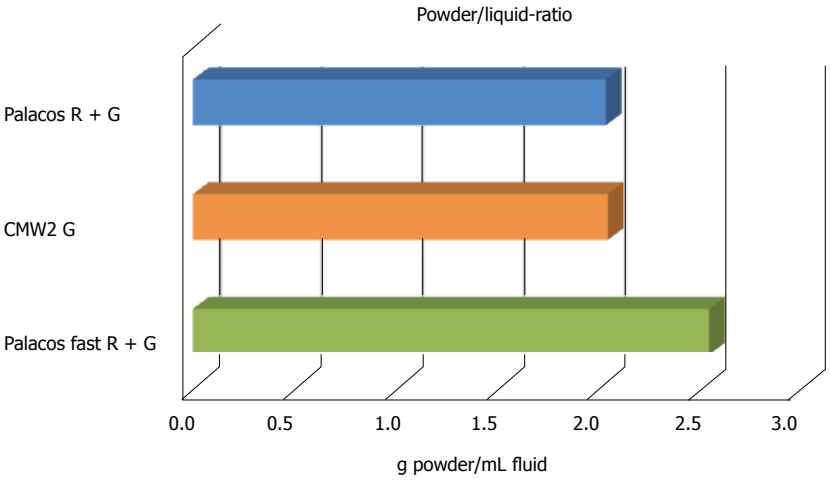

Figure 4 Graphical presentation of powder/liquid ratio of all tested cements. Data is presented as absolute.

DISCUSSION

Fast-setting high viscosity cements have gained popularity in clinical applications owing to their advantageous handling properties and possible associated cost saving potential. Economically the rapid use immediately after mixing and the quick setting is of importance. In the United Kingdom and Australia such fast-setting cements

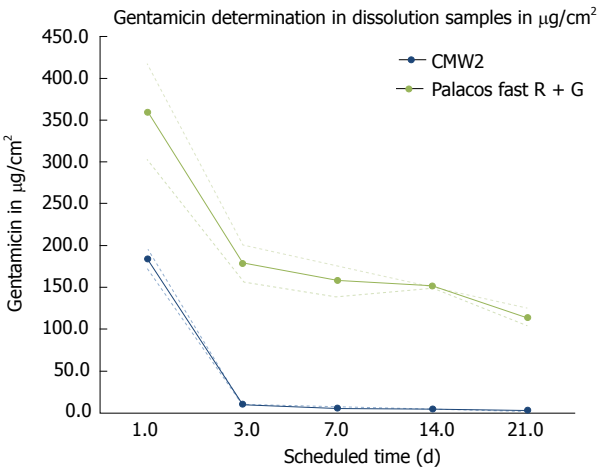

Figure 5 Graphical presentation of elution profile of CMW® 2G (in blue) and Palacos® fast R + G (in green) (specimen surface 3.1 cm²). Data is presented as mean ± SD.

are now widely used[2,5].

Palacos® fast R + G and CMW® 2G were characterised by different mechanical and handling properties when compared to standard-setting high viscosity PMMA cements. The key question, is whether such fast-setting behaviour lends itself to use in all cement clinical applications for bone cement? The relatively short mixing, moderate working and setting phases when compared to standard-setting high viscosity may be less favourable in some scenarios such as femoral stem insertion when the downside of incomplete insertion would be detrimental to the outcome of the surgical procedure. None the less the fact that these cements will have set whilst standard versions are still in their working phase does offer some potential benefits to the surgeon, as detailed in the introduction.

The altered handling characteristics of CMW® 2G are the clinically corollary of the special PMMA bead formulation together with an increased content of BPO[28]. In contrast, Palacos® fast R + G utilises an increased powder-liquid (polymer to monomer) ratio in combination with an increased BPO content to achieve the different handling properties.

Both tested fast setting cements are characterised by a short doughy/waiting phase with Palacos® fast R + G being ready to handle immediately after mixing. During THA these properties might be advantageous such as allowing better component position control during cup insertion with less extrusion and movement of the cement. The viscosity within the working or application phase is ideal for good cement penetration into the cancellous bone. Surgical technique must be altered to allow the use of fast-setting cements because the viscosity increases quickly and results in an earlier setting.

With regards to the handling properties of the two cements tested, Palacos® fast R + G may offer some benefits to surgeon over CMW® 2G. The latter is workable from about 60 s until 4 min after the start of mixing. The material sets at approx 5 min[20]. The viscosity at the end of the working phase is high and the cement becomes warmer quickly. Palacos® fast R + G is workable immediately after mixing at 35-40 s until 4 min after the start of mixing. This results in a slightly longer working phase at 23 ℃. It is expected that these differences in the handling behaviour of the tested fast setting cements will be significantly higher at lower ambient temperatures.

Fast-setting cements can be used immediately after mixing during TKA in a sequential cementing technique. Before touching the cement users should be aware that CMW® 2G is sticky for slightly longer than Palacos® fast R + G. High viscosity fast-setting cements do not penetrate the cancellous bone as deeply as their standard-setting versions. The higher the monomer (liquid) content in a PMMA cement, the higher the temperature reached during setting[29]. The higher powder-liquid ratio of Palacos® fast R + G results in a lower peak temperature in comparison to CMW® 2G. This might protect against thermal damage of the bone with use of the Palacos® fast R + G cement.

To our knowledge, only two fast-setting high viscosity cements are marketed today. Another cement is marketed as a fast setting cement - Simplex®P SpeedSet® (Stryker®). This is not a high viscosity fast-setting cement as studied in this paper, but rather represents a slightly faster-setting version of their medium viscosity Simplex P[30].

The altered setting behavior of Simplex®P Speed Set® is achieved by using smaller copolymer particles which leads to an increased surface area of the powder beads. Such a change of the polymeric composition produces a more viscous material. Further, a higher BPO content is used to speed up the polymerisation reaction, leading to a faster setting time in comparison with the original Simplex ®P cement[31]. The handling properties of Simplex®P Speed Set® are markedly different from those of standard viscosity cements, such as Palacos® R + G. Simplex®P SpeedSet® is characterised by a doughing time of 2.53 min, a working time of approximately 4.8 min and a setting time of 8.2 min according to FDA510 (k) K 053198[28]. The reference, the standard viscous Palacos® R + G showed a working time of approximately 4 min, a doughing of approximately 55 s and a setting of 6 to 7 min. Due to this, Simplex®P SpeedSet® is not a high viscosity fast-setting cement.

The clinical success of cemented arthroplasty relies upon the strength of the interfaces between the bone, the cement and the implants. Registry figures have confirmed the efficacy of combining implants and cements with optimal mechanical properties and design (NJR 2015). When assessing a new type of cement one must ensure that they will be able to withstand the varying loads they will encounter *in vivo*. The minimum requirements for mechanical properties on an acrylic cement to be used in human applications are described in ISO 5833 and DIN 53435[23,24]. Both the fast-setting cements we tested in this study fulfilled these requirements. In addition, it was noted that Palacos® fast R + G had a statistically significant higher ISO compressive strength (MPa) than CMW® 2G.

Nevertheless, quasistatic tests on PMMA cements usually conveys similar strength values between brands.

Dynamic mechanical testing of cements probably offers more clinically relevant information relevant to the long-term survival of cemented implants. Such properties include visco-elastic properties and fatigue testing[9]. Fatigue behaviour of PMMA cement was tested in this study because it is more sensitive to acrylic variation and can frequently distinguish between material differences in composition or preparation[32]. Palacos® fast R + G showed higher fatigue strength according to ISO 16402. This may depend upon the different sterilisation techniques used in the preparation of the two cements tested explains these differences. CMW® 2G powder is sterilised by gamma irradiation, whereas Palacos® cements are sterilised by Ethylene oxide (ETO). Irradiation has been shown by other authors to reduce the molecular weight of the polymer beads by half, which results in lower fatigue strengths of the resultant cement[33,34].

In revision surgery for prosthetic joint infection, local antibiotic delivery is a proven component of treatment in the form of hand-made antibiotic-loaded cement spacers and beads[35,36]. Fast-setting cements may be preferable for this indication if they appropriate handling and elution characteristics? Firstly, the highly viscous dough of fast setting cements after mixing allows an easy manual application without the cement sticking to the gloves. Secondly, both cements tested showed standard bi-phasic elution of the antibiotic *in vitro*. Palacos® fast R + G showed superior gentamicin release at all stages, despite a lower antibiotic content in comparison to CMW® 2G. Palacos® fast R + G contains the same hydrophilic co-polymers that are present in Palacos® R + G. It is these co-polymers in combination with the special polymer/monomer ratios of Palacos® cements that accounts for the increased antibiotic release compared with other cement brands[37]. This phenomenon has been described by numerous authors for the standard-setting Palacos® R + G and it would appear to hold true for the fast-setting version as well[7,38].

The use of eligible, fast-setting high viscosity PMMA cements are already described in national joint registries for both knee and hip arthroplasty[5,6]. Palacos® fast R + G and CMW® 2G are both highly suitable for their specified surgical indications as they afford a time-saving measure without detriment to the mechanical properties. Both are compliant with international standards and we have described in this study their relative handling and mechanical properties in order to inform surgeons so that they might apply them to their practice.

Due to Palacos® fast R + G's shorter doughy/waiting phase compared to CMW® 2G, it is ready to apply immediately after mixing. During surgeries Palacos® fast R + G allows better component position control during cup insertion with less extrusion and movement of the cement compared to CMW® 2G.

A higher powder-liquid ratio of Palacos® fast R + G results in a lower peak temperature compared to CMW® 2G, which might protect against thermal damage of the bone with use of the Palacos® fast R + G cement.

Palacos® fast R + G had a statistically significant higher ISO compressive strength (MPa) than CMW® 2G, it also showed higher fatigue strength according to ISO 16402, likely due to different sterilisation techniques. Palacos® fast R + G also showed a much higher gentamicin release profile at all stages, despite a lower antibiotic content compared to CMW® 2G.

COMMENTS

Background

Polymethylmethacrylate (PMMA) cements provide reliable fixation of the implants in joint arthroplasty. Fast-setting high viscosity cements exist that have altered setting characteristics compared to standard setting cements.

Research frontiers

PMMA is widely used for implant fixation in orthopaedic and trauma surgery. Bone cements also act as space-filler and elastic buffer, distributing forces evenly between prosthesis and bone.

Innovations and breakthroughs

Fast-setting PMMA cements offer benefits to both surgeon and patient based on their handling properties. These benefits might include reduced operative time and therefore economic advantage and decreasing risk of infection, also due to better antibiotic release because of special polymer/monomer ratio.

Application

Fast-setting PMMA bone cements have gained popularity in knee arthroplasty and hip replacement surgery as described in the United Kingdom and Australian National Joint Registries over the last years.

Terminology

The chemical composition of PMMA cements accounts for its mechanical and handling properties. The polymerization reaction of PMMA is divided in to four phases: Mixing, waiting, working and setting. Bone cements are classified based upon the amount of time they spend in each of these phases. Fast-setting cements are characterised by a short mixing, moderate working and very short hardening phase.

Peer-review

The study is very well executed and presented.

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ORIGINAL ARTICLE

Basic Study

Augmented reality: The use of the PicoLinker smart glasses improves wire insertion under fluoroscopy

Takafumi Hiranaka, Takaaki Fujishiro, Yuichi Hida, Yosaku Shibata, Masanori Tsubosaka, Yuta Nakanishi, Kenjiro Okimura, Harunobu Uemoto

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Abstract

AIM

To demonstrate the feasibility of the wearable smart glasses, PicoLinker, in guide wire insertion under fluoroscopic guidance.

METHODS

Under a fluoroscope, a surgeon inserted 3 mm guide wires into plastic femurs from the lateral cortex to the femoral head center while the surgeon did or did not wear PicoLinker, which are wearable smart glasses where the fluoroscopic video was displayed (10 guide wires each).

RESULTS

The tip apex distance, radiation exposure time and total insertion time were significantly shorter while wearing the PicoLinker smart glasses.

CONCLUSION

This study indicated that the PicoLinker smart glasses can improve accuracy, reduce radiation exposure time, and reduce total insertion time. This is due to the fact that the PicoLinker smart glasses enable surgeons to keep their eyes on the operation field.

Key words: Smart glasses; Imaging; Wearable devices; Fluoroscopy; Guide wire insertion

Core tip: Smart glasses are a kind of wearable device that has a head-mounted monitor enabling augmented reality. The fluoroscopic video was displayed on the head-mounted monitor of the smart glasses, PicoLinker. A surgeon was asked to insert 3 mm guide wires into plastic femoral bones under fluoroscopic control while wearing the PicoLinker smart glasses or by viewing the conventional fluoroscope monitor. Total insertion time, radiation exposure time and tip apex distance were shorter while wearing the PicoLinker smart glasses than while viewing the conventional monitor. Smart glasses are an innovative device that enables surgeons to keep their eyes on the operation field during procedures carried out under fluoroscopic control.

Hiranaka T, Fujishiro T, Hida Y, Shibata Y, Tsubosaka M, Nakanishi Y, Okimura K, Uemoto H. Augmented reality: The use of the PicoLinker smart glasses improves wire insertion under fluoroscopy. *World J Orthop* 2017; 8(12): 891-894 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/891.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.891

INTRODUCTION

Wearable technology has entered the medical field and will change surgery dramatically. Wearable smart glasses are a kind of computer that displays information on a head-mounted display. For procedures performed under fluoroscopic guidance, the head-mounted display enables surgeons to perform procedures under fluoroscopic control while keeping their eyes on the operative field. Google Glass® (Google Inc., Mountain View, CA, United States) is the most well-known wearable glasses and has been used for various medical purposes such as medical education[1,2], surgery navigation[3,4] and as vital sign monitors[5]. However, it is not commercially available for general use. PicoLinker (Westunitis Co., Ltd., Osaka, Japan) (Figure 1) is a kind of wearable glasses that can display images or videos that are on existing monitor screens, on the head-mounted monitor. Unlike Google Glass, PicoLinker can capture video from various types of video sources *via* a transmission box that is connected to PicoLinker and contains various types of video connectors. We assumed that PicoLinker can be used as an alternative screen for fluoroscopic images. This technology is a kind of augmented reality (AR) where virtual images are added on real images. Virtual reality is where the wearer can see completely virtual or synthesized images in a completely shielded eyewear without viewing the real image. Through the AR, the wearer (operator) can obtain additional information (fluoroscopic video) simultaneously with the real image (operation field). Using this device, the operator can glance at the fluoroscope video on the PicoLinker smart glasses while keeping his/her eyes on the operation field. This would improve accuracy, reduce radiation exposure, and reduce the procedure time. The aim of this pilot study was to evaluate the effectiveness of PicoLinker in guide wire insertion into an artificial femoral head under fluoroscopic control.

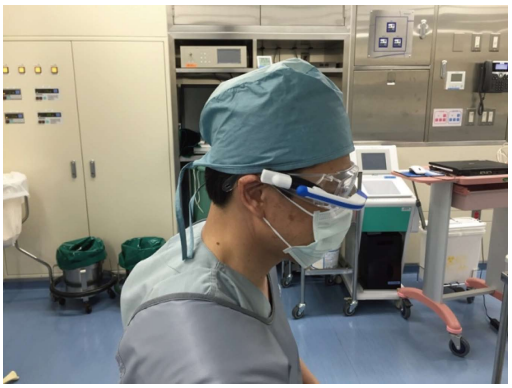

Figure 1 An operator wearing the PicoLinker (wearable smart glasses).

MATERIALS AND METHODS

Wearable device

The PicoLinker is a kind of wearable smart glasses and contains a prism monitor with resolution of 428 × 240 pixels. PicoLinker can be mounted on any type of normal glasses and is connected to a video box by a wire cable. The video box has six types of video-connectors: HDMI, USB, VGA, video composite, S-video composite, and encrypted and secured micro-SD slot. Various types of monitors such as a fluoroscope monitor can be connected to the video box, and can be viewed by the operator on the prism monitor of PicoLinker. Although most types of video lines can be connected, in the case where there is no available connector nor video signals, a video camera can be placed in front of the existing monitor so that the screen image can be transferred to the prism monitor *via* the video box. The prism screen is set on normal glasses. In the present study, a fluoroscope monitor was connected to the video box of PicoLinker so that the surgeon could view the fluoroscopic video through PicoLinker.

Evaluation of wire insertion

A surgeon performed guide wire insertion into five plastic femoral bones (Sawbone®, Sawbones Inc., Malmo, Sweden). The operator was instructed to introduce a Kirschner wire of 3.0 mm in diameter using an electric driver from the lateral cortex of the femur towards the femoral head, parallel to the femoral neck axis on anteroposterior view, under fluoroscopic control with the aim of minimizing the tip apex distance (TAD)[6]. The driver was initially placed beside the operator. The operator was instructed to pick up the driver, pick up the wire with the driver, find the best insertion point, and advance the drill into the femoral head. The drill insertion was performed ten times with PicoLinker (Wearable group) (Figure 2) and another ten times without PicoLinker while viewing the conventional fluoroscope

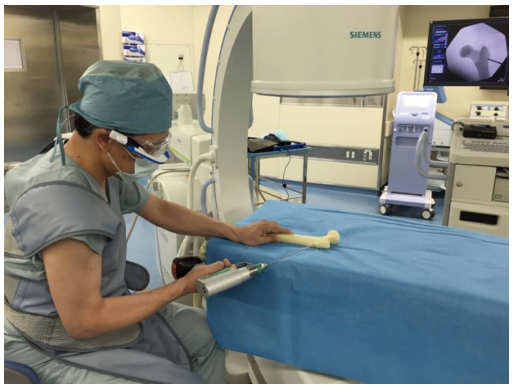

Figure 2 The operator inserting a 3.0 mm Kirschner wire in a plastic femoral bone under a fluoroscope while viewing the fluoroscopic video on PicoLinker.

Figure 3 The operator inserting a 3.0 mm Kirschner wire in a plastic femoral bone under a fluoroscope without PicoLinker, while viewing a conventional fluoroscope monitor.

monitor (Conventional group) (Figure 3). The time from picking up the wire to completion of insertion, total radiation time and the TAD on anteroposterior view were measured and evaluated.

Statistical analysis

Results are expressed as the mean. The significance of differences between the groups was evaluated using unpaired *t*-test. A level of $P < 0.05$ was considered to be significant. Statistical analyses were performed using Microsoft Excel 2016 (Microsoft Corp., Redmond, WA, United States).

RESULTS

TAD, radiation exposure time and total insertion time were significantly shorter in the Wearable group than in the Conventional group [2.6 mm (mean) *vs* 4.1 mm, $P = 0.02$; 11.6 s *vs* 15.0 s, $P = 0.00001$; and 14.5 s *vs* 19.3 s, $P < 0.00001$, respectively].

DISCUSSION

Smart glasses are an innovative device for medical purposes that can be used in emergency surgery and surgical education including live streaming as well as remote instruction and monitoring. Although many papers on this device have been reported, evidence on the usefulness of the device has seldom been reported. Chimenti *et al*[7] reported a similar study using Google Glass in which an operator inserted Kirschner wires into cadaveric phalangeal and metacarpal bones. The results showed reductions in radiation time and operation time. Their results were similar to our results, which also showed reductions in radiation time and operation time. In addition, we found that the accuracy of pin insertion was significantly improved using PicoLinker. This is due to the fact that the operator can see both the operation field and fluoroscopic images without moving his/her eyes and head.

Numerous medical procedures are performed under images displayed on monitor screens. In most such procedures, the operator needs to take his/her eyes off from the operation field to see the monitor (Figure 3). In addition to fluoroscopy, vital sign monitor, endoscope, and computer navigation as well as conventional images such as X-ray image, computed tomography and magnetic resonance imaging are images on monitors. Using the PicoLinker allows the operator to keep his/her eyes on the operative field while seeing the images (Figure 2).

Unlike Google Glass, PicoLinker has a video box that can be connected by various types of connectors. Furthermore, even if there is no available connector from a monitor, a video camera can be used to capture the monitor images and the images can be transferred to PicoLinker; consequently, the images on all types of monitors can be transferred to PicoLinker. In addition to connectivity, the simple structure is another advantage of PicoLinker over Google Glass. The PicoLinker contains no more than a prism monitor. It has no CPU, camera nor battery; therefore, it has a light weight and battery life is never a problem. As PicoLinker is connected to a video source *via* a wire cable, there is no image delay. On the other hand, Google Glass images are transferred *via* the internet, and therefore a certain degree of latency is inevitable. Commercial availability is another distinct advantage of PicoLinker over Google Glass.

Nearly all reports on the use of smart glasses for medical purposes have involved the use of Google Glass. However, some other devices are available for surgery. We reported another type of smart glasses, InfoLinker (Westunitis Inc., Osaka, Japan), which has both a head-mounted monitor and head-mounted video camera and can connect to the internet for surgical video streaming[8]. This device is suitable for sending images in which the operator can see the same images through a head-mounted video camera. Although Google Glass has been used for this purpose, there are some advantages of the InfoLinker over Google Glass such as internet connection flexibility, battery durability and usability. Both PicoLinker and InfoLinker are currently available in Japan. They will soon become available in other countries.

Limitations of this study were that the trial was done by a single surgeon and the relatively small trial numbers. Nevertheless, the superiority of the use of PicoLinker smart glasses was demonstrated. The results on the usefulness of PicoLinker are encouraging. Further usage is expected.

COMMENTS

Background

There are few reports on head-mounted visualization of video from a fluoroscope monitor. Most operators have to see the fluoroscopic video on a fluoroscope monitor apart from the operation field. This may cause technical difficulties and inconvenience to the operator.

Research frontiers

Smart glasses are an innovative tool for visualization and image recording using a head-mounted monitor and head-mounted camera. Nearly all medical articles on smart glasses have involved the use of Google Glass. Although Google Glass can be utilized in various medical settings, head-mounted visualization of fluoroscopic video has rarely been reported.

Innovations and breakthroughs

The authors have presented a new type of smart glasses named PicoLinker. It is already commercially available in Japan and will soon be available in other countries. PicoLinker has some advantages over Google Glass with regard to direct image transfer *via* cable connection without image latency, its simple and light body, and unlimited battery life. The introduction of PicoLinker to the medical field will inspire new ideas to improve surgeries.

Peer-review

This is an interesting study testing a devise "coming from the future".

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ORIGINAL ARTICLE

Case Control Study

Season of the year influences infection rates following total hip arthroplasty

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Abstract

AIM

To research the influence of season of the year on peri-prosthetic joint infections.

METHODS

We conducted a retrospective review of the entire Medicare files from 2005 to 2014. Seasons were classified as spring, summer, fall or winter. Regional variations were accounted for by dividing patients into four geographic regions as per the United States Census Bureau (Northeast, Midwest, West and South). Acute postoperative infection and deep periprosthetic infections within 90 d after surgery were tracked.

RESULTS

In all regions, winter had the highest incidence of

periprosthetic infections (mean 0.98%, SD 0.1%) and was significantly higher than other seasons in the Midwest, South and West ($P < 0.05$ for all) but not the Northeast ($P = 0.358$). Acute postoperative infection rates were more frequent in the summer and were significantly affected by season of the year in the West.

CONCLUSION

Season of the year is a risk factor for periprosthetic joint infection following total hip arthroplasty (THA). Understanding the influence of season on outcomes following THA is essential when risk-stratifying patients to optimize outcomes and reduce episode of care costs.

Key words: Hip arthroplasty; Healthcare; Infection; Outcomes; Season

Core tip: Season of the year when a total hip arthroplasty is performed may affect 90-d post-operative outcomes in certain regions of the United States. Furthermore, there appears to be a difference of the effect of seasonal variation on the outcomes as superficial infections have different patterns compared to deep peri-prosthetic joint infection.

Rosas S, Ong AC, Buller LT, Sabeh KG, Law T, Roche MW, Hernandez VH. Season of the year influences infection rates following total hip arthroplasty. *World J Orthop* 2017; 8(12): 895-901 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/895.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.895

INTRODUCTION

Total hip arthroplasty is one of the most common orthopaedic procedures in the United States, with over 600000 performed annually[1,2]. Though this procedure has societal and personal benefits for patients, it is not without risks[3]. Complications following THA range from increased length of stay to circulatory collapse and death. While minor and major complications are infrequent[4,5] their impact on readmissions and post-discharge care represents a significant portion of the episode payment[6]. Factors increasing the likelihood of complications are of great interest, as risk minimization strategies have been shown to reduce overall cost in THA[7]. Hospital type, surgeon volume, comorbidities and other modifiable risk factors have recently been studied in great detail[4,8-13]. However, non-modifiable risk factors have also been elucidated as important for pre-operative risk stratification[14-17].

Recently, the influence of seasonality on outcomes in various surgical subspecialties has been investigated[14,18-21]. How season or climate impacts outcomes following THA remains unknown, with the only evidence originating from a single institution, retrospective study by Kane *et al*[22] who demonstrated an association between summer and infection. In the United States, seasonality affects aspects of life in a variety of manners[23]. Winter months encourage a sedentary lifestyle, changes eating patterns and results in fewer follow up visits[24-27]. In contrast, the increased temperatures and humidity of summer months improves microbe survivorship, increases vitamin D levels, encourages being outdoors and overall activity levels[28]. Given the impact of seasonality on such diverse aspects of life, this study sought to elucidate the influence of season of the year and geographic location on outcomes following THA at a national level. To improve the relevance of this study, we chose to compare differences in the incidence of postoperative infections within the 90-d period, simulating an episode of care period as put forth by the Comprehensive Care for Joint Replacement (CJR) Model.

MATERIALS AND METHODS

We conducted a retrospective case-control, level of evidence Ⅲ study, evaluating the effects of season of the year on two types of infections following THA. This was achieved by analysis of the Medicare patient database. The query was performed through the Pearldiver Supercomputer (Warsaw, IN, United States). The supercomputer allows identification of patient records through international classification of disease (ICD) ninth revision codes. Patients were then stratified by season of surgery. The seasons were defined as follows: Spring (March, April and May), summer: (June, July and August), fall (September, October and November), winter (December, January and February). Demographical data including age, gender and region of the United States were the surgery was performed was gathered at baseline. Geographical region was classified according to the United States Census Bureau as follows: Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin. Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island and Vermont. South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia and West Virginia. West: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming.

Patients and outcomes were tracked for 90 d. Using previously described methodology; ICD-9 codes were used to identify complications[9-11,29,30]. The following outcomes were tracked: acute post-operative infection (998.5), osteomyelitis (730) and infection of orthopaedic device (996.66). Infections were then subdivided into acute postoperative infection (ICD-998.5) and deep infection (ICD-996.66 and 730). This methodology

Table 1 Study patient demographics

	NE	MW	WE	SO
Female	61.60%	61.10%	60.60%	61.40%
Male	38.40%	38.90%	39.40%	38.60%
Age (yr)	9%	9%	9%	12%
⩽ 64	9%	9%	9%	12%
65-69	23%	24%	26%	24%
70-74	22%	22%	23%	22%
75-79	21%	21%	20%	20%
80-84	16%	15%	14%	14%
⩾ 85	10%	9%	9%	8%

NE: North East; MW: Mid West; WE: West; SO: South.

Table 2 Incidence of acute postoperative infections at 90 d following total hip arthroplasty

Location	Spring	Summer	Fall	Winter	χ^2
North East	1.41%	1.35%	1.35%	1.47%	0.281
Mid West	1.54%	1.59%	1.51%	1.60%	0.39
South	1.60%	1.68%	1.58%	1.64%	0.277
West	1.25%	1.59%	1.31%	1.43%	< 0.001
Mean	1.45%	1.55%	1.44%	1.54%	
SD	0.16%	0.14%	0.13%	0.10%	

of separating infections has also been previously described[9-11,29,30]. The incidence of complications was compared through Chi-squares with Yates corrections given the large sample size of the study. Statistical analysis was conducted through SPSS version 20 (IBM, Armonk, NY, United States). An alpha value less than 0.05 was deemed statistically significant.

RESULTS

A cohort representative of 1311672 patients who underwent THA between 2005 and 2014 was identified. The seasonal distribution of procedures was similar: 25% in the spring, 26.9% in the summer, 25% in the fall and 24% in the winter. Regional volume varied significantly ($P < 0.001$) with the south performing the majority of surgeries (35%) followed by the mid-west (28%), the northeast (19%) and the west (18%) (Table 1).

There was a significant difference in the incidence of acute postoperative infections by season in the West (Table 2). The greatest incidence in the West was following surgeries performed in the summer (1.59%), which was significantly greater than all other seasons ($P < 0.001$ for all) (Figure 1). There was no difference in acute postoperative infections when stratified by season in the other regions.

Our analysis demonstrated that season of the year had a significant effect on periprosthetic joint infections in two out of the four regions, Midwest and South (Table 3). The mean incidence in the Northeast and West was 0.85% (range 0.82% to 0.91%, $P = 0.358$) and 0.86% (range 0.84% to 0.89%, $P = 0.680$), respectively.

Table 3 Incidence of periprosthetic infections at 90 d following total hip arthroplasty

Location	Spring	Summer	Fall	Winter	χ^2
North East	0.82%	0.83%	0.84%	0.91%	0.358
Mid West	0.97%	0.97%	0.88%	1.04%	0.013
South	1.06%	1.06%	0.96%	1.10%	0.007
West	0.84%	0.84%	0.88%	0.89%	0.68
Mean	0.92%	0.92%	0.89%	0.98%	
SD	0.11%	0.11%	0.05%	0.10%	

The Midwest region had the highest incidence of periprosthetic infections in the winter 1.04%, which was significantly higher than the fall (0.88%, $P = 0.001$) but not higher than other seasons ($P = 0.175$ *vs* the summer and $P = 0.155$ *vs* the spring). There were no significant differences when comparing the remaining seasons. In the South, the highest incidence of periprosthetic infections was also seen in the winter (1.1%), which was significantly higher than the fall 0.96% ($P < 0.001$) but not than the summer or spring, both 1.06% ($P = 0.377$ and 0.344 respectively). In the South, the fall had a lower incidence, 0.96%, compared to the spring ($P = 0.018$) and to the summer ($P = 0.005$) (Figure 2).

DISCUSSION

This study sought to determine the effect of season of the year, a non-modifiable risk factor, on infections following THA. This was achieved by scrutinizing the entire Medicare population from 2005 to 2014 for the outcomes of interest during the 90-d post-operative period. Our analysis of over 1 million patients demonstrated that acute postoperative infections are significantly affected by season in certain geographical regions. These results are similar to the work of Kane *et al*[22], who reported infection rates during summer of 4.7%, fall 2.4%, winter 1.5% and spring 0.5%. Although the authors did not differentiate between deep and superficial infections, they highlight that humidity; colonization and the implementation of new house staff ("July effect") might be responsible for the reported findings. Similarly, various studies have demonstrated a seasonal variation in the rates of surgical site infections from Staphylococcus aureus, which is the main cause of superficial infections among orthopaedic patients[14,19,31,32]. The seasonal influence of the microbes in conjunction with increased sweat gland output, skin hydration, and elevated temperatures may all contribute to the seasonal variation observed here[20,28,32]. Conversely, the relative consistency of the weather in the South, with warmer year-round temperatures, may account for the lack of statistically significant variation in this region. Previous studies have found differences in infection rates are more pronounced in particular regions of the United States, which was also reported in the present study[32].

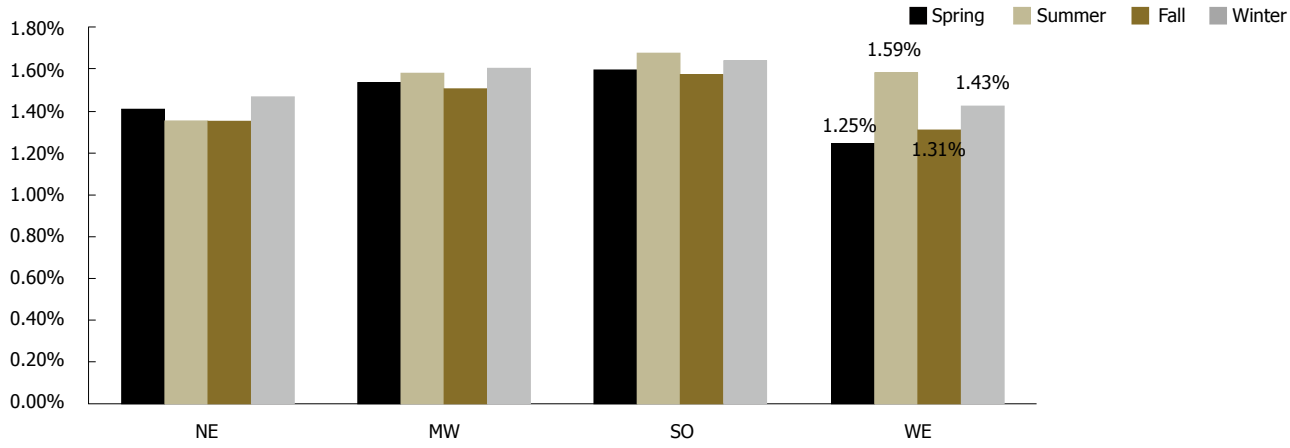

Figure 1 Incidence of acute post-operative infection following total hip arthroplasty by region of the United States. Values are shown for the region, which had a significant difference. There was a significant difference in the incidence of acute postoperative infections by season in the West ($P < 0.001$). NE: North East; MW: Mid West; WE: West; SO: South.

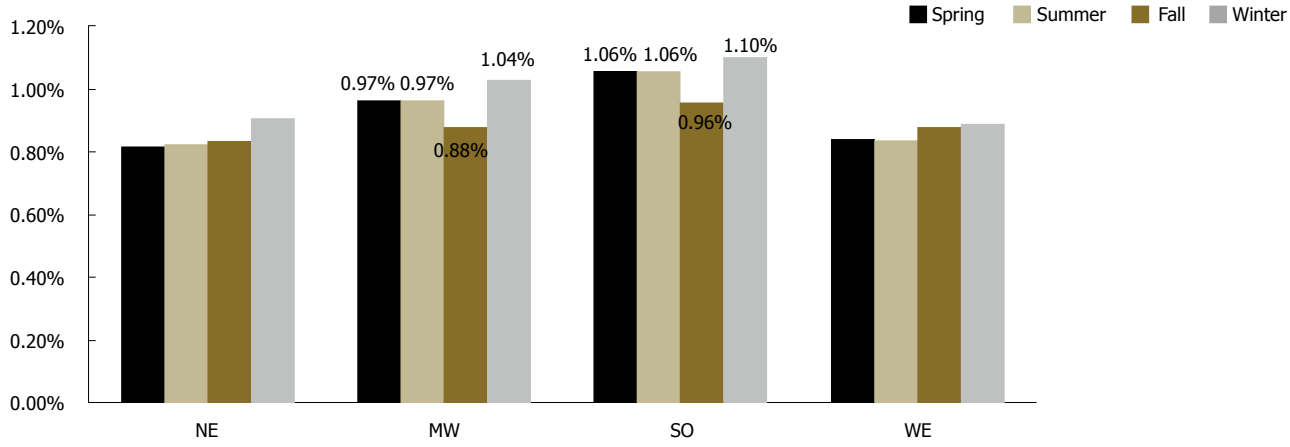

Figure 2 Incidence of periprosthetic infection following total hip arthroplasty by region of the United States. Values are shown for the regions, which had a significant difference. There was a significant difference in periprosthetic joint infections in two out of the four regions, Midwest and South ($P = 0.013$ and $P = 0.007$ respectively). NE: North East; MW: Mid West; WE: West; SO: South.

The overall incidence of periprosthetic joint infections reported in this study (0.89%-0.98%) is similar to epidemiological studies by Kurtz *et al*[33] who reported an overall incidence of 2% with variation by training center from 0.61% in rural hospitals to 0.73% at urban-teaching hospitals to 1.18% in Urban-non-teaching hospitals[34]. This study also found a significant variation in the total number of procedures performed when stratified by geographic region, with the South performing the highest volume of cases. Thakore *et al*[35] reported similar results with the number of average discharges billed to Medicare at each hospital highest in the Midwest, followed by the South, Northeast and West. Similarly, this study demonstrated a seasonal variation in the incidence of infection in certain regions of the United States. The Midwest and the South were found to have higher rates of infection in the winter (1.04% and 1.1%, respectively). Previous studies in spine surgery have found a greater incidence of infectious complications in the summer (4.1%) followed by the fall (3.9%)[31]. However, these authors did not differentiate between superficial and deep infections and classified patients based on the surgical site infection classification. Similar findings were also reported by Kestle *et al*[36], who concluded that there is an increased risk of infections attributable to the "July effect," based on data from 737 patients treated in Canada. Nonetheless, these articles did not analyse a national sample stratified by region and potential reasons for the higher periprosthetic infection rate seen in the winter include longer length of stay because of travel/discharge difficulties, decreased patient compliance with post-operative care or difficulty making follow up appointments. The "July" effect which refers to incoming house staff lack of experience has been suggested as a cause of increased infections following surgical management of certain entities, but this has not held true in the arthroplasty literature[31]. Although our study did not stratify by hospital type (teaching *vs* non-teaching), demonstration that periprosthetic joint infections are more common in the winter suggests incoming residents may not be at fault[14,18].

Although our study demonstrates certain differences in infection rates by season of the year and by region,

we demonstrated that "superficial infections" have different variations that "deep infections" which although controversial, may be due to various reasons: first, the increased risk of superficial infections in the summer may be related to the increased in temperature as has been postulated by Anthony *et al*[37] in their large population-based study of the National Inpatient Sample. The authors conducted a comprehensive examination of the NIS and accounted for patient factors, hospital factors and weather variations with their models. Furthermore, the authors state that bacteria can colonize different skin areas at different concentration as temperature varies. Unfortunately, less is known about the seasonality of deep infections. Some authors have demonstrated a seasonal variation in bacteraemia in hospitalized patients, but bacteraemia does not always cause a joint infection and as such limited information can be extracted from this[38]. Thus, with such little evidence available no definite conclusion can be made of why such variation exists.

This study is not without its limitations. Being a retrospective review, there is potential for selection bias due to the way patients were stratified. This bias was minimized, as the number of THAs in each group was similar. As a large database study, another source of selection bias might have been the coding of the procedures and/or the outcomes, which is beyond the author's control. Although we relied on previously published literature regarding the identification of the outcomes, it is possible that coding errors may have influenced our results. However, the importance of coding on reimbursements, decreases this likelihood. Time-lead bias may also play a part in the significance of our results as the outcomes are tracked for 90 d following the procedures that occurred within a 3-mo period and thus we cannot account for whether a procedure was performed at the beginning or end of that 3-mo period that comprised a season of the year.

In conclusion, season of the year, which is a non-modifiable risk factor, influences the rate of postoperative infections following THA in some regions of the United States. Superficial, acute post-operative infections are more commonly seen after THAs performed in the summer and periprosthetic joint infections more frequently occur in THAs performed in the winter. Understanding that seasonality is a risk factor for periprosthetic joint infection following THA is essential when risk stratifying patients that are a part of a bundled payment reimbursement model.

ARTICLE HIGHLIGHTS

Research background

Limited information is available in regard to the correlation between season of the year when a surgery is performed to the outcomes of the surgery. Weather variations may account for different bacterial patterns that may lead to infection. Thus, we studied the effects of season of the year on the infectious outcomes after total hip arthroplasty in the United States Medicare patient population.

Research motivation

Due to the large effect on morbidity, mortality and cost that infections can cause, it is important to study modifiable and non-modifiable risk factors for adverse outcomes after surgery. By identifying a seasonal variation in post-operative outcomes, one may ultimately use this information to delay elective surgery.

Research objectives

The purpose of this study was to determine if season of the year when a total hip arthroplasty is performed had an effect on 90-d post-operative superficial and deep infections among Medicare beneficiaries in the United States. The study identified certain seasonal differences that should promote research on this subject through prospective studies.

Research methods

The authors conducted a retrospective review of the entire Medicare files and stratified patients by region and season when the surgery was performed. The authors evaluated the 90-d post-operative period after the procedure to determine the incidence of these complications. The authors analyzed the entire Medicare records from 2005 to 2014. Comparative statistical analysis was used to compare the 90-d incidences reported by international classification of disease 9th edition code tracked in the patient file.

Research results

There was a significant difference in the incidence of acute postoperative infections by season in the West. The greatest incidence in this region (West) was following surgeries performed in the summer (1.59%), which was significantly greater than all other seasons ($P < 0.001$ for all). Our analysis demonstrated that season of the year had a significant effect on periprosthetic joint infections in two out of the four regions, Midwest and South. These results help demonstrate that variation exists in certain regions of the United States by season of the year and that more research is needed on this non-modifiable risk factor.

Research conclusions

There were no previous articles in the literature describing seasonal variation of outcomes after lower extremity arthroplasty. The new findings of this study is: Season of the year may influence post-operative outcomes after total hip arthroplasty. This study proposes the new theories that seasonal variation of these outcomes varies and that the seasonal variability between superficial infection and peri-prosthetic infection exists. This study offered the original insights into the current knowledge by providing evidence that there is regional and seasonal variation in outcomes. This study proposed the new hypotheses that temperature and weather variations may lead to different infectious complications after hip arthroplasty. The authos proposed the new methods that prospective trials to investigate the effect of not only season of the year when the surgery is performed affect the outcomes but also weather. We found the new phenomena that certain regions of the United States have different post-operative complication rates of infectious outcomes after THA when stratified by season of the year when the surgery was performed. Through experiments in this study, the authors confirmed the hypotheses that seasonal variation exists in infectious outcomes after THA in certain regions of the United States. In the future, non-modifiable risk factors may play a role in the outcome of THA such as season of the year when the surgery is performed.

Research perspectives

Season of the year when surgery is performed may have an effect on complication rates after THA. Future studies should create models that account for weather and seasonal variations in the study of outcomes after arthroplasty procedures.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Do Not Resuscitate status as an independent risk factor for patients undergoing surgery for hip fracture

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Abstract

AIM

To determine morbidity and mortality in this specific patient group and also to assess for any independent associations between Do Not Resuscitate (DNR) status and increased post-operative morbidity and mortality.

METHODS

We conducted a propensity score matched retrospective analysis using de-identified data from the American College of Surgeons' National Surgical Quality Improvement Project (ACS NSQIP) for all patients undergoing hip fracture surgery over a 7 year period in hospitals across the United States enrolled in ACS NSQIP with and without Do Not Resuscitate Status. We measured patient demographics including DNR status, co-morbidities, frailty and functional baseline, surgical and anaesthetic

procedure data, post-operative morbidity/complications, length of stay, discharge destination and mortality.

RESULTS

Of 9218 patients meeting the inclusion criteria, 13.6% had a DNR status, 86.4% did not. Mortality was higher in the DNR status compared to the non-DNR group, at 15.3% *vs* 8.1% and propensity score matched multivariable analysis demonstrated that DNR status was independently associated with mortality (OR = 2.04, 95%CI: 1.46-2.86, $P < 0.001$). Additionally, analysis of the propensity score matched cohort demonstrated that DNR status was associated with a significant, but very small increased likelihood of post-operative complications (0.53 *vs* 0.43 complications per episode; OR = 1.21; 95%CI: 1.04-1.41, $P = 0.004$). Cardiopulmonary resuscitation and unplanned reintubation were significantly less likely in patients with DNR status.

CONCLUSION

Whilst DNR status patients had higher rates of post-operative complications and mortality, DNR status itself was not otherwise associated with increased morbidity. DNR status appears to increase 30-d mortality via ceilings of care in keeping with a DNR status, including withholding reintubation and cardiopulmonary resuscitation.

Key words: Do Not Resuscitate; Consent; Perioperative; Outcomes; Mortality; Hip fracture

Core tip: We present a large, multi-institution retrospective cohort study which examines the independent association of Do Not Resuscitate (DNR) status with perioperative outcomes during hip fracture surgery. We find that DNR status independently predicts overall rates of complications and mortality at 30 d without other clear sources of morbidity. Our conclusions place this work in the context of other literature on the outcomes for patients with DNR status during the perioperative period, exploring the data among other surgical populations and hypotheses for this effect.

Brovman EY, Pisansky AJ, Beverly A, Bader AM, Urman RD. Do Not Resuscitate status as an independent risk factor for patients undergoing surgery for hip fracture. *World J Orthop* 2017; 8(12): 902-912 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/902.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.902

INTRODUCTION

Do Not Resuscitate (DNR) status documents that a decision has been made to withhold certain resuscitative measures in the event of cardiorespiratory arrest. This typically includes withholding chest compressions and endotracheal intubation. DNR status documents a patient's advance refusal of resuscitative procedures, due to expressed wishes or beliefs, or where cardiopulmonary resuscitation would fail to restore a quality of life compatible with the patient's goals of care[1-3]. DNR status is most common when patients have multiple, severe co-morbidities, extreme frailty, or end stage diseases[4-6].

DNR status does not prevent surgery, despite the potential need for endotracheal intubation or inotropic support during anesthesia. The American Society of Anaesthesiologists' Ethics Committee guidance of 2013 states: "an essential element of preoperative preparation and perioperative care for patients with DNR orders … is communication among involved parties. …The status of these directives should be clarified or modified based on the preferences of the patient"[7]. Patients with DNR status can undergo a range of emergency, urgent or elective surgical procedures to prolong life or improve quality of life. However, as DNR status frequently coincides with narrowed goals of care, procedures tend to be life sustaining or palliative, rather than elective.

The true incidence and composition of surgery in patients with DNR status is unknown. One recent analysis identified 22% of all surgeries in patients with DNR status were lower limb orthopedic procedures[8]. Hip fracture fixation is the most common indication for hip surgery at the older extreme of age, and ortho-geriatric patient outcomes have been the focus of recent national quality improvement initiatives[9-12]. However, outcomes after hip fracture surgery specifically in the DNR status population are unknown.

It is also unclear whether DNR status itself independently and negatively impacts major outcomes such as morbidity and length of stay[13-16]. DNR status only directs actions in the event of cardiopulmonary arrest. The "failure to treat" hypothesis, describing inadequate (non-resuscitative) treatment of patients because of DNR status, has been suggested but with inconclusive evidence[17]. The aim of this study is to describe the incidence and distribution of DNR status in patients undergoing hip fracture surgery and to determine whether DNR status is an independent risk factor for worse outcomes on 30 d follow up.

MATERIALS AND METHODS

Data source

The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) is a data registry of cases reported from approximately 400 participating sites. ACS-NSQIP is a well-validated database and incorporates data from patients' medical charts, with data entry overseen by a designated Surgical Clinical Reviewer (SCR) at each site. Institutional Review Board (Brigham and Women's Hospital, Boston, MA, United States) approval was obtained for analysis of the data and was exempted from the

consent requirement due to the de-identified nature of the data.

Study sample

The 2007-2013 NSQIP was compiled into a single data file containing 306 variables across 2.8 million surgical cases. All cases recording patients under age 18, trauma cases, transplant surgeries, cases where the patient is American Society of Anesthesiologists (ASA) physical status class 6, representing a brain-dead organ donor are excluded from NSQIP. We isolated all admissions for hip fracture surgery using all listed ICD codes (Appendix 1) and Current Procedural Terminology (CPT) codes (included in Table 1 with case mix data). All cases failing to report the "do not resuscitate" variable or CPT code were excluded from the analysis. Patient demographic data were collected for age, ASA physical status (PS) class, sex, race, ethnicity, height, weight, and body mass index. Preoperative comorbidity data were collected for functional status prior to surgery, defined as ability to perform activities of daily living (ADL), baseline dyspnea, diabetes mellitus (insulin and non-insulin dependent); smoking status within one year prior to admission; presence of chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease (defined as a composite of a history of angina, myocardial infarction, percutaneous coronary interventions or previous cardiac surgery), hypertension, chronic kidney disease, cerebrovascular accidents, pre-operative weight loss of greater than 10% in the 6 mo prior to surgery, sepsis physiology and a previous operation within the past 30 d. Additional pre-operative laboratories, including the creatinine, albumin, hematocrit, platelet count and international normalized ratio (INR) were collected.

We calculated a frailty score for each patient undergoing hip fracture surgery to assess for presence of any baseline differences in pre-morbid status between the DNR and non-DNR status groups. We used a variation of the well-known Charlson Comorbidity Index[18-21]. The Canadian Study of Health and Ageing (CSHA)[22] Clinical Frailty Scale is a 7 point index, modified from the Charlson Comorbidity Index. It has been validated previously using NSQIP data, and has been modified for use with data collected within the NSQIP dataset[23].

Data collection for the surgical procedure included the primary surgical CPT code, surgical wound classification, total anesthesia and surgical time and anesthesia type. To assess for independent association between preoperative patient demographic, comorbidity and frailty variables and DNR status, we conducted univariable and multivariable regression analysis. For the logistic regression, odds ratios (OR) were reported with their associated 95% CI. OR not including 1.00 in their 95%CI were considered statistically significant and were included in the multivariable regression analysis.

We collected binary outcomes data for the following postoperative events up to 30 d after surgery: Death, return to the operating room, superficial and deep space surgical site infections, post-operative pneumonia, unplanned intubation, failure to wean from the ventilator, progressive renal insufficiency and acute renal failure requiring dialysis, urinary tract infections, cerebrovascular accidents, myocardial infarction, post-operative bleeding requiring transfusion of packed red blood cells, deep venous thrombosis requiring therapy, pulmonary embolism and post-operative sepsis. Additional data on discharge destination (Home, Skilled Care, or Rehabilitation facility) and total length of stay were also collected. All outcomes were reported as percentages, with the numerator defined as the absolute count reporting a given outcome and the denominator defined as the total number of cases reporting any outcome for that variable. To assess for the associations between DNR status and post-operative outcomes, we developed a propensity score matched cohort in which patients were matched by propensity for DNR status. We performed univariable and multivariable regression analysis on the matched cohort and OR not including 1.00 in their 95%CI were considered statistically significant.

Statistical analysis

R Project for Statistical Computing (R version 3.2.3) was used to perform all statistical analysis. Differences between cohorts were assessed using the Pearson chi squared test for categorical variables and using the Student's *t*-test for continuous variables due to the assessment of normality. However, for the variable length of stay, assessment of the distribution of data was non-normal; thus a Wilcoxon rank sum test was performed on this variable. For all demographic, comorbidity, and operative characteristics, a univariable logistic regression model was fitted to assess the association of each variable with DNR status. Of note, the database does not report any postoperative outcomes (including death) occurring more than 30 d after surgery. Additionally, for variables with a large continuous range, the following assumptions were made; platelet count assumes a change of 100000, while the morbidity and mortality risk scores assume a change of 10%. For anesthesia and surgical operating time, the regression model assumes a time interval change of 10 min.

Multivariable logistic regression propensity score matched model

For our primary analysis, we applied a propensity score matched logistic regression model accounting for propensity for DNR status. The matched cohort was developed using a propensity scoring method in which we incorporated statistically significant variables from the unmatched model into a propensity score model. A 1:1 greedy, nearest neighbor matching strategy was employed utilizing the MatchIt library, producing successful matching of 725 patients who were DNR

Table 1 Surgical case mix of hip fracture surgery performed on Do Not Resuscitate and non Do Not Resuscitate status patients

Surgical specialty	Translation	DNR			Not DNR			*P* value
		num	denom	%	num	denom	%	
27236	Open treatment of femoral fracture, proximal end, neck, internal fixation or prosthetic replacement	210	725	28.966	223	725	30.759	0.994
27245	Treatment of intertrochanteric, per-trochanteric, or sub-trochanteric femoral fracture; with intramedullary implant	173	725	23.862	171	725	23.586	
27125	Hemiarthroplasty, hip, partial (*e.g.*, femoral stem prosthesis, bipolar arthroplasty)	111	725	15.31	104	725	14.345	
27244	Treatment of intertrochanteric, per-trochanteric, or sub-trochanteric femoral fracture; with plate/screw type implant, with or without cerclage	91	725	12.552	99	725	13.655	
27235	Percutaneous skeletal fixation of femoral fracture, proximal end, neck	48	725	6.621	44	725	6.069	
27130	Arthroplasty, acetabular and proximal femoral prosthetic replacement (total hip arthroplasty)	20	725	2.759	19	725	2.621	
27248	Open treatment of greater trochanteric fracture, with or without internal or external fixation	9	725	1.241	5	725	0.69	
27506	Open treatment of femoral shaft fracture, with or without external fixation, with insertion of intramedullary implant, with or without cerclage and/or locking screws	8	725	1.103	12	725	1.655	
27187	Prophylactic treatment (nailing, pinning, plating or wiring) with or without methylmethacrylate, femoral neck and proximal femur	6	725	0.828	4	725	0.552	
27454	Osteotomy, multiple, with realignment on intramedullary rod, femoral shaft (*e.g.*, Sofield type procedure)	5	725	0.69	4	725	0.552	
27507	Open treatment of femoral shaft fracture with plate/screws, with or without cerclage	5	725	0.69	8	725	1.103	
27511	Open treatment of femoral supracondylar or trans-condylar fracture without intercondylar extension, with or without internal or external fixation	5	725	0.69	6	725	0.828	
27228	Open treatment of acetabular fracture(s) involving anterior and posterior (two) columns, includes T-fracture and both column fracture with complete articular detachment, or single column or transverse fracture with associated acetabular wall fracture, with internal fixation	3	725	0.414	4	725	0.552	
27513	Open treatment of femoral supracondylar or trans-condylar fracture with intercondylar extension, with or without internal or external fixation	3	725	0.414	1	725	0.138	
27122	Acetabuloplasty; resection, femoral head (*e.g.*, Girdlestone procedure)	2	725	0.276	2	725	0.276	
27138	Revision of total hip arthroplasty	2	725	0.276	2	725	0.276	
27165	Osteotomy, intertrochanteric or sub-trochanteric, including internal or external fixation and/or cast	2	725	0.276	0	725	0	
27509	Percutaneous skeletal fixation of femoral fracture, distal end, medial or lateral condyle, or supracondylar or trans-condylar, with or without intercondylar extension, or distal femoral epiphyseal	2	725	0.276	1	725	0.138	
27132	Conversion of previous hip surgery to total hip arthroplasty	1	725	0.138	1	725	0.138	
27134	Revision of total hip arthroplasty	1	725	0.138	0	725	0	
27254	Open treatment of hip dislocation, traumatic, with acetabular wall and femoral head fracture, with or without internal or external fixation	1	725	0.138	1	725	0.138	
27450	Osteotomy, femur, shaft or supracondylar; with fixation	1	725	0.138	3	725	0.414	
27514	Open treatment of femoral fracture, distal end, medial or lateral condyle, with or without internal or external fixation	1	725	0.138	1	725	0.138	

DNR: Do Not Resuscitate.

to 725 patients who were not DNR. Success of the matching process was evaluated using Student's *t*-test for continuous variables and Pearson's χ^2 test for categorical variables. We found only one statistically significant difference between the cohorts after matching, which suggested that the matched groups may have hematocrit values that differed by approximately 1.3% (OR = 0.87; *P* = 0.017; see Table 2).

For the logistic regression on the matched cohorts, odds ratios (OR) were reported with associated 95%CI. OR not including 1.00 in the 95%CI were considered statistically significant. To assess the association specifically between length of stay and DNR status, a Cox proportional hazard model was fitted, incorporating the demographic and comorbidity co-variables as described above to generate a hazard ratio (HR). The model was right censored with death as a completing event.

RESULTS

Study population

The ICD codes included in the analysis are shown in Appendix 1. A total of 9218 cases met inclusion criteria (Figure 1). Of these, 1256 (13.6%) were patients with DNR status, and 7962 (86.4%) were patients without DNR status. Unmatched univariate and multivariable analysis demonstrated that patients undergoing hip fracture surgery with DNR status were more likely to be female, aged over > 80 years, unreported race/ethnicity, BMI < 18.5, dyspneic with moderate exertion or rest, ASA class Ⅲ or Ⅳ, partially or totally dependent for

Table 2 Propensity score matched cohorts, matched by propensity for Do Not Resuscitate status

Surgical specialty	Translation	DNR			Not DNR			*P* value
		num	denom	%	num	denom	%	
27236	Open treatment of femoral fracture, proximal end, neck, internal fixation or prosthetic replacement	322	1252	25.719	1873	7758	24.143	< 0.001
27245	Treatment of intertrochanteric, pertrochanteric, or sub-trochanteric femoral fracture; with intramedullary implant	297	1252	23.722	1799	7758	23.189	
27125	Hemiarthroplasty, hip, partial (*e.g.*, femoral stem prosthesis, bipolar arthroplasty)	233	1252	18.61	1178	7758	15.184	
27244	Treatment of intertrochanteric, pertrochanteric, or subtrochanteric femoral fracture; with plate/screw type implant, with or without cerclage	213	1252	17.013	914	7758	11.781	
27235	Percutaneous skeletal fixation of femoral fracture, proximal end, neck	66	1252	5.272	550	7758	7.089	
27130	Arthroplasty, acetabular and proximal femoral prosthetic replacement (total hip arthroplasty)	29	1252	2.316	377	7758	4.859	
27248	Open treatment of greater trochanteric fracture, with or without internal or external fixation	15	1252	1.198	132	7758	1.701	
27506		10	1252	0.799	197	7758	2.539	
27187		6	1252	0.479	71	7758	0.915	
27511		6	1252	0.479	102	7758	1.315	
22318		5	1252	0.399	23	7758	0.296	
27454		5	1252	0.399	7	7758	0.09	
27507		5	1252	0.399	68	7758	0.877	
27254	Open treatment of hip dislocation, traumatic, with acetabular wall and femoral head fracture, with or without internal or external fixation	4	1252	0.319	141	7758	1.817	
27509		4	1252	0.319	17	7758	0.219	
27513		4	1252	0.319	50	7758	0.644	
23615		3	1252	0.24	12	7758	0.155	
27122		3	1252	0.24	3	7758	0.039	
27165		3	1252	0.24	44	7758	0.567	
27228		3	1252	0.24	20	7758	0.258	
27514		3	1252	0.24	48	7758	0.619	
27138		2	1252	0.16	18	7758	0.232	
27759		2	1252	0.16	1	7758	0.013	
23470		1	1252	0.08	2	7758	0.026	
27132		1	1252	0.08	13	7758	0.168	
27134		1	1252	0.08	14	7758	0.18	
27177		1	1252	0.08	4	7758	0.052	

DNR: Do Not Resuscitate.

activities of daily living or diagnosed with hypertension, diabetes, COPD, CHF, PVD, prior stroke, weight loss, or sepsis (Table 3). Comparison between the groups in the unmatched cohort also suggested that patients with DNR status were more likely to have surgery booked as emergent, to receive a neuraxial or regional anesthetic, have a shorter anesthetic and operative time, and a higher modified Charlson score. These factors were used to construct the propensity score matched cohort as described above. The propensity matched groups are shown in Table 2.

Risk prediction

Using the ACS-NSQIP calculator, the average pre-operative risk prediction within the DNR status group was a mortality of 10% [Standard deviation (S.D) 10%] and morbidity of 15% (S.D 7%). In the non-DNR status group, using the ACS-NSQIP risk prediction calculator the average predicted mortality was 4% (S.D 6%) and morbidity of 11% (S.D 6%).

Surgical case mix for hip fracture surgery in DNR and non-DNR populations

Table 1 shows the commonest 23 CPT codes encountered for hip fracture surgery in the matched cohorts. Ninety-seven point six percent of all DNR patients and 95% of all non-DNR patients had hip fracture surgery classed by one of these CPT codes. The remaining minority (2.4% of DNR and 5% of non-DNR) had other hip fracture surgery CPT codes not listed, and these patients were still included in the analysis. Table 3 also demonstrates the propensity score matched case mix of procedures and the distribution within DNR and non-DNR status groups. The numbers of patients per CPT code were too small to conduct regression analysis. However, ranking CPT codes by frequency demonstrated very similar surgical case mixes in terms of CPT codes between the DNR and non-DNR groups, with the same 10 CPT codes accounting for over 95% of cases and occurring in the same order of frequency, with several low volume exceptions. This suggests there were minimal differences and a high correlation between the surgical case mixes encountered across the two groups, however the degree or significance of differences beyond this were not analysed further. CPT codes were not included in multivariable regression modelling.

Operative and anesthetic comparisons in DNR and non-DNR populations undergoing hip fracture surgery

Table 2 demonstrates various surgical and anaesthetic

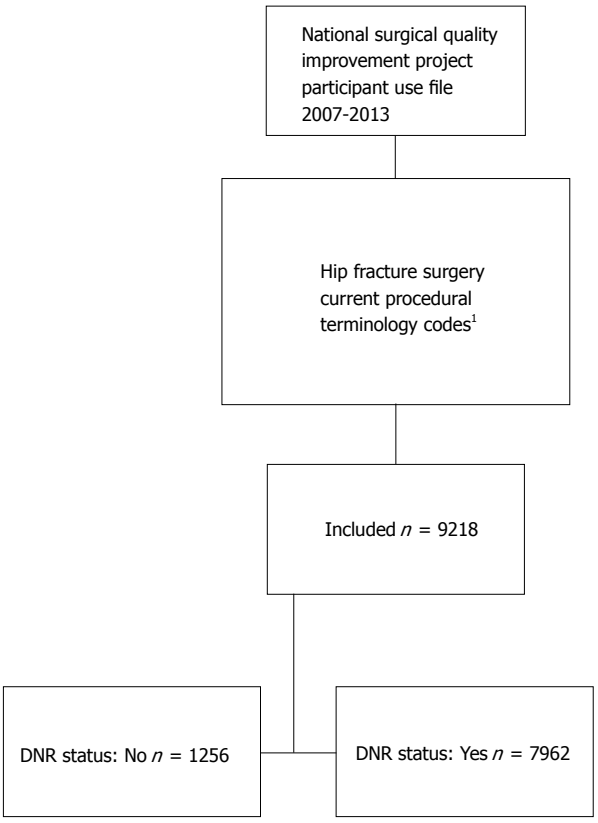

Figure 1 Study population. [1]See Appendix 1. DNR: Do Not Resuscitate.

factors between the matched groups. Multivariable regression demonstrated no increased likelihood for patients with DNR status to have a hip fracture surgery as an emergency procedure. DNR status was not independently associated with shorter surgical time (OR = 0.99, CI 0.99-1.00) or anesthetic time (OR = 0.99, 95%CI: 0.99-1.00). DNR status also did not appear to impact anesthesia modality: Compared to general anaesthesia, spinal anesthesia was not more likely in the DNR patient group compared to the non-DNR patient group in the propensity score matched analysis (OR = 0.96, 95%CI: 0.75-1.22).

Post-operative 30 d outcomes: Mortality

Table 4 presents outcomes up to 30 d postoperatively between the propensity matched cohorts. Mortality was higher in DNR status patients than in non-DNR status patients undergoing hip fracture surgery, at 15.3% *vs* 8.1% of patients. Multivariable regression demonstrated DNR status was independently associated with mortality (OR = 2.04, 95%CI: 1.46-2.85, $P < 0.001$). DNR status was not associated with return to the OR on multivariable regression.

Post-operative 30 d outcomes: Morbidity

Our analysis of the propensity score matched cohort found one difference with respect to post operative morbidity. Patients with DNR status had a slightly higher average number of complications per hospitalization (0.53 *vs* 0.43; OR = 1.213, 95%CI: 1.04-1.41). Although DNR patients appeared more likely to experience superficial surgical site infections (OR = 21.3; 95%CI: 1.25-364), this was likely an artifact of no events for the non-DNR patients and was no difference was seen with deep surgical site infections or dehiscence rates. DNR patients were less likely to experience reintubation (OR = 0.253; 95%CI: 0.09-0.69), or cardiac arrest with CPR (OR = 0.115; 95%CI: 0.03-0.52). Mean length of stay in the DNR group was no different between the propensity score matched groups.

DISCUSSION

Our study aimed to examine post-operative mortality and morbidity in patients with DNR status undergoing hip fracture surgery. We also aimed to determine whether DNR status was independently associated with increased morbidity or whether DNR status purely decreased utilisation of CPR and reintubation, without affecting other postoperative outcomes. We found that mortality was over two times greater in the DNR status group, with DNR status independently predicting mortality after patient groups were matched for other underlying comorbidities using propensity scoring methods. However, relatively few sources of morbidity were independently associated with DNR status. Although overall complication rates were slightly higher, rates of reintubation and cardiac arrest with CPR were much lower among patients with a DNR order in place. This raises the question of how we reconcile the increased rate of mortality observed among the DNR cohort in the setting of an isolated, modest overall rate of complications but no clear source of morbidity.

Historically, some surgeons and anesthesiologists have considered perioperative DNR status controversial, given the interventional procedures and unique physiologic changes that occur during anesthesia and the way clinicians manage these events. In light of this, both the American College of Surgeons[24] and American Society of Anesthesiologists[7] have produced consensus statements to guide perioperative management of DNR status. These emphasize communication and individualized management plans, including suspending, then reinstating DNR status post-operatively, if in accordance with a patient's wishes.

The impact of DNR status on surgical outcomes has been examined previously in the wider surgical cohort and in specific specialty groups such as patients undergoing vascular surgery[25,26]. Kazaure *et al*[25] demonstrated similar patient associations with having DNR status (white, female, > 85) and also demonstrated high mortality (nearly 1 in 4) in surgical patients with DNR status. However, in contrast to our findings, they demonstrated significantly higher morbidity rates in DNR *vs* non DNR patients. These higher rates of morbidity were not replicated in our hip fracture specific study, and therefore may imply that in our orthopedic cohort a DNR status did not negatively

Table 3 Demographics, co-morbidities and functional baseline of Do Not Resuscitate and non Do Not Resuscitate status patients undergoing hip fracture surgery

Categ.	DNR			Not DNR			OR (95%CI)	*P* values
	Num	Denom	%	Num	Denom	%		
Age, mean (SD)	85.1		6.7	77.55		12.3	1.098 (1.088-1.109)	< 0.001
(0, 65)	26	1256	2.1	1188	7962	14.9	Reference	< 0.001
(65,80)	169	1256	13.5	2384	7962	29.9	3.239 (2.131-4.923)	
(80,100)	1061	1256	84.5	4390	7962	55.1	11.043 (7.445-16.381)	
Sex								
Male	313	1254	25.0	2395	7950	30.1	Reference	< 0.001
Female	941	1254	75.0	5555	7950	69.9	1.296 (1.131-1.486)	
Demographics								
White	781	1215	64.3	6008	7544	79.6	Reference	< 0.001
Black	11	1215	0.9	371	7544	4.9	0.228 (0.125-0.417)	
Asian	3	1215	0.2	94	7544	1.2	0.246 (0.078-0.777)	
Other	4	1215	0.3	31	7544	0.4	0.993 (0.349-2.819)	
Not reported	416	1215	34.2	1040	7544	13.8	3.077 (2.686-3.525)	
Hispanic	18	824	2.2	314	6677	4.7	0.453 (0.28-0.732)	0.001
BMI								
Mean (SD)	24.1		5.5	25.3		6.5	0.966 (0.953-0.978)	< 0.001
(0, 18.5)	110	913	12.0	630	7076	8.9	1.261 (1.007-1.579)	< 0.001
(18.5, 25)	454	913	49.7	3279	7076	46.3	Reference	
(25, 30)	244	913	26.7	1976	7076	27.9	0.892 (0.756-1.052)	
(30, 100)	105	913	11.5	1191	7076	16.8	0.637 (0.51-0.795)	
Functional status								
No dyspnea	1098	1256	87.4	7136	7961	89.6	Reference	0.015
Dyspnea with moderate exertion	116	1256	9.2	652	7961	8.2	1.156 (0.94-1.423)	
Dyspnea at rest	42	1256	3.3	173	7961	2.2	1.578 (1.12-2.224)	
Independent	491	1251	39.2	4726	7917	59.7	Reference	< 0.001
Partially dependent	579	1251	46.3	2583	7917	32.6	2.158 (1.896-2.456)	
Totally dependent	181	1251	14.5	608	7917	7.7	2.865 (2.369-3.466)	
ASA class								
1-no disturb/2-mild disturb	108	1256	8.6	1739	7951	21.9	0.388 (0.315-0.478)	< 0.001
3-severe disturb	779	1256	62.0	4866	7951	61.2	Reference	
4-life threat/5-moribund	369	1256	29.4	1346	7951	16.9	1.712 (1.492-1.965)	
Comorbidities								
Hypertension	908	1256	72.3	5413	7962	68.0	1.229 (1.076-1.402)	0.002
Diabetes	184	1256	14.7	1468	7962	18.4	0.759 (0.643-0.897)	0.001
COPD	181	1256	14.4	899	7962	11.3	1.323 (1.114-1.571)	0.001
CHF	55	1256	4.4	234	7962	2.9	1.512 (1.12-2.041)	0.006
CAD	212	1256	16.9	1340	7962	16.8	1.004 (0.856-1.176)	0.966
PVD	25	1256	2.0	235	7962	3.0	0.668 (0.44-1.013)	0.056
CKD	29	1256	2.3	214	7962	2.7	0.856 (0.578-1.267)	0.436
Stroke	229	1256	18.2	1023	7962	12.8	1.512 (1.292-1.771)	< 0.001
Weight loss	31	1256	2.5	119	7962	1.5	1.668 (1.118-2.488)	0.011
Sepsis	204	1249	16.3	931	7892	11.8	1.46 (1.238-1.721)	< 0.001
Recent surgery	12	1256	1.0	114	7962	1.4	0.664 (0.365-1.207)	0.177
Labs								
Creatinine	1.09		0.8	1.08		0.9	1.015 (0.946-1.088)	0.664
Hematocrit	30.7			30.1			1.01 (0.986-1.034)	0.394
Platelets	212			208			1.04 (0.977-1.107)	0.196
Surgical urgency								
Emergent	428	1256	34.1	2194	7962	27.6	1.359 (1.197-1.542)	< 0.001
Surgical complexity								
Work RVU	17.45		2.0	17.46		2.7	0.998 (0.975-1.021)	0.841
Anesthesia								
General	796	1255	63.4	6028	7959	75.7	NA	< 0.001
Neuraxial/regional	446	1255	35.5	1876	7959	23.6	1.8 (1.586-2.044)	
Other	13	1255	1.0	55	7959	0.7	1.79 (0.974-3.291)	
Anesthesia time	117.9		48.1	128.8		58.5	0.996 (0.995-0.997)	< 0.001
Operation time	61.4		43.8	70.2		43.5	0.994 (0.992-0.996)	< 0.001
Modified charlson score	2.44		1.4	2.03		1.5	1.207 (1.16-1.255)	< 0.001

DNR: Do Not Resuscitate.

impact outcomes or morbidity to the degree described in the predominantly general surgery (63%) cohort which they analysed. Aziz *et al*[26] investigated outcomes of patients undergoing vascular surgery with DNR status and also demonstrated higher mortality in DNR patients, but found similarity in rates of complications between

Table 4 Thirty-days outcomes after hip fracture surgery in DNR and non-DNR status patients

Outcomes	DNR			Not DNR			OR (95%CI)	*P* values
	Num	Denom	%	Num	Denom	%		
Death	111	725	15.3	59	725	8.1	2.04 (1.459-2.851)	< 0.001
Reoperation/return OR	22	725	3.0	17	725	2.3	1.309 (0.689-2.487)	0.417
Failure to wean from vent	4	725	0.6	7	725	1.0	0.558 (0.161-1.934)	0.364
Reintubation	5	725	0.7	19	725	2.6	0.253 (0.093-0.688)	0.004
Superficial SSI	10	725	1.4	0	725	0.0	21.294 (1.245-364.078)	0.002
Deep incisional SSI	3	725	0.4	2	725	0.3	1.466 (0.242-8.901)	0.654
Organ/space SSI	2	725	0.3	2	725	0.3	1.011 (0.142-7.196)	1
Dehiscence	1	725	0.1	0	725	0.0	3.00 (0.122-73.870)	0.317
Pneumonia	25	725	3.4	34	725	4.7	0.725 (0.428-1.23)	0.232
Acute kidney injury	3	725	0.4	4	725	0.6	0.754 (0.168-3.383)	0.705
Renal failure requiring dialysis	3	725	0.4	2	725	0.3	1.5 (0.249-9.034)	0.654
CVA	4	725	0.6	5	725	0.7	0.798 (0.213-2.994)	0.738
Cardiac arrest with CPR	2	725	0.3	16	725	2.2	0.115 (0.025-0.523)	0.001
Acute MI	16	725	2.2	13	725	1.8	1.245 (0.594-2.608)	0.574
Transfusion	169	725	23.3	139	725	19.2	1.243 (0.964-1.603)	0.054
Venous thromboembolism	9	725	1.2	14	725	1.9	0.621 (0.265-1.457)	0.293
UTI	45	725	6.2	41	725	5.7	1.061 (0.683-1.649)	0.657
Sepsis	14	725	1.9	23	725	3.2	0.595 (0.303-1.17)	0.134
Number of complications	Mean		SD	Mean		SD	OR (95%CI)	*P*-values
	0.53		0.65	0.43		0.61	1.213 (1.043-1.409)	0.004
Length of stay	Mean		SD	Mean		SD	HR (95%CI)	*P*-values
	6.4		5.0	6.74		5.3	2.133 (0.469-0.871)	0.219

DNR: Do Not Resuscitate.

the two groups, except for graft failure, a procedure specific complication. This demonstrates the importance of procedure specific information in discussing risk with patients.

Other emerging literature supports our findings of relatively high mortality among patients with DNR orders who undergo surgery. A recent study by our group[8] examined outcomes among DNR patients undergoing a variety of the most common procedures done for this patient population using NSQIP data. The most common procedures among DNR patients focused on symptom relief but were also associated with higher rates of 30 d mortality (but not morbidity) when compared to non-DNR matched controls[8]. In another analysis focused on DNR patients undergoing hip surgery, the urgency of the procedure (emergent *vs* non-emergent) was found to cause no independent increase in 30-d morbidity, while DNR status itself again demonstrated high 30-d mortality rates in excess of those predicted by the NSQIP risk calculator[27].

Patients undergoing hip fracture surgery comprise a diverse patient group, making risk stratification important[28,29]. High quality perioperative care and subsequent recovery particularly in the most elderly and medically complex patients presents a growing challenge for an ageing population[10-12]. Ours is among the emerging literature to measure hip fracture surgery outcomes in the presence of a DNR status and quantify the impact of this important risk factor in this common condition. Our analysis demonstrates that at present, 13.6% of all patients undergoing hip fracture surgery have DNR status. This incidence was previously unknown, despite the growing awareness of the higher risk orthogeriatric population. The burden of mortality and morbidity in this population therefore may present a sizeable and specific opportunity for quality improvement[30]. It may also identify a skills gap or systems gap in broaching discussions about end of life wishes in a pre-emptive, comprehensive, acceptable and sensitive fashion. Shared surgical decision making is an emerging topic in the literature, and there have been research and policy agendas proposed for improved perioperative code status discussion between providers involved in perioperative care and patients as well as their families[31].

We report that patients with DNR status undergoing hip fracture surgery were more likely to be female, aged over > 80 years, dyspneic with moderate exertion or rest, ASA class Ⅲ or Ⅳ, partially or totally dependent for activities of daily living or diagnosed with hypertension, diabetes, COPD, CHF, PVD, prior stroke, weight loss, or sepsis and this is in keeping with patterns described elsewhere[4,25,32,33]. Similar to previous reports on DNR status, we also found patients with DNR status were less likely to report their race/ethnicity and more likely to be underweight (BMI < 18.5)[33-35]. This could also reflect physician inconsistency in discussing end of life and resuscitation status as well as ethnic variations in fragility fractures or even of life expectancy[36,37].

Concern has been expressed previously that DNR status may carry inadvertent care provider bias, or the so-called "failure to rescue" hypothesis. This could lead to inadequate or insufficient care, extending beyond withholding CPR or intubation and ventilation[14]. Our study was not designed to evaluate this specifically, however propensity score matching and regression analysis created a model to compare outcomes in patients with and without DNR status, controlling for

age, gender, race, ethnicity, ASA class, functional status, albumin levels and presence of multiple independently significant comorbidities. Additionally, our model matched patients using a frailty index, which may have further eliminated differences between the matched groups based on physical status alone.

Our study found that patients with DNR status had slightly shorter mean anesthesia and surgery times in the unmatched analyses. This may reflect an effort to reduce operative or anesthetic time for higher risk patients, by selecting more senior or experienced staff, or less complex operative procedures[38]. We found the rates of spinal anesthesia were higher for patients who were DNR. This may reflect ongoing debate as to whether spinal anesthesia out-performs general anesthesia in specific patient groups[39,40]. Potential benefits from regional anesthesia, such as reduced respiratory and neurological complications, and reduced opiate consumption and side effects may be more pronounced in high risk patients. This finding was despite the fact that some contraindications to spinal anesthesia, such as anticoagulation, may be more prevalent[39].

Limits of the study and summary

The primary limit to this study is fundamental to the retrospective data review design that we were obligated to by the dataset. We were not able to control selection of patients for the surgeries as a result, and therefore sought to address these limitations by our statistical methods, as described above.

The surgical case mix was similar for both groups, though due to a relatively small sample size this could not be analysed in detail. The 10 most common procedures appeared in approximately the same order for both groups, and no gross discrepancies were apparent to visual inspection of the relative proportions. Although our data was able to describe the case mix of procedures undertaken in this population, we were not able to discern sufficient level of detail to describe all aspects of the procedures performed. For instance, although we describe an approximately 15% incidence of total hip arthroplasty, the data set does not provide specific details on the techniques used to accomplish the surgery (*e.g.*, use of cementing agent type, specific screw or prosthesis hardware type). This must be recognized as one of the specific limitations of the study in addition to the general limitations of retrospective administrative and clinical datasets.

Although the emerging literature in this area suggests that shared decision making is a crucial aspect of care for patients with DNR status, our data sources did not allow us to investigate the surgical decision making that preceded the operations among DNR patients in this cohort. Thus, we cannot comment on the specific decision making process that was used in deciding to undergo surgery for hip fracture among these patients. However, this would be a valuable area of future investigation.

However, the mortality and morbidity demonstrated in this study provides a useful reference point for specific discussions about risks of hip fracture surgery, for informed consent, end of life discussions, and for planning perioperative care in this high risk demographic. Importantly, while mortality was higher in DNR status patients, morbidity, defined by post-operative complications, either individually or overall, was generally not higher in the DNR status patients. Indeed, the reduced rate of CPR and unplanned intubation is both expected and consistent with findings in general and other surgical specialities[8]. It is unclear why a small number of patients with DNR status did undergo such resuscitative procedures, or what the events leading to this were. Taken together, it does not seem that an excess burden of post-operative adverse events cannot adequately explain the increased mortality and suggests the need for further research to understand what unmeasured variables account for these consistent differences in outcome. Our findings support the need for routine, systematic, perioperative discussion with hip fracture patients regarding their goals of care in the event of post-operative morbidity leading to cardiopulmonary arrest. Hip fracture surgery has high perioperative mortality, however this data suggests DNR status is effective in reducing specific interventions such as CPR and reintubation, without appearing to increase overall morbidity in the first 30 d after surgery.

ARTICLE HIGHLIGHTS

Research background

Relatively little is known about the exact mechanism through which Do Not Resuscitate (DNR) status affects patient outcomes during the perioperative period. The approach of surgical and anesthesia societies has been to treat DNR status as a component of the decision to undergo surgery or as a means of framing surgical goals and expectations with patients and their families. Depending on patients' goals, DNR status may even be reversed during the perioperative period. However, little is known about how preoperative DNR status affects morbidity and mortality during the perioperative period, if at all.

Research motivation

Patients in the orthogeriatric population who are undergoing hip fracture fixation surgery may be at increased risk for morbidity and/or mortality. Given that these patients have already made a premeditated decision to limit cardiopulmonary resuscitative aspects of their medical care, they may also benefit from additional counselling with regard to any additional risks that may apply to their surgical population.

Research objectives

This study seeks to describe the incidence and distribution of DNR status in patients undergoing hip fracture surgery and to determine whether DNR status is an independent risk factor for worse outcomes on 30-d follow up. The study's objective was realized by analysis of propensity matched groups of patients in a large retrospective cohort. The study seeks to support an emerging field of literature which describes the unique perioperative outcomes among patients with preoperative DNR/DNI status.

Research methods

A large, national, US-based retrospective cohort database was used to identify patients undergoing surgical fixation for hip fracture across a variety of geographic and hospital settings. Characteristics of this cohort were examined

for unmatched groups of patients with and without DNR/DNI orders, as well as for groups of matched on their propensity for having a DNR/DNI order.

Research results

This study demonstrates that when comparing groups of patients that have been matched on propensity for DNR/DNI status, having a DNR/DNI order was independently associated with mortality (OR = 2.04, 95%CI: 1.46-2.86, $P < 0.001$). Additionally, DNR/DNI status was associated with a very slight increased risk of perioperative complications without otherwise showing significantly different incidences of morbidity between the matched groups.

Research conclusion

New findings contributed by this study include insight in the role of DNR/DNI status as an independent predictor of perioperative mortality among patients undergoing hip fracture fixation surgeries. Notably, these matched groups did not demonstrate associations between DNR/DNI status and perioperative morbidity. Given that rates of CPR and reintubation were markedly lower in the DNR/DNI group, we demonstrate that there may be a "ceilings of care" effect in this context. The findings also raises a question as to whether a "failure to rescue" mechanism may be active among these patients in the perioperative period. Regardless, the results of this study raise questions for future research which will hopefully yield additional insight into the mechanisms driving increased mortality among patients with DNR/DNI status who are undergoing surgery for hip fracture. In the immediate term, these findings will assist clinicians in appropriately counselling patients who may have a DNR/DNI order and are undergoing surgery for hip fracture.

Research perspectives

Future research will hopefully yield additional insight into the mechanisms driving increased mortality among patients with DNR/DNI status who are undergoing surgery for hip fracture.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Anterolateral rotatory instability *in vivo* correlates tunnel position after anterior cruciate ligament reconstruction using bone-patellar tendon-bone graft

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Author contributions: Tashiro Y designed the study, performed surgeries and followed up patients; he analyzed the data and drafted the manuscript; Okazaki K assisted designing the study, performed surgeries and followed up patients; he revised the manuscript; Murakami K performed subjective and objective data collection, assisted data analysis and evaluation; Matsubara H and Osaki K performed kinematic data collection, assisted data analysis and evaluation; Iwamoto Y helped grant writing, directed all clinical aspects and co-supervised the entire research; Nakashima Y directed all clinical aspects and supervised the entire research.

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Abstract

AIM

To quantitatively assess rotatory and anterior-posterior instability *in vivo* after anterior cruciate ligament (ACL) reconstruction using bone-patellar tendon-bone (BTB) autografts, and to clarify the influence of tunnel positions on the knee stability.

METHODS

Single-bundle ACL reconstruction with BTB autograft was performed on 50 patients with a mean age of 28 years using the trans-tibial (TT) (n = 20) and trans-portal (TP) (n = 30) techniques. Femoral and tibial tunnel positions were identified from the high-resolution 3D-CT bone models two weeks after surgery. Anterolateral rotatory translation

was examined using a Slocum anterolateral rotatory instability test in open magnetic resonance imaging (MRI) 1.0-1.5 years after surgery, by measuring anterior tibial translation at the medial and lateral compartments on its sagittal images. Anterior-posterior stability was evaluated with a Kneelax3 arthrometer.

RESULTS

A total of 40 patients (80%) were finally followed up. Femoral tunnel positions were shallower ($P < 0.01$) and higher ($P < 0.001$), and tibial tunnel positions were more posterior ($P < 0.05$) in the TT group compared with the TP group. Anterolateral rotatory translations in reconstructed knees were significantly correlated with the shallow femoral tunnel positions (R = 0.42, $P < 0.01$), and the rotatory translations were greater in the TT group (3.2 ± 1.6 mm) than in the TP group (2.0 ± 1.8 mm) ($P < 0.05$). Side-to-side differences of Kneelax3 arthrometer were 1.5 ± 1.3 mm in the TT, and 1.7 ± 1.6 mm in the TP group (N.S.). Lysholm scores, KOOS subscales and re-injury rate showed no difference between the two groups.

CONCLUSION

Anterolateral rotatory instability significantly correlated shallow femoral tunnel positions after ACL reconstruction using BTB autografts. Clinical outcomes, rotatory and anterior-posterior stability were overall satisfactory in both techniques, but the TT technique located femoral tunnels in shallower and higher positions, and tibial tunnels in more posterior positions than the TP technique, thus increased the anterolateral rotation. Anatomic ACL reconstruction with BTB autografts may restore knee function and stability.

Key words: Anterior cruciate ligament; Patellar tendon; Bone-patellar tendon-bone; Rotatory instability; Magnetic resonance imaging; Tunnel position; Anatomic; Single-bundle

Core tip: Anterolateral rotatory instability was quantitatively assessed in 40 anterior cruciate ligament-reconstructed knees with bone-patellar tendon-bone autografts using a Slocum anterolateral rotatory instability test in open magnetic resonance imaging 1-1.5 years after surgery, and correlated to tunnel positions evaluated by high resolution computed tomography scan 2 wk after surgery. Femoral tunnel positions were shallower ($P < 0.01$) and higher ($P < 0.001$), and tibial tunnel positions were more posterior ($P < 0.05$) in the trans-tibial (TT) group, compared with the trans-portal (TP) group. Anterolateral rotatory translations were significantly correlated with the shallow femoral tunnel positions, and they were greater in the TT group (3.2 ± 1.6 mm) than in the TP group (2.0 ± 1.8 mm) ($P < 0.05$).

Tashiro Y, Okazaki K, Murakami K, Matsubara H, Osaki K, Iwamoto Y, Nakashima Y. Anterolateral rotatory instability *in vivo* correlates tunnel position after anterior cruciate ligament reconstruction using bone-patellar tendon-bone graft. *World J Orthop* 2017; 8(12): 913-921 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/913.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.913

INTRODUCTION

It is the goal of anterior cruciate ligament (ACL) reconstruction to restore normal knee function and kinematics, finally achieving patient's return to sports and daily activities. Recently, anatomic ACL reconstruction which reproduces dimensions, fiber orientations and insertion sites of the native ACL has been reported to improve knee stability and clinical outcomes after surgery[1-4]. Oblique fiber orientation based on anatomical location of bone tunnels is more favorable for controlling rotation, as well as resisting anterior tibial force, compared with a vertical graft orientation[5,6]. ACL reconstruction creating femoral tunnels independently from tibial tunnels has been shown to locate femoral tunnels more closely to anatomical footprint than the trans-tibial (TT) technique[7-9]. A double-bundle technique has been one of the popular methods to perform anatomic ACL reconstruction, principally using soft tissue grafts such as hamstring tendon[10-13]. However, anatomic single-bundle technique has developed recently, showing comparable outcomes as double-bundle techniques[14-17]. Therefore, it may be possible that single-bundle ACL reconstruction with bone-patellar tendon-bone (BTB) grafts, which is based on the modern concept of ACL anatomy[18-21], could restore close to normal ACL function.

One of the great advantages of BTB autograft is its better graft-tunnel healing, as well as the stable initial fixation with bone block, compared with other soft tissue grafts[22-25]. Although several original studies have reported kinematics after ACL reconstruction with BTB grafts, they were based on cadaveric specimens measured by testing machine or robotic system[5,6,26-28], which could not reflect better graft-tunnel healing of BTB grafts. Recent *in vivo* studies using BTB grafts have introduced the anatomic single-bundle technique, which locates bone tunnels within the native insertion site, and have shown favorable clinical results after for ACL reconstruction, but the degree of rotatory instability was mainly assessed by manual pivot-shift test[18,29-31], not quantitatively. Only a few studies from limited research groups so far have reported quantitative results of rotatory instability after anatomic ACL reconstruction using BTB grafts[32-34]. Therefore, it would be clinically relevant to assess *in vivo* rotatory instability objectively after ACL reconstruction using BTB autografts.

For the surgical technique of creating femoral tunnels, we had used the TT technique until 2010, modifying the position and orientation of the graft more obliquely[12,35,36]. But this technique sometimes made it difficult for us to place femoral tunnels within the

Table 1 Baseline data of the two groups

	TT group	TP group	Significance
n	20	30	
Period of surgery	Apr 2009-Dec 2010	Aug 2010-Mar 2013	
Age	29 ± 9	27 ± 9	NS
Height (cm)	171.3 ± 7.1	171.7 ± 6.0	NS
Weight (kg)	73.8 ± 6.9	75.5 ± 12.2	NS
Lysholm score	65 ± 11	63 ± 14	NS

Mean ± SD is shown. TT: Trans-tibial; TP: Trans-portal; NS: Not significantly.

anatomical footprint[9,37-40], thus since the late 2010, we've shifted to the trans-portal (TP) technique, which enables femoral tunnel placement independently from tibial tunnels[8,41,42]. In addition, we have utilized open MRI to assess anterolateral rotatory instability of ACL-deficient and ACL-reconstructed knees since 2005, and have shown its usefulness in quantification[35,43-45].

The purpose of this study was to: (1) Compare the knee stability *in vivo* after ACL reconstruction using BTB autografts *via* TT and TP techniques; and (2) clarify the influence of tunnel position on the knee stability. We hypothesized that: (1) The TP technique would show less instability; and (2) tunnel positions may affect knee stability after single-bundle ACL reconstruction using BTB autografts.

MATERIALS AND METHODS

From April 2009 to March 2013, single-bundle primary ACL reconstruction was performed on 52 knees with a BTB autograft. Patients with any history of significant injury to other knee ligaments, articular cartilage and bilateral ACL cases (2 knees) were excluded. Consequently, 50 patients with a mean age of 28 years (range: 17-45) were enrolled. All patients were male. TT technique was used in 20 knees from April 2009 to 2010, and TP technique was used in 30 patients from August 2010 to March 2013 (Table 1). A computed tomography (CT) scan was performed with 1-2 mm slices in order to determine tunnel positions 2 wk after surgery. Anterolateral rotatory instability *in vivo* was assessed quantitatively in 40 patients (80%) using open MRI an average of 1.2 years (range: 1.0-1.5 years) after surgery. All aspects of this study was approved by the institutional review board (IRB) of our university (ID: 24-108), and all subjects gave their informed consent before they were included.

Surgical technique

The subjects underwent arthroscopic ACL reconstruction at a median of 6 wk after the injury. An arthroscopic leg holder was utilized to hold the affected knee in 90º of flexion. A 10-mm BTB autograft was harvested. The anterolateral portal was positioned as high as the inferior pole of the patella so that it gave an excellent arthroscopic view over the tibial footprint of the ACL.

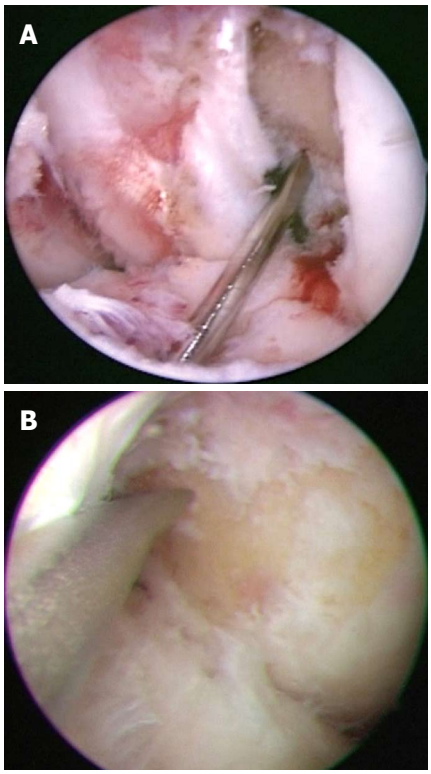

Figure 1 Arthroscopic techniques for creating the femoral tunnel. A: Arthroscopic view of trans-tibial technique in left knee is shown. The femoral guide wire was centered at the 1:30-2:00 o'clock position; B: Left knee. In trans-portal technique, the anteromedial portal was used to visualize the lateral wall of the intercondylar notch. The far medial accessory portal was used to directly access to the center of the anterior cruciate ligament femoral insertion site.

The tibial tunnel was targeted in the center of the native ACL insertion site, avoiding impingement during knee extension.

In the TT group, a femoral guide wire was inserted *via* the tibial tunnel, and then it was centered at the 1:30-2:00 o'clock position for the left knees (10:00-10:30 for right) (Figure 1A). The femoral tunnel was drilled trans-tibially with the knee in 90° of flexion. In the TP group, the anteromedial portal was used to allow optimal visualization of the lateral wall of the intercondylar notch, including the ACL femoral insertion site[13,41]. In addition, the accessory medial portal was established far medially, just above the anterior horn of the medial meniscus, in a position allowing direct access to the center of the ACL femoral insertion site and avoiding damage to articular cartilage during femoral drilling (Figure 1B). A guide wire was introduced through the accessory medial portal and placed at the center of femoral insertion site. The femoral tunnel was drilled using a 2.4-mm straight guide pin and rigid drills, with the knee kept in maximal flexion.

In all cases, the BTB graft was fixed to the femur using extracortical fixation (EndoButton CL BTB, Smith and Nephew Endoscopy). Tibial side was fixed with interference screws (Softsilk 1.5 Fixation Screws, Smith and Nephew Endoscopy). A notch plasty was not performed in any of our patients. All of the patients underwent a standard rehabilitation program with early

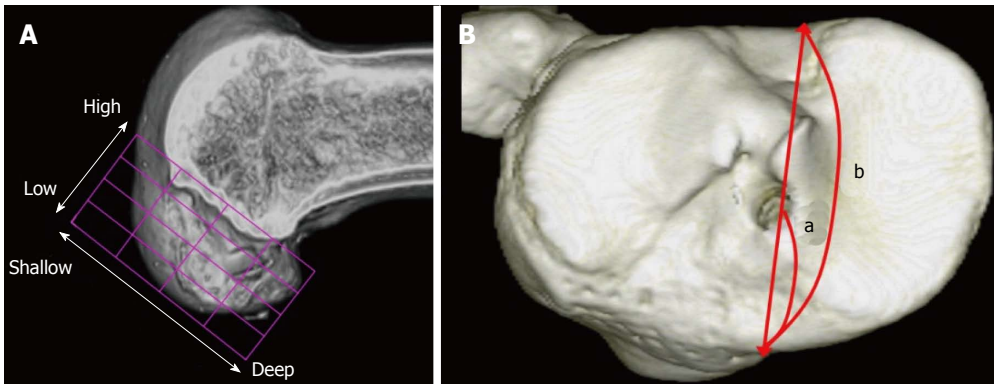

Figure 2 Evaluation of tunnel positions in femur and tibia. A: 3D CT-based model of a femoral bone tunnel after an ACL reconstruction. Tunnel position was assessed according to the quadrant method[46]. Depth = (distance from the posterior edge to tunnel center along Blumensaat's line/total length of the lateral condyle) × 100%. Height = (distance from Blumensaat's line to tunnel center/total height of the intercondylar roof) × 100%; B: For tibial side, Staubli's technique was used[47]. Anterior-posterior position = (a/b) × 100%. a: Distance from anterior edge to tunnel center; b: Anteroposterior length of the tibia plateau. ACL: Anterior cruciate ligament.

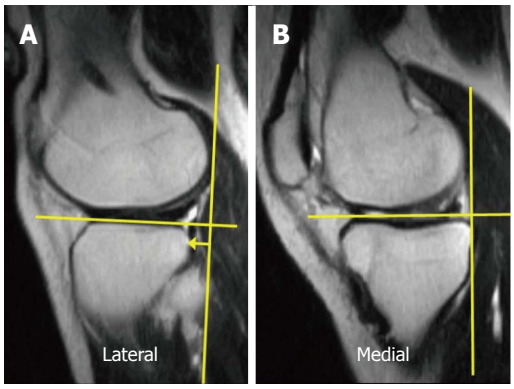

Figure 3 The anterior translation of the tibia with respect to the femoral condyle was measured on sagittal MR images of the (A) lateral compartment and (B) medial compartment, respectively. As a landmark for the center of the lateral compartment, slices that included the medial edge of the fibula were selected. For the center of the medial compartment, slices with the attachment of the medial head of the gastrocnemius were selected.

weight bearing and range of motion exercise. Sports activities were permitted 9 mo after the reconstruction, if the patients had regained functional strength and stability.

The locations of the femoral and tibial tunnel aperture centers were identified from 3D bone models generated from the high-resolution CT scan two weeks after surgery. Femoral tunnel positions were measured according to the quadrant method (Figure 2A)[46]. For the tibial side, the technique of Staubli and Rauschning was used for the measurement (Figure 2B)[47]. A commercially available medical imaging software (Real INTAGE, Cybernet Systems Co, Ltd, Tokyo, Japan) was used in these analysis.

Evaluation of anterolateral rotatory instability

The assessment of *in vivo* anterolateral rotatory instability (ALRI) was performed by applying the Slocum ALRI test[48] to stress the tibia rotating anteriorly and internally in a horizontal open MRI Scanner, as previously described[35,43-45]. The MRI system used in this study was an open MRI at 0.4 T (APERTO, Hitachi Medical Co, Tokyo, Japan). Briefly, the patient was kept in a semilateral recumbent position on the table. The hip and knee of the contra lateral side were flexed. The affected knee was placed in 10° of flexion and the medial side of the foot was rested on a pad so that the weight of the leg was borne on the heel and the knee sagged into valgus. The examiner placed his one hand on the distal femur and the other hand on the proximal tibia from the posterior side. He pushed the fibular head anteriorly with his thumb to increase the stress that makes the tibia rotate anteriorly and internally.

The anterior translation of the tibia with respect to the femoral condyle was measured on sagittal images scanned at each center of the medial and lateral compartments, respectively, in order to evaluate rotatory instability (Figure 3). The image plane scanned under stress was adjusted to the same sagittal plane scanned before stress, using the Interactive Scan Control (ISC) software program. The ISC program determines the image plane interactively on the basis of fluoroscopic images displayed on a user interface with an update time of 2 s, including the scan time. The MRI operator can change the image plane, oblique angle and phase encoding direction during the scan. It usually takes less than 3 min from applying stress to completing the scan, including the fine-tuning of the plane, when the ISC is used. The anterolateral rotatory translation, determined from anterolateral minus anteromedial tibial translation, was calculated to assess ALRI. Side-to-side differences of anterolateral tibial translation and anteromedial tibial translation were also analyzed, respectively. High intra- and inter-observer reproducibility (correlation coefficient = 0.98, 0.91, respectively) have been demonstrated between 2 successive examinations in our previous study, using this assessment technique[43].

The subjective knee function was assessed with the Lysholm scores and Knee injury and Osteoarthritis Outcome Score (KOOS) scales[49,50]. Anterior-posterior

Table 2 Tunnel positions of the femur and the tibia by postoperative computed tomography

		TT technique (%)	TP technique (%)	Significance
Femur	Depth	34.0 ± 4.9	29.7 ± 4.9	$P < 0.01$
	Height	30.3 ± 5.6	39.3 ± 7.3	$P < 0.001$
Tibia	Anterior-posterior	47.1 ± 7.5	42.0 ± 4.9	$P < 0.05$

Mean ± SD. TT: Trans-tibial; TP: Trans-portal.

Table 3 Clinical outcomes and knee stability parameters

	TT technique	TP technique	Significance
Lysholm score	94 ± 7	95 ± 7	NS
KOOS subscale			
Symptoms	89 ± 9	90 ± 12	NS
Pain	87 ± 7	89 ± 8	NS
ADL	92 ± 12	96 ± 10	NS
Sport/Rec	82 ± 14	84 ± 9	NS
QoL	78 ± 13	80 ± 11	NS
Re-injury (ipsilateral)	0	0	NS
Kneelax3			NS
Side-to-side diff. (mm)	1.5 ± 1.3	1.7 ± 1.6	
MRI analysis			
Anterolateral rotatory translation			
Affected side (mm)	3.2 ± 1.6	2.0 ± 1.8	$P < 0.05$
Contra-lateral side (mm)	2.4 ± 1.6	2.5 ± 2.7	NS
Side-to-side diff. (mm) of			
Anteromedial tibial translation	0.6 ± 0.8	1.4 ± 2.3	NS
Anterolateral tibial translation	1.4 ± 1.6	0.9 ± 1.9	NS

Mean ± SD is shown. TT: Trans-tibial; TP: Trans-portal; Anterolateral rotatory translation: Anterolateral minus anteromedial tibial translation; NS: Not significantly.

stability was evaluated with a Kneelax3 arthrometer (MR Systems, Haarlem, The Netherlands) at 134 N anterior force.

Statistical analysis

Femoral and tibial tunnel positions were compared between TT and TP groups using Student's *t*-test. The side-to-side differences of tibial translations, anterolateral rotatory translation and clinical outcomes were also compared between the 2 groups using Student's *t*-test. The relationships between tunnel positions and knee stability parameters were analyzed using Pearson's correlations. For those statistical analyses, the StatView 5.0 software (SAS Institute Inc., Cary, NC, United States) was used with a significance level of $P < 0.05$. All statistical analyses of this study were reviewed by a biomedical statistician.

RESULTS

Femoral tunnels were located significantly shallower ($P < 0.01$) and higher ($P < 0.001$) in the TT group, compared with the TP group. Tibial tunnel positions in the TT group were significantly posterior than those of the TP group ($P < 0.05$) (Table 2).

In open MRI analysis, the anterolateral rotatory translation (= anterolateral minus anteromedial tibial translation) of the affected knees were 3.2 ± 1.6 mm in the TT group and 2.0 ± 1.8 mm in the TP group, and significantly larger in the TT group ($P < 0.05$). The side-to-side differences of anterolateral tibial translation were 1.4 ± 1.6 mm in the TT group and 0.9 ± 1.9 mm in the TP group (N.S.). There was no significant difference in the side-to-side difference of Kneelax3 arthrometer, Lysholm scores, KOOS and re-injury rate between the two groups (Table 3).

The anterolateral rotatory translation were significantly correlated with the shallow (distal and anterior in anatomy) femoral tunnel position (R = 0.42, $P < 0.01$), while the correlation between the side-to-side differences of Kneelax3 arthrometer and shallow femoral tunnel positions was weak and not statistically significant (R = 0.27, $P = 0.14$) (Table 4). Femoral and tibial tunnel positions are plotted in both groups, according to the quadrant method and Staubli's technique, together with the relationship with stability results of MRI and Kneelax3 arthrometer (Figure 4).

DISCUSSION

We aimed to clarify *in vivo* rotatory knee stability as well as the anterior-posterior stability after ACL reconstruction using BTB autografts, and correlate knee stability to tunnel positions. The most important findings of this study were that the anterolateral rotatory translations (= anterolateral minus anteromedial tibial translation) were significantly correlated with the shallow (distal and anterior in anatomy) femoral tunnel positions. A previous *in vivo* study has also reported that ACL reconstruction using BTB autografts with non-anatomic tunnel position resulted in significantly increased positive pivot-shift test cases, compared with those with anatomic tunnel positions at 1-year follow-up[30]. Another robotic study using cadaveric knees has reported that anatomic ACL reconstruction with rectangular BTB grafts restored knee kinematics better than the one with oval femoral tunnels located in shallower and higher positions[6], and these were consistent with our study.

Comparison between TT and TP groups showed shallower and higher femoral tunnel positions, more posterior tibial tunnel positions and increased anterolateral rotatory translation in the TT group. Previous studies have reported that it is more difficult for TT technique to locate femoral tunnels anatomically and restore normal kinematics, compared with TP technique[7-9,37,41,42],

Table 4 Correlations between tunnel positions and knee stability

		Femur		Tibia
		Shallow (+)-Deep (-)	Low (+)-High (-)	Posterior (+)-Anterior (-)
Kneelax3	Corr (R)	0.27	-0.02	0.15
side-to-side differences	Significance	NS (P = 0.14)	NS	NS
MRI analysis				
Anterolateral	Corr (R)	0.42	-0.13	0.12
rotatory translation	Significance	P < 0.01	NS	NS

Anterolateral rotatory translation: Difference of anterior tibial translation between lateral minus medial compartment; NS: Not significantly.

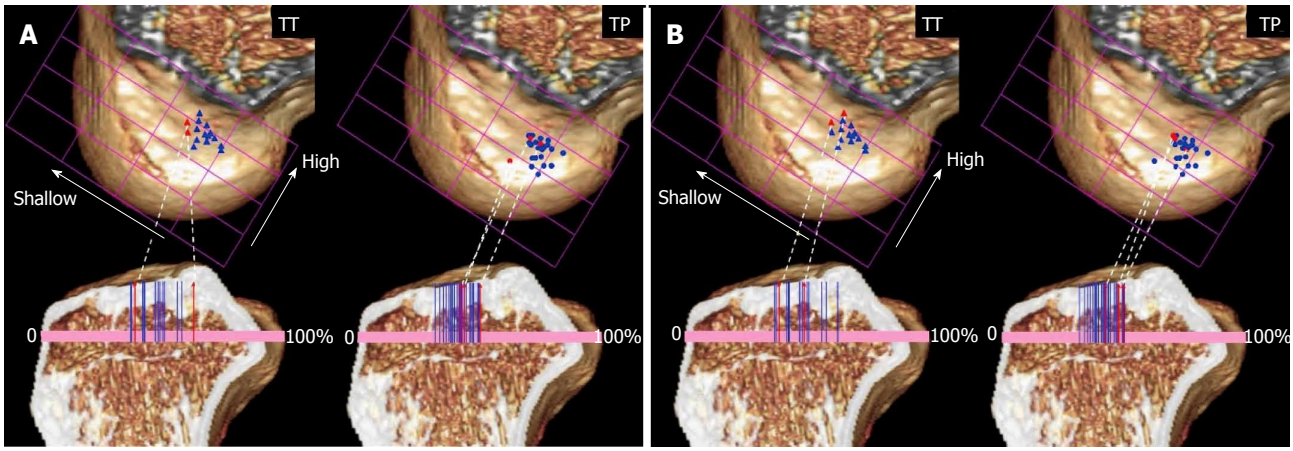

Figure 4 Tunnel positions in trans-tibial and trans-portal group are plotted for the femur and the tibia. A: Blue and red markers mean the side-to-side differences of Kneelax3 arthrometer of the case were under 3 mm (blue) and over 3 mm (red), respectively; B: Blue and red markers mean the side-to-side differences of anterolateral tibial translation were under 3 mm (blue) and over 3 mm (red), respectively. TT: Trans-tibial; TP: Trans-portal.

whereas no significant difference was found in side-to-side differences of Kneelax3 measurement, anterolateral and anteromedial tibial translation in MRI, or other clinical outcomes. The reasons why these stability parameters and clinical outcomes showed no difference between the two techniques may be that the TT-techniques we used did not locate femoral tunnels in "high-noon" isometric position, but located them in oblique positions which are mostly within the femoral footprint, as shown in Figure 4, thus the two groups resulted in less than 2 mm of mean side-to-side difference of anterolateral tibial translation and Kneelax3 measurement with small differences. A recent study using modified TT technique has reported similar anatomic femoral tunnel positions and good clinical results which are comparable to TP technique[51], although TT technique still runs a risk of creating posterior tibial tunnels and resulting vertical graft orientation[52,53]. A vertical graft orientation, created by shallow femoral tunnels and posterior tibial tunnels, may result in residual rotatory knee instability[40,54].

It is well known that merits of using a BTB autograft are its stable initial fixation and good bone-graft healing[23-25]. BTB cases in our cohort also showed sufficient stability within 2 mm of mean side-to-side difference of anterior tibial translation in rotatory and anterior-posterior evaluation and excellent clinical outcomes. To our knowledge, only a few studies so far have reported quantitative assessment of rotatory instability *in vivo* after anatomic ACL reconstruction using BTB autografts[32-34]. Most of the previous studies about BTB grafts were *in vitro* kinematic study using cadaveric specimens[5,6,26-28], or *in vivo* study evaluated by manual testing of pivot-shift[18,29-31]. We added the quantitatively assessed evidence of rotatory instability after anatomic ACL reconstruction using BTB autografts to the current knowledge. Our results suggest that anatomical placement of BTB autografts would restore knee stability and function after ACL reconstruction.

One of the limitations of this study was that all the subjects included were male patients, thus it might have affected the results[55]. However, recent large cohort studies have reported gender is not a risk factor for knee instability or revision after ACL reconstruction[56-58]. Secondly, our sample size was relatively small. It was because we usually used hamstring grafts for female patients and for those who had habits of frequent kneeling. The size might not be enough to detect small differences of anterolateral tibial translation between the two techniques.

Anterolateral rotatory instability *in vivo* significantly correlated shallow (distal and anterior in anatomy) femoral tunnel positions after ACL reconstruction using BTB autografts. TT technique located femoral tunnels in shallower and higher positions, and tibial tunnels in more posterior positions than the TP technique, thus increased the anterolateral rotation in reconstructed

knees. Clinical outcomes and knee stability in both techniques were overall satisfactory with less than 2 mm of side-to-side differences in rotatory and anterior-posterior instability. As for clinical relevance, anatomic reconstruction of the ACL using BTB autografts may restore knee function and stability.

COMMENTS

Background

Anatomic single-bundle anterior cruciate ligament (ACL) reconstruction using bone-patellar tendon-bone (BTB) autograft may restore close to normal ACL function. However, quantitative studies showing *in vivo* rotatory instability after anatomic ACL reconstruction using BTB graft are sparse.

Research frontiers

In vivo anterolateral rotatory instability (ALRI) can be assessed quantitatively by applying the Slocum ALRI test in a horizontal open MRI Scanner.

Innovations and breakthroughs

This study added the quantitatively assessed evidence of rotatory instability after anatomic ACL reconstruction using BTB autografts to the current knowledge.

Applications

It was suggested that anatomical placement of BTB autografts would restore knee stability and function after ACL reconstruction.

Terminology

ALRI: Anterolateral rotatory instability.

Peer-review

The manuscript is well-written.

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ORIGINAL ARTICLE

Retrospective Study

Evaluation of 1031 primary titanium nitride coated mobile bearing total knee arthroplasties in an orthopedic clinic

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Author contributions: All authors equally contributed to this article; Breugem SJM and Linnartz J wrote the paper, analysed the data; Sierevelt I evaluated the data, performed a critical review and did the final approval; Breugem SJM, Bruijn JD and Driessen MJM designed the study and performed the critical revision and editing and performed the final approval of the final version.

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Abstract

AIM

To evaluate the influence of the titanium nitride (TiN) coating on the results of a total knee arthroplasty (TKA).

METHODS

A total of 910 patients (338 men; 572 woman), with a mean age of 65 (range 36-94) undergoing 1031 primary TKAs were assessed. Clinical evaluation and patient-reported outcomes were gathered one year after surgery. The questionnaires included the Knee injury and Osteoarthritis Outcome Score (KOOS)-Dutch version, Visual Analogue Scale (VAS) pain scores in rest and during active knee movement, VAS-satisfaction scores, and EQ-5D-3L health scores. This was aimed to assess the overall knee function and patient satisfaction, and to enable us to make a gross comparison to other TKAs.

RESULTS

At a mean follow-up of 46 mo (range 1-92) the overall implant survival was 97.7% and 95.1% for any operative reason related to the implant. Twenty-three knees (2.2%) required revision surgery. Arthrofibrosis was the most common indication for a re-operation. The clinical evaluation and patient-reported outcomes revealed good to excellent patient satisfaction and function of the

arthroplasty. The median postoperative VAS-pain scores on a scale of 0-100, at one year after surgery were 1 in rest and 2 during movement.

CONCLUSION

The TiN coated, mobile bearing TKA results are excellent and similar to those of other widely used TKA designs. Residual pain of the knee remains a concern and the TiN coating in combination with the mobile bearing does not seem to be the simple solution to this problem. Future research will have to show that the coating gives a better survival than the cobalt chrome version.

Key words: Total knee arthroplasty; Titanium nitride coating; Mobile bearing; Pain; Satisfaction and survival

Core tip: The titanium nitride coated, mobile bearing total knee arthroplasty (TKA) results are excellent and similar to those of other widely used TKA designs.

Breugem SJM, Linnartz J, Sierevelt I, Bruijn JD, Driessen MJM. Evaluation of 1031 primary titanium nitride coated mobile bearing total knee arthroplasties in an orthopedic clinic. *World J Orthop* 2017; 8(12): 922-928 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/922.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.922

INTRODUCTION

Total knee arthroplasty (TKA) is the golden standard treatment for treating patients with end stage Osteoarthritis, and although very successful, approximately 10% of patients experience residual pain[1]. In the last 20-30 years much research have been done and many theories have been proposed to explain this residual pain. Today most TKA manufacturers use approximately the same design, but small differences in the used materials and coatings, make each arthroplasty unique. Each small change to a well renowned arthroplasty system needs to be evaluated.

Although fixed bearing designs have revealed a high degree of clinical success over the past decades, implant loosening and polyethylene wear were regularly causes for failure[2,3]. In the 1970's, Buechel and Pappas introduced the (LCS-system) mobile bearing in TKAs, hereby trying to reduce polyethylene contact stress and therefore wear[4]. Although the mobile bearing achieves excellent results, literature is not clear whether a mobile bearing is better than a fixed bearing TKA. Some studies show a difference, yet others show no significant differences between fixed- and mobile bearing TKAs[5-9]. Today most femur and tibia components used, are made of cobalt-chromium-molybdenum (CoCrMo) alloy[10].

Titanium nitride (TiN) is a ceramic, which is regularly used as a coating to enhance other materials with the properties of TiN. This coating is administered to a wide variety of implants used in cardiac-, neurologic-, dental- and orthopaedic surgery[11-13]. Beneficial properties of TiN include hardness, more scratch resistant, a smoother surface, less adhesion to polyethylene and a more wettable surface[10,14-16]. The TiN coating is thought to reduce the wear of Polyethylene and the potential for wear debris induced osteolysis, which today is still a considerable cause for revision surgery[2,3]. Furthermore *In vitro* studies have shown that Cobalt en Chrome ions can induce an inflammatory response, thus induce pain and swelling[10]. Adding the TiN coating to the CoCrMo TKA system, is thought to reduce the release of Cobalt and Chrome ions[10].

The primary goal is to report if the TiN coating in a mobile bearing TKA has any influence on the clinical outcome, patient satisfaction and the mid term implant survival of the TKA. This TiN TKA has been used in several clinics the last decade. Yet, little is published or reported about the clinical outcome and survival[10,14,15].

MATERIALS AND METHODS

All patients that had received a primary ACS® (Implantcast, Buxtehude, Germany) TiN mobile bearing TKA, between February 2007 and April 2012 in our clinic, were included in this study. The data for all included patients was collected up until October 2014, by utilizing the clinics' database and by contacting patients if any necessary data was missing. No patients were excluded on the basis of the severity of their disease or deformity of the knee. Patient sex, age, BMI, ASA-class (American Society of Anaesthesiology), arthroplasty side, component sizing and use of posterior stabilised components were gathered as baseline patient characteristics. Informed consent was obtained from all individual participants included in this study.

The Primary endpoints were defined as true revisions, defined as exchange of the tibial and/or femoral component, and secondary resurfacing of the patella. Secondary endpoints were defined as "revision for any reason" and included also open and arthroscopic arthrolysis, exchange of the polyethylene liner, and realignment of the patella. All patients were asked to complete a questionnaire at 1 year following primary TKA. The questionnaire included the Knee injury and Osteoarthritis Outcome Score (KOOS)-Dutch version[17], Visual Analogue Scale (VAS) pain scores in rest and during active knee movement, VAS-satisfaction scores, and EQ-5D-3L health scores. This was aimed to assess the overall knee function and patient satisfaction, and to enable us to make a gross comparison to other TKAs.

Operative technique

Three orthopaedic surgeons within the same orthopedic clinic performed all TKAs, with osteoarthritis being the most common indication for surgery. Patients underwent either a general- or spinal-anaesthetic and all patients

Table 1 Comparisons of clinical outcomes 1 year after primary total knee arthroplasty (medians with interquartile ranges)

	Arthroplasty *in situ* (n = 663)	Revised (n = 8)	P value
KOOS-pain	92 (72; 100)	64 (42; 72)	< 0.01
KOOS-sympt	86 (71; 93)	68 (56; 78)	< 0.01
KOOS-adl	89 (70; 97)	59 (51; 75)	< 0.01
KOOS-sport	40 (15; 70)	33 (6; 65)	0.56
KOOS-qol	69 (50; 88)	38 (38; 55)	< 0.01
VAS-pain (rest)	1 (0; 7)	8 (1; 61)	0.06
VAS-pain (activity)	2 (0; 13)	18 (3; 40)	0.03
VAS-satisfaction	91 (70; 100)	45 (14; 38)	< 0.01
EQ-5D	0.84 (0.78; 1.0)	0.76 (0.35; 0.78)	< 0.01
EQ-5D-VAS	80 (70; 90)	71 (50; 89)	0.26

KOOS: Knee injury and osteoarthritis outcome score; VAS: Visual analogue scale.

received a locally infiltrated anaesthetic (LIA) at the end of surgery. All patients received perioperative antibiotic prophylaxis for 24 h. A straight longitudinal incision was made to expose the knee joint. A surgical tourniquet was used during all TKAs. All prostheses were fixed using bone cement. Postoperative thrombo-profylaxis was administered in the form of daily subcutaneous injections with Low Molecular Weight Heparin (LMWH) and use of a Trombo Embolism Deterrent (TED) stocking during 4 wk after surgery. Physical therapy was prescribed generally starting two weeks after surgery.

Statistical analysis

Survival analyses were performed using the Kaplan-Meier methods and cumulative survival rates were calculated with 95%CI for both true revision and revision for any reason as endpoints. Patients who died with the implant intact or who were lost to follow up were identified from patient files, and the follow-up time for these patients was censored at the date of death or last clinical or telephone based contact. Multivariate Cox regression analysis was performed to assess the association between potential risk factors (age, BMI, ASA, component sizing and indication) and revision. The KOOS, VAS-pain and satisfaction, and EQ-5D scores are described as medians with accompanying interquartile ranges (IRQ). Comparisons between the revision and non-revision group were performed by use of Mann Whitney *U*-tests. Statistical analysis was performed with the use of SPSS 24.0 (Armonk, NY: IBM Corp). A P-value < 0.05 was considered statistically significant.

RESULTS

A total of 910 patients with 1031 Primary ACS arthroplasties, performed by 3 orthopaedic surgeons, were identified from the database. This included 338 male (37.1%) and 572 female (62.9%) patients, with a mean age of 65.4 years (range 36-94) at time of surgery.

The arthroplasties were performed in 52.7% (n = 543) on the right side, and in 47.3% (n = 488) on the left. A total of 121 patients had received bilateral arthroplasty between 2007 and 2012. Mean BMI was 28.7 (range 20.4-47.3). 26.3% of patients had an ASA-score of 1, 67.8% had an ASA-score of 2 and 5.9% had an ASA-score of 3.

Clinical outcomes at 1 year after surgery

A total of 671 patients (65%) had filled out the questionnaires at one year after primary TKA (Table 1). The KOOS measured at 1 year after surgery showed generally good levels of function during activities of daily life (ADL), pain, and symptoms with a median scores of 89 (IQR: 70-97), 92 (IQR: 72-100), 86 (IQR: 71-93), respectively. The domains "sport/rec" and "QoL" had median values of 40 (IQR: 15-70) and 69 (IQR: 50-88), respectively. In all but the "sports and recreational function" subscale of the KOOS, patients without required revision surgery scored significant higher scores (P-value < 0.01) then the revision group (Table 1).

The median postoperative VAS-pain scores on a scale of 0-100, at one year after surgery were 1 in rest and 2 during movement of the joint in the non-revision group. The patients that required a revision operation scored significantly higher VAS scores during activity (P = 0.03).

Overall patient satisfaction levels were good, revealing a median VAS-satisfaction score of 91 (IQR: 70-100) out of 100 in the non-revised, *vs* 45 (IQR: 14-38) out of 100 in the revision group at one year following primary surgery. This difference was statistically significant (P < 0.01).

At one year after surgery patients reported high levels of health-related quality of life. There was a significant difference (P < 0.01) in the EQ-5D scores between the revised and non-revised TKA scores, with the revision group showing lower scores corresponding with a lower quality of life (Table 1).

Component sizing

Table 2 shows the overall use of arthroplasty sizes utilised in this study. Size 4 femoral and tibial components were the most frequently implanted (both 38%) with a 10 mm thick liner (53%). Twelve female knee replacements were done using a Gender-specific, also known as a Slim-variety, arthroplasty. In 18 cases, use of a Posterior Stabilised (PS) femoral component with matching PS-liner was deemed necessary to acquire a peri-operative stable knee joint. All but two TKAs were primarily implanted without a patellar component. In these two cases peri-operative patellar tracking was suboptimal due to heavy wear and severe deformation of the patella and/or trochlea. The size of the components was not significantly associated with revision rates for component exchange as well as revisions for any reason (0.22 < P < 0.72).

Survival analysis

The mean follow-up period of all 1031 patients was 46 mo, ranging from 1 to 92 mo. Overall arthroplasty

Table 2 Implant component sizing (n = 1031)

Component size femur	n (%)	Component size tibia	n (%)	Size liner	n (%)
2	5 (0.5)	3	57 (5.6)	10	545 (53)
3	257 (25.0)	4	386 (37.6)	12.5	394 (38.2)
4	390 (37.9)	5	287 (27.9)	15	80 (7.8)
5	280 (27.2)	6	221 (21.5)	17.5	8 (0.8)
6	97 (7.4)	7	76 (7.4)	20	2 (0.2)
Missing	2	Missing	4	Missing	2

survival for component exchange was 97.7% (95%CI: 97.2-98.2) and 95.1% (95%CI: 94.4-95.8) for revision for any reason. Seventeen patients (18 TKAs) had died due to causes unrelated to knee surgery after a mean follow-up of 30.1 mo (range: 9 to 56) (Figure 1).

A total of 23 (2.2%) TKAs required revision surgery of at least one component of the TKA or addition of a patellar button. All revisions were performed within the first three years postoperatively. Mean time to revision was 21 mo (range: 3 to 36). Revision of six tibial components was performed due to malpositioning at primary surgery, two of which also required addition of a patellar button. In five cases revision was required following a traumatic event, resulting in periprosthetic bone fractures, and muscle-/ligament tears. One of which, revision of the femoral component was necessary at 27 mo, after a fracture of the femur was caused during manipulation under narcosis, at five months after primary TKA. Revision surgery was performed on 2 patients due to infection of the TKA. Revision surgery of the total joint was performed in two stages with addition of antibiotic treatment. These treatments proved successful as the revised TKAs are still implanted.

Isolated Patellofemoral (PF) pain occurred in four patients after TKA and required addition of a patellar component. Two patients had PF pain accompanied by non-traumatic instability and required polyethylene exchange along with the addition of a patellar component. One patient reported PF pain and instability after a traumatic event for which PE exchange and addition of a patellar component was performed. Arthrofibrosis combined with PF pain was seen in four patients. In these cases addition of a patellar component was done along with an arthrolysis and in three cases removal of the liner was necessary to release the posterior capsule. An implantation of a patellar component was necessary to improve patellar tracking along the trochlea.

Revision for other reasons in terms open and arthroscopic arthrolysis, exchange of the polyethylene liner, and realignment of the patella, was performed in an additional 27 patients (2.6%), resulting in a total amount of 50 revisions for any reason (4.8%) with a mean time to revision of 18 mo (range 1 to 36). Of these 27 procedures, seventeen knees (34% of all revisions for any reason) required an open release for which the PE needed to be removed, eight knees (16%) required an open arthrolysis without PE exchange, one knee (2%) was arthroscopically released and in one knee (2%) an arthroscopic lavage was done, followed by antibiotic treatment due to an infection of the knee.

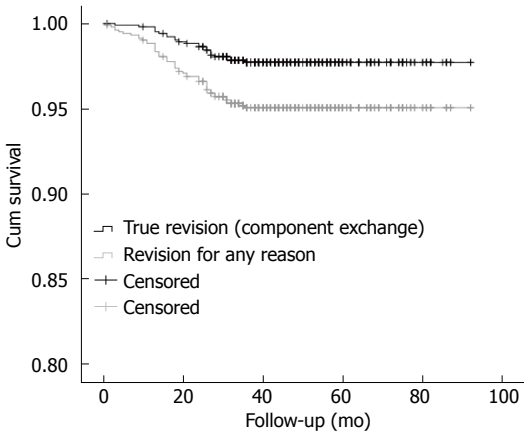

Figure 1 Kaplan-Meier survival curves of the ACS total knee arthroplasty for both True revision (component exchange and revision for any reason).

Five patients required open arthrolysis with exchange of the polyethylene liner. In three of these cases no clear improvement of the ROM was achieved by a manipulation under anaesthesia (MUA). One patient suffered from periarticular ossifications (PAO's), which were excised at 13 mo after surgery and therefore required polyethylene exchange. In one case, the patient had complaints of a large fabella for which removal of the PE was needed to gain access for excision. Five patients suffered from joint instability after a traumatic event, and four patients had complaints of instability following primary surgery without any clear trauma. One early infection (within 1 mo) was treated with arthroscopic lavage followed by an additional treatment. Of the eight TKAs that received an open procedure without PE exchange, seven patients underwent arthrolysis for arthrofibrosis, of which two cases required additional realignment of the patella without implantation of a patellar button. One patient had complaints of a Corpus Liberum (CL) that required removal. On inspection, there was no visible damage caused by the CL.

In one case amputation of the lower limb was necessary within the first month after surgery, due to a rupture of a pseudo-aneurysm. This lead to a compartment syndrome, which was detected too late due to an epidural anaesthesia.

MUA was performed in 33 knees (3.2%) at a mean follow up time of 4.1 (range 1-8) mo. In three cases MUA was followed by an open release, for which PE exchange was also necessary and in one case by component exchange. All TKAs that required MUA suffered from arthrofibrosis that limited the functional Range of Motion (ROM) of 90 degrees of flexion or full extension. Patient age, gender, BMI and ASA-class were not significantly associated with true revision as well as revision for any reason ($0.38 < P < 0.99$).

DISCUSSION

In this large retrospective review of a TiN coated mobile

bearing TKA, good to excellent scores were achieved and a very low pain scores. A median postoperative VAS pain scores in a scale of 0-100, at one year after surgery were 1 in rest and 2 during movement of the joint. The median reported KOOS-pain scores were 92. These reported pain scores seem to be comparable with the reported VAS-pain scores reported by Moon *et al*[18] of 1.4 (in de "Buechel and Pappas" total knee group) and 1.8 (in the "NexGen-LPS" total knee group). Therefore the results of the TiN coated mobile bearing TKA concur with the results of the CoCrMo mobile bearing TKA, and are not superior or inferior to the CoCrMo mobile bearing TKA[18,19].

It was suggested in the literature, that the TiN coating could protect the synovium of the knee for the release of Co and Cr ions[10]. *In vitro* studies have shown that Co en Cr ions can induce an inflammatory response, thus induce pain and swelling[10]. Van Hove *et al*[10] compared the TiN coating to a CoCrMo mobile bearing TKA and found no difference in postoperative pain scores or inflammation between the two groups. So the hypothesis that the TiN coating could make a difference in the direct post operative period, does not seem to be the case, our results are comparable to the CoCrMo mobile bearing TKA.

Another reason for our group to use the mobile bearing TKA is the low number of patients with anterior knee pain or PF pain after a TKA. Resurfacing or nor resurfacing the patella during primary TKA still remains controversial[1,20]. Anterior knee pain after TKA could have multiple causes and is not solely caused by not resurfacing the patella during primary surgery. In our series all but two TKAs in this study were implanted without the use of a patellar component. Later 10 Patients (1.0%) suffered from PF pain and required a secondary resurfacing of the patella. Thus in our series, more than 1000 knees were not resurfaced with a patella, this may further support the theory that resurfacing of the patella is not strictly necessary in primary mobile bearing TKA[20-22]. There are some limitations in this study with regard to this dilemma. We did not specifically ask questions regarding PF pain or quantify that amount of pain. Although the completed questionnaires can give some insight in the overall knee function and pain scores, they do not isolate PF pain. We only have data on PF pain if this resulted in the secondary resurfacing of the patella.

Patient satisfaction were good, revealing a median VAS-satisfaction score of 91 (IQR 70-100) out of 100 in the non-revised, *vs* 45 (IQR: 14-38) out of 100 in the revision group at one year following primary surgery. This difference was statistically significant ($P < 0.01$). At one year after surgery patients reported high levels of health-related quality of life. There was a significant difference ($P < 0.01$) in the EQ-5D scores between the revised and non-revised TKA scores, with the revision group showing lower scores corresponding with a lower quality of life. The impact of a revision or secondary operation can be revealed in this way.

The TiN coating of the CoCrMo TKA could be beneficial to patients with a metal allergy, especially those with a known nickel sensitivity[23]. This precludes them from receiving a CoCrMo alloyed arthroplasty. Due to the increase in the number of TKAs performed annually; the amount of patients with a painful well-implanted TKA is also thought to increase. If a patient is known with a metal allergy, it is advised to perform an anallergic implant, like the TiN coated implants.

MUA was performed in 33 (3.2%) cases, and this is in unison with the widely reported prevalence of 1.3%-12%[8]. For all but 3 patients in our study, a single MUA followed by intensive physical therapy was sufficient to improve ROM to a functional level of > 90 degrees of flexion and full extension. An additional open release was necessary in the above-mentioned three patients following MUA to regain a functional ROM.

The TiN coating is thought to reduce the wear of Polyethylene and the potential for wear debris induced osteolysis, which today is still a considerable cause for revision surgery[2,3]. This is thought to be due to the beneficial properties of TiN coating, they include: The hardness, more scratch resistant, a smoother surface, less adhesion to polyethylene and a more wettable surface[10,14-16]. In this series a survival of 97.7% at a mean follow-up period of 46 mo was found. This is comparable to the survivorship of other TKAs. The survival of conventional knee arthroplasties, using fixed bearing implants, ranges from 90%-95% of > 10 years[18]. Beuchel *et al*[19] reported a 20 year survival of the LCS cemented rotating platform TKA of 97.7%. Jordan *et al*[24] reported survivorship of 94.8% at 8 years of the meniscal-bearing TKA. All retrieved polyethylene liners were inspected for wear during revision surgery. There were no reports of significant wear of the retrieved liners. The mean revision period of 21 mo is however, arguably too short to reveal high levels, if any, of polyethylene wear. Whether or not the addition of a TiN coating of a mobile bearing TKA reduces polyethylene wear and thus enhance the survival of the arthroplasty needs to be further investigated in the upcoming years.

Results of this study should be interpreted taking into account the limitations inherent to retrospective studies. Additionally, the response rate of completed questionnaires was 65%. This percentage might be susceptible to selection bias. A limitation of our study is due to lack of pre-operative pain scores, it is however not possible to quantify the improvement of patient reported pain after TKA.

In conclusion the ACS TiN mobile bearing TKA is a reliable arthroplasty yielding good to excellent clinical results, with a high level of function and low revision rates at a mean follow-up of 46 mo after surgery. Based on the outcomes of this study, the use of the ACS TiN coated, mobile bearing TKA appears to be justified and will be used as our primary TKA. Further research is necessary to investigate long-term survival of the arthroplasty and whether or not the addition of the TiN

coating is beneficial for polyethylene wear.

ARTICLE HIGHLIGHTS

Research background

Evaluate the influence of the titanium nitride (TiN) coating on the results of a total knee arthroplasty (TKA).

Research motivation

Very little is known about the influence of the TiN coating on the results of a TKA.

Research objectives

Evaluate the overall clinical outcome, evaluating pain and patient satisfaction and the mid-term implant survival.

Research methods

A total of 910 patients (338 men; 572 woman), with a mean age of 65 (range 36-94) undergoing 1031 primary TKAs were assessed. Clinical evaluation and patient-reported outcomes were gathered one year after surgery. The questionnaires included the Knee injury and Osteoarthritis Outcome Score (KOOS)-Dutch version, Visual Analogue Scale (VAS) pain scores in rest and during active knee movement, VAS-satisfaction scores, and EQ-5D-3L health scores. This was aimed to assess the overall knee function and patient satisfaction, and to enable us to make a gross comparison to other TKAs.

Research results

At a mean follow-up of 46 mo (range 1-92) the overall implant survival was 97.7% and 95.1% for any operative reason related to the implant. Twenty-three knees (2.2%) required revision surgery. Arthrofibrosis was the most common indication for a re-operation. The clinical evaluation and patient-reported outcomes revealed good to excellent patient satisfaction and function of the arthroplasty. The median postoperative VAS-pain scores on a scale of 0-100, at one year after surgery were 1 in rest and 2 during movement.

Research conclusion

The TiN coated, mobile bearing TKA results are excellent and similar to those of other widely used TKA designs. Residual pain of the knee remains a concern and the TiN coating in combination with the mobile bearing does not seem to be the simple solution to this problem. Future research will have to show that the coating gives a better survival than the cobalt chrome version.

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ORIGINAL ARTICLE

Retrospective Study

Acetabular cup version modelling and its clinical applying on plain radiograms

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Author contributions: Kovalenko A designed the study and analyzed data; Bilyk S performed three-dimensional modeling part; Denisov A revised the manuscript for important intellectual content and in couple with expert-doctor from United States made the translation in English.

Institutional review board statement: The study "Acetabular cup version modelling and its clinical applying on plain radiograms" was approved by the Institutional Review Board (IRB) of the Vreden Scientific Orthopedic Institute, Saint-Petersburg, Russian Federation.

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

Conflict-of-interest statement: Dr. Denisov has nothing to disclose. Dr. Kovalenko has nothing to disclose. Dr. Bilyk has nothing to disclose.

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Abstract

AIM

To measure the sensitivity and specificity of the cup version assessment by using only anteroposterior hip and pelvis views, evaluate the incidence of inadequate cup version in patients with repeated dislocations after total hip arthroplasty (THA).

METHODS

Radiographic retrospective analysis of 2 groups of patients, with follow up of 6-60 mo, after undergoing primary THA. First group of 32 patients (20 female, 12 male) with unilateral THA (32 hips) required early revision arthroplasty for reasons of dislocation. The mean age and mode were 59 (from 38 to 83) and 66 ages respectively. The average body mass index (BMI) was 24.2 (from 17.7 to 36.3), mode 23.9. Second group was consisted of 164 patients (101 female, 63 male) without dislocations during the follow-up period (170 hips). Among them 6 patients required bilateral THA. The mean age was 60 (from 38 to 84) and mode 59. BMI was 24.8 (17.2-36.8), mode 25.2. Clinical significance of the cup anteversion sign was estimated with cross tabulation 2 × 2.

RESULTS

The value of the χ^2 yates was 10.668 ($P < 0.01$).

Sensitivity of SAI (sign of anteversion insufficiency) was 29% (95%CI: 9%-46%), and specificity was 92% (95%CI: 88%-96%). Relative risk of dislocation in patients with SAI was 3.4 (95%CI: 1.8-6.3).

CONCLUSION

This method provides the surgeons with the ability to perform a reliable and simple qualitative assessment of the acetabular component version. It can be useful during patient examination with early loosening of the implant, dislocations, and impingement. Additionally, it can provide necessary information during planning of revision surgery, especially when considering question about cup replacement, although final assessment of the cup position should be done with a computed tomography scan.

Key words: Hip arthroplasty; Acetabular component; Retroversion; Dislocation

Core tip: The acetabular cup position is a crucial factor of normal function and implant survival. Several methods to determine cup anteversion are described. Among them are mathematical methods based on a standard anteroposterior (AP) view, modifications of a cross-table lateral views, and computed tomography-scan. Latter two methods are not always available or practical in outpatient setting. The purpose of our study was to estimate sensitivity, specificity of the cup version assessment by using only AP hip and pelvis views. Our findings suggest that inadequate anteversion sign appears when the anteversion angle is less than half the angle between X-ray beams in the AP hip and pelvis views.

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INTRODUCTION

Compared to most other orthopedic interventions, total hip arthroplasty (THA) is only a first step in a lengthy journey. Successful patient outcome relies heavily on the implant, which requires regular observation to assess the prosthesis and surrounding tissues. It is well known that bearing surface wear rate and prosthesis stability are dependent upon proper component positioning[1-3]. Thus, timely recognition of component malposition is a major goal in the postoperative period. Early awareness may allow for a timely correction of acetabular cup position and expedited return to daily activities without undesirable effects of improper component alignment. Two main parameters that must be taken into account while assessing acetabular component position are inclination and anteversion. Inclination is a measure of the angle between longitudinal axis (line drawn between the teardrops) and acetabular axis (cup tilt). Cup version measurement, on the other hand, poses a greater challenge.

Calculation of this angle can be achieved via several techniques. These methods are based on the evaluation of a visible ellipse on anteroposterior (AP) view as a result of cup rotation. Previously described techniques by Pradhan, Acland, Lewinnek are often used[4], as well as specialized software which can provide calculation of cup version[5], and even orthopedic grid calipers which approximate this calculation[6]. However, none of these techniques can differentiate cup ellipse appearance in patients with same degree of anteversion *vs* retroversion. This issue can be resolved by using a cross-table lateral view or computed tomography (CT) scan[7], both of which are seldom used due to challenge with patient position in the early postoperative period and concerns for radiation exposure.

To measure the sensitivity and specificity of the cup version assessment by using only AP hip and pelvis views and evaluate the incidence of inadequate cup version in patients with repeated dislocations after THA.

MATERIALS AND METHODS

Cup shadows in retroversion and anteversion were reproduced on AP hip and pelvis views using Autodesk 3ds Max software (Autodesk, Inc., San Rafael, CA, United States) (Figure 1). Difference in angles of cup version, which may be seen as a result of difference between X-ray beams centered on AP hip and pelvis views, were subsequently analyzed. The distance from the beam source to the screen was 100 cm, the distance from the cup model to the screen was 15 cm, and the cup diameter was 50 mm. Cup version angles ranged from -20 to 20 degrees in one degree intervals. The shift of the source beam between AP pelvis and AP hip views was 12 cm. Acquired data was used for radiographic retrospective analysis of 2 groups of patients, with follow up of 6-60 mo, after undergoing primary THA.

First group of 32 patients (20 female, 12 male) with unilateral THA (32 hips) required early revision arthroplasty for reasons of dislocation. The mean age and mode were 59 years (38-83) and 66 years respectively. Average BMI was 24.2 (17.7-36.3), mode 23.9.

Second group consisted of 164 patients (101 female, 63 male) without dislocations during the follow-up period (170 hips). Among them 6 patients required bilateral THA. The average age was 60 years (38-84) and mode 59 years. BMI was 25.1 (17.2-36.8), mode 25.2. Clinical significance of cup anteversion sign was estimated with cross tabulation 2 × 2.

RESULTS

Three-dimension modelling revealed that the widths

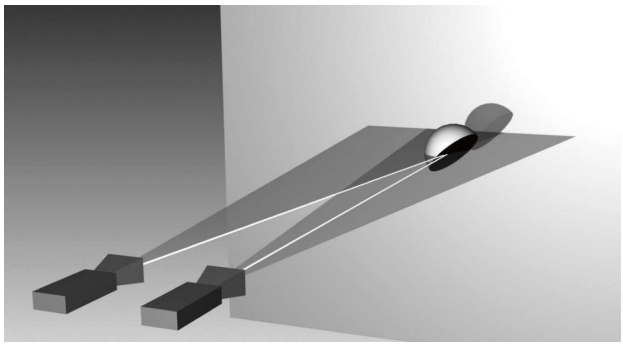

Figure 1 The scheme of model of anteroposterior pelvis view (X-ray source on the left) and anteroposterior hip view (X-ray source on the right) for acetabular cup of left hip.

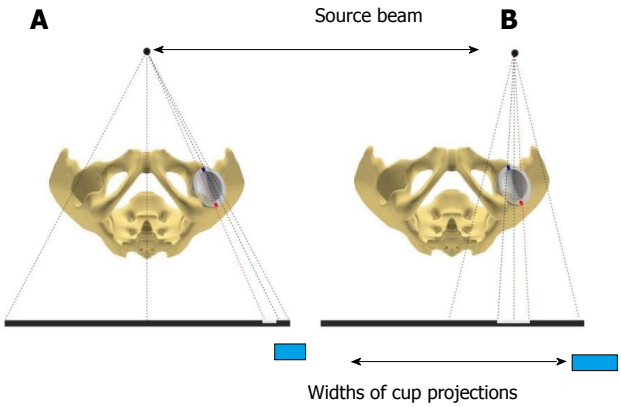

Figure 2 Different width of cup projections in pelvic and hip anteroposterior views. A: Pelvic anteroposterior views; B: Hip anteroposterior views.

of the ellipse-shaped shadow formed by the projection of the cup base to the screen are distinct in different views (Figure 2). The shadow ellipse width appears less pronounced in AP pelvis view as compared to AP hip view when the cup is anteverted (Figure 3). On the other hand, the observed shadow profile is greater in AP pelvis view as compared to AP hip view when cup is retroverted (Figure 4). A sign of retroversion was also noted when true anteversion angle did not exceed 1/2 of the angle between X-ray beam in different views (AP hip and AP pelvis). Ellipse width profiles were equal between 2 projections at the point where true anteversion was 3.5 degrees (Figure 5).

Doubling the distance of medialization of the source beam (12 to 24 cm) from the AP hip to AP pelvis position, this threshold increased in a linear manner from 3.5 degrees to 7 degrees. Retro- or anteversion angle was confirmed with a CT scan among patients having indications for revision arthroplasty (Figure 6). For discrete X-rays assessment, we assigned expression of sign shown on Figure 2 to the sign of anteversion (SA), and all others options (Figures 3 and 4) to sign of anteversion insufficiency (SAI). Thus, two options were available in assessment of cup position on X-rays-SA and SAI. Findings are presented in Table 1.

The value of the χ^2 yates was 10.668 ($P < 0.01$). Sensitivity of SAI was 29% (95%CI: 9%-46%), and specificity was 92% (95%CI: 88%-96%). Relative risk of dislocation in patients with SAI was 3.4 (95%CI: 1.8-6.3).

Predictiveness (positive predictive value) of SAI (predictive probability dislocation appearance) was 0.20 (95%CI: 0.09-0.38). Counter-predictiveness (Counter-negative predictive value) of SA (predictive probability dislocation absence) was only 0.046 (95%CI: 0.026-0.081) (Figure 7).

DISCUSSION

The method of this investigation was described by Markel *et al*[8] in 2007. However, the authors only described the technique and recommended it's use as a screening tool without reporting its sensitivity and specificity.

Threshold value for the sign inversion corresponds to the cup anteversion value that is equal to 1/2 of the X-ray beam angle penetrating the acetabular component in AP hip and AP pelvis views. The threshold value was only 3.5° in baseline conditions of our experiment. The version sign can appear retroverted in the cases when true cup anteversion is less than the threshold values. Thus, the sign can point to retroversion while the cup is, in fact, anteverted. However, in such cases, anteversion value will be out of Lewinnek's safety zone of 10°-20°[9] and further imaging would be encouraged. For these cases, we recommend the use of special views or a CT-scan to refine implant position.

In clinical practice threshold value, will depend on the patient anthropometric parameters which affect cup distance to the X-ray detector and the distance between centers of pelvis and hip joint. Nevertheless, two-fold shift in the beam source, compared to our model baseline condition, leads to increase in sign of inversion threshold up to 7°. This either corresponds to patient with a pelvis twice as wide than average[10] or, to a beam centered in front of a contralateral joint instead of symphysis pubis, which is unlikely. In addition, method accuracy can be affected by improper beam centering during radiography.

Low sensitivity (29%) and predictiveness (positive predictive value) of SAI (20%) can be explained by multifactorial causes of dislocation such as stem position, offset, muscle insufficiency and comorbidities. On other hand, specificity of SA (92%) points to a high probability to find SA in a patient without dislocation. Furthermore, counter-predictiveness (counter-negative predictive value) of SA points to the probability that dislocation can occur with frequency of only 4.6%. This data leads us to believe that these radiographic signs have a strong clinical relevance and can be useful in orthopedic practice.

X-ray assessment immediately after surgery or during outpatient follow-up, when lateral view is not available, can be limited to evaluation of cup inclination and ellipse presence that suggests about probable

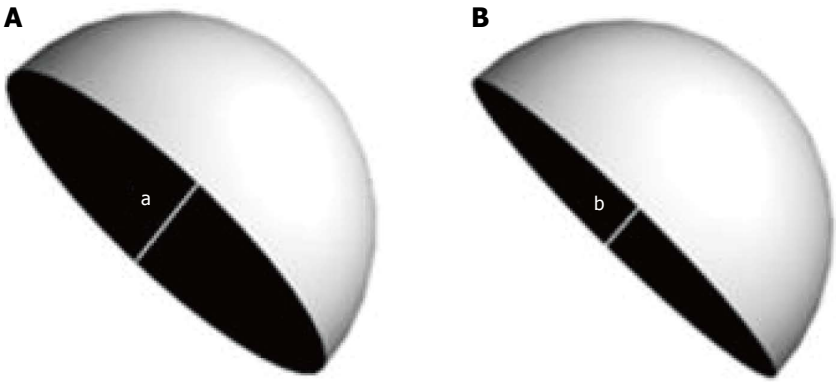

Figure 3 Acetabular component with anteversion angle of 20 degrees. A: Acetabular component image for hip AP view; B: Acetabular component image for pelvic AP view, a > b. AP: Anteroposterior.

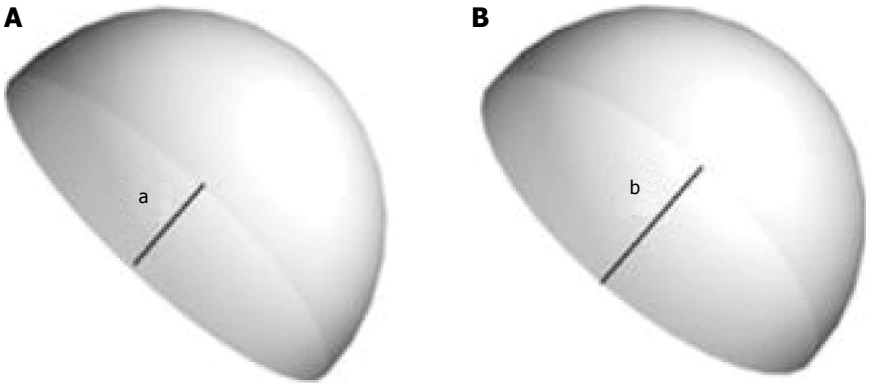

Figure 4 Acetabular component with retroversion angle of 20 degrees. A: Acetabular component image for AP hip view; B: Acetabular component image for AP pelvic view, a < b. AP: Anteroposterior.

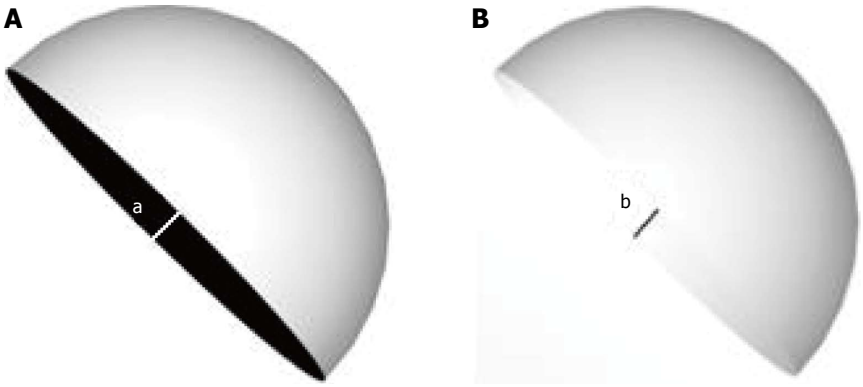

Figure 5 Acetabular component views with anteversion angle equal to half angle between rays of the beam. A: Acetabular component image for hip AP view; B: Acetabular component image for pelvic AP view. Equal width of ellipse in both views, a = b. AP: Anteroposterior.

cup version. However, a bias exists because of a two-dimensional nature of conventional X-ray views. Additional comparison of cup position on AP hip and AP pelvis views allows to avoid this bias. This simple method is useful as a screening assessment of post-op cup position and, in outpatient and remote follow-up. Furthermore, it can be used for X-ray assessment in patients with early components loosening, dislocations, impingement and preoperative revision planning, especially when there is a possibility of avoiding an acetabular cup revision. In the last example provided, we recommend performing a CT-scan for additional analysis.

On the other hand, high incidence of retroversion sign confirms clinical relevance of this method in the group of patients who required early revision surgery for the reason of hip dislocations. Postoperative radiographic evaluation is usually limited to measuring of inclination and cup ellipse, may be indirect evidence of anteversion. Such assessment methodology can

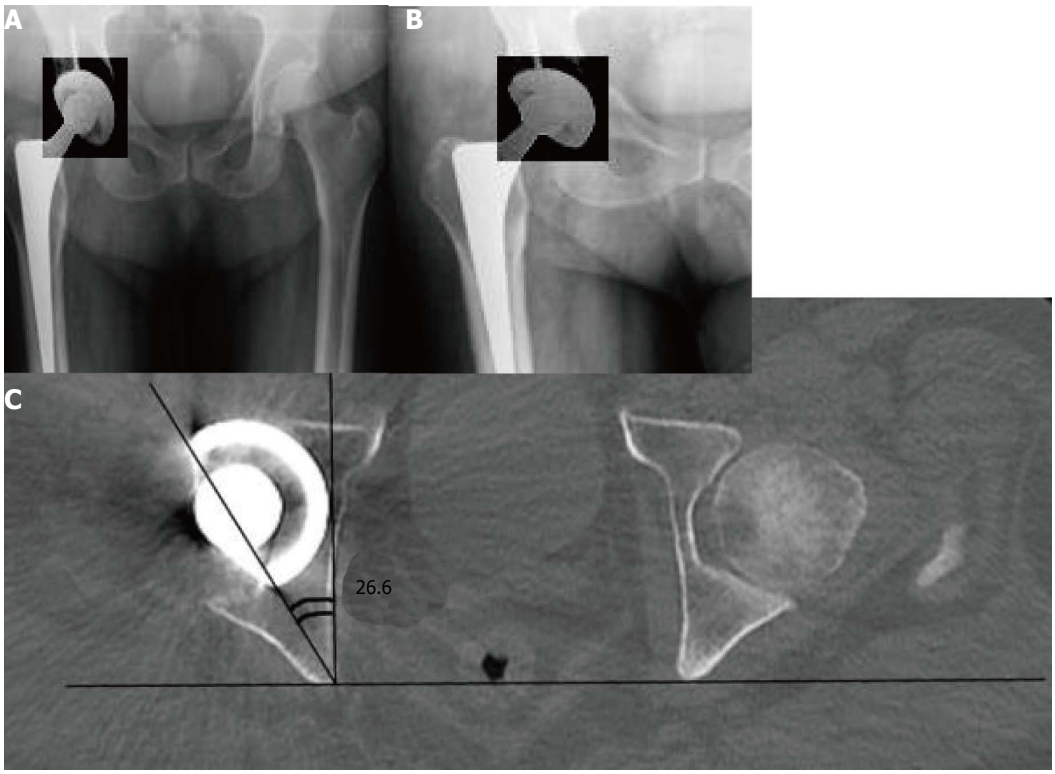

Figure 6 Retroversion sign in a patient with recurrent hip dislocations (enhanced contrasting applied to provide better recognition of acetabular cup ellipse). A: AP Pelvic view; B: AP hip views; C: CT-scan of the same patient confirming acetabular component retroversion. AP: Anteroposterior.

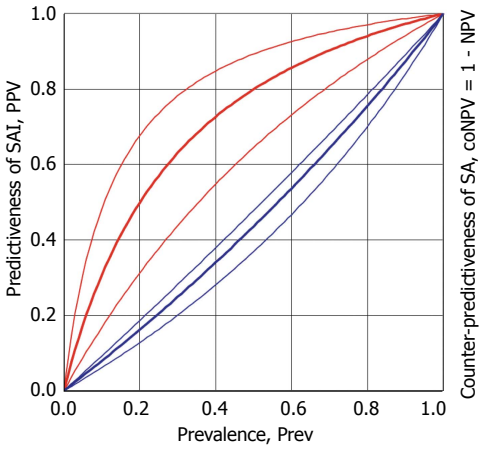

Figure 7 Predictiveness of sign of anteversion insufficiency appearance and counter-predictiveness of sign of anteversion appearance. SAI: Sign of anteversion insufficiency; SA: Sign of anteversion.

have an error due to plain radiography imaging features described above. Additional comparison of pelvic AP and hip AP view allows the possibility to eliminate this error during radiographic evaluation and decreases the probability of early hip joint instability. This simple radiographic test can be used both for screening assessment of acetabular cup version on postoperative images and in outpatient setting.

This method provides surgeons with ability to use it as a screening examination because of the simplicity of the acetabular component version qualitative assessment. It can be useful during patient examination with suspicion of the implant malposition, early implant loosening, dislocations and impingement to provide with the argument for obtaining CT scan. Additionally, it can provide necessary information during planning of revision surgery, especially when considering question about cup replacement, although final assessment of the cup position should be done with a CT scan.

Table 1 Prevalence of sign of anteversion insufficiency and sign of anteversion in patients with absence and recurrence of dislocations after primary total hip arthroplasty

X-ray diagnostic conclusion	Dislocation		Total
	Yes	No	
SAI	9	12	21
SA	23	158	181
Total	32	170	202

SAI: Sign of anteversion insufficiency; SA: Sign of anteversion.

ARTICLE HIGHLIGHTS

Research background

Correct cup positioning is one of the crucial factors of preventing hip luxation after total hip arthroplasty (THA). It can be estimated using simple radiographic views (AP of pelvis and hip) and calculating of the cup inclination angle.

Research motivation

Some techniques can provide calculation of cup version, however none of these techniques can differentiate cup ellipse appearance in patients with same degree of anteversion *vs* retroversion. It can be resolved by using a cross-table

lateral view or CT scan, both of which are seldom used due to challenge with patient position in the early postoperative period and concerns for radiation exposure and sometimes not available in orthopedic practice.

Research objectives

The authors measured the sensitivity and specificity of the cup version assessment by using AP hip and pelvis views, evaluated the incidence of inadequate version in patients with repeated dislocations after THA. The authors believe that estimation of simple radiographic anteversion sign can be used for screening assessment for further obtaining of additional examinations in case of cup malposition and repeated dislocations (as one of the provoking factor).

Research methods

Cup shadows in retroversion and anteversion were reproduced on AP hip and pelvis views using Autodesk 3ds Max software (Autodesk, Inc., San Rafael, CA, United States). Difference in angles of cup version, which may be seen as a result of difference between X-ray beams centered on AP hip and pelvis views, were subsequently analyzed. Acquired data was used for analysis of 2 groups of patients, with follow up of 6-60 mo, after undergoing primary THA.

Research results

The value of the χ^2 yates was 10.668 ($P < 0.01$). A sign of retroversion was also noted when true anteversion angle did not exceed 1/2 of the angle between X-ray beam in different views (AP hip and AP pelvis). Sensitivity of SAI was 29% (95%CI: 9%-46%), and specificity was 92% (95%CI: 88%-96%). Relative risk of dislocation in patients with SAI was 3.4 (95%CI: 1.8-6.3).

Research conclusions

Results of our study showed high specificity of the sign of anteversion inclination 92% and low sensitivity (29%) due to other risk factors of hip dislocation.

Research perspectives

In this article were not studied other factors provoking hip dislocation. That is way for future perspectives, the authors want to determine the current role of the cup malposition in comparison with other factors of hip luxation.

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ORIGINAL ARTICLE

Observational Study

Deepening trochleoplasty combined with balanced medial patellofemoral ligament reconstruction for an adequate graft tensioning

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Author contributions: von Engelhardt LV, Lahner M, Spahn G and Jerosch J contributed to study conception and design; von Engelhardt LV and Weskamp P contributed to the data acquisition and analysis; von Engelhardt LV, Weskamp P, Lahner M, Spahn G and Jerosch J contributed to the data interpretation and writing of the article; all authors approved.

Institutional review board statement: The study was reviewed and approved by the Ethical Committee of the University of Witten/Herdecke (Study No. 108/2015).

Informed consent statement: All persons involved in this study gave their informed consent prior to study inclusion.

Conflict-of-interest statement: All authors have no interests, commercial or otherwise, which represent a conflict of interest in relation to this study.

Data sharing statement: No additional data are available.

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Abstract

AIM

To evaluate our modified deepening trochleoplasty combined with a balanced medial patellofemoral ligament (MPFL) reconstruction for soft tissue alignement.

METHODS

Thirty-three knees with with recurrent patellar dislocations and a trochlear dysplasia in 30 patients (m/f = 12/21, mean age 24 ± 9 years) underwent a combination of a modified deepening trochleoplasty and a balanced MPFL reconstruction for a medial soft tissue alignement. After a mean follow-up period of 29 ± 23 mo, patients' return to sports, possible complications as well as the clinical outcomes using the Kujala, International Knee Documentation Committee (IKDC) and Lysholm scoring were evaluated. Moreover, patients' satisfaction with the general outcome, the cosmetic outcome, the pre- and postoperative pain and a potential avoidance behaviour were assessed with additional standardized questionnaires

which also included different visual analog scales.

RESULTS

There were no signs of a persistent instability. The Kujala score improved from a mean of 64 ± 16 points to 94 ± 9 points, the Lysholm score improved from a mean of 63 ± 17 to 95 ± 6 points and the IKDC score from 58 ± 11 to 85 ± 12 points, $P < 0.0001$, respectively. The assessment of pain using a visual analog scale showed a significant pain reduction from a mean of 4.8 ± 2.0 to 1.3 ± 3.4 points ($P < 0.0001$). Two of 26 cases (92%) who were engaged in regular physical activity before surgery did not return to full sporting activities. One patient felt that his sport was too risky for his knee and reported an ongoing avoidance behaviour. The other patient preferred to wait for surgery of her contralateral knee. Of the eight patients who were not engaged in sporting activities before surgery, three started regular sporting activities after surgery. In 31 of the 33 cases (94%), the patients were very satisfied with the clinical outcome of the surgery. Regarding the cosmetic results, no patients felt impaired in their self-confidence and in their clothing decisions.

CONCLUSION

Our technique shows a good clinical outcome in terms of the common scorings as well as in terms of pain, return to sports and patient satisfaction.

Key words: Trochlea dysplasia; Medial-patellofemoral ligament; Patellofemoral instability; Patella dislocation; Trochleoplasty

Core tip: Patients with recurrent patella dislocations typically have an insufficiency of the medial patellofemoral ligament (MPFL), which is an additional instability factor in a symptomatic trochlear dysplasia. Following a trochleoplasty, the articulation of the patella is changed to a more medial and dorsal mechanical position. As a consequence, a balanced alignment of the medial soft tissue restraints during a trochleoplasty is very reasonable to achieve an adequate stabilization. The combination of a modified Bereiter trochleoplasty and our MPFL reconstruction technique allowing a simple intra-operative tensioning shows encouraging results.

von Engelhardt LV, Weskamp P, Lahner M, Spahn G, Jerosch J. Deepening trochleoplasty combined with balanced medial patellofemoral ligament reconstruction for an adequate graft tensioning. *World J Orthop* 2017; 8(12): 935-945 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/935.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.935

INTRODUCTION

In flexion angles of more than 30°, the patella is predominantly guided by the trochlear groove. Between 30° of flexion and the full extension, both the medial patellofemoral ligament (MPFL) and the trochlear groove stabilize the patella[1,2]. In trochlear dysplasia, the trochlea is shallow, flat, or dome shaped, leading to an inadequate resistance to lateral patellar dislocations. Therefore, it has been described to be a major risk factor for patellofemoral instability[3]. Trochlear dysplasia is described in less than 2% of the population, whereas it occurs in up to 85% of patients with patellar instability[4]. An isolated MPFL reattachment or reconstruction in the presence of a severe dysplasia of the trochlea shows a relatively poor clinical outcome and leads to an increased risk for a recurrent instability with persistent apprehension and/or dislocations[5-10]. Therefore, a severe dysplasia of the trochlea should be addressed when corresponding clinical findings are present.

Following an acute patellar dislocation, the MPFL is ruptured with a frequency of more than 90%, which can cause recurrent dislocations and/or a significant instability[1,11,12]. During a trochleoplasty, the intra-operative impression that the patella is moved to a more medial and dorsal mechanical position has been proven by a computed tomography (CT) study on corrective postoperative changes[13]. As a logical consequence, a MPFL plastic surgery seems advisable, not only to address a torn, insufficient ligament, but also because a balancing and alignment of the medial soft tissue restraints is necessary (Figure 1). Therefore, our technique of a MPFL reconstruction allowing a simple intra-operative testing and adjustment of the graft tension[14], might be convenient especially in cases with a combined trochleoplasty. This might help in minimizing common complications of MPFL reconstructions, such as an overtensioning with anterior knee pain and/or motion deficits, patellar fractures, *etc*. or an undertensioning with an ongoing instability[6,15,16]. This study was necessary to explore our combination of a deepening trochleoplasty and our technique of a balanced MPFL reconstruction for a medial soft tissue alignment. Our hypothesis is that this technique provides reasonable advantages.

MATERIALS AND METHODS

Ethical considerations

This study has been approved by the Ethical Committee of the University of Witten/Herdecke (Study No. 108/2015) and was carried out in accordance with the ethical standards laid down in the Declaration of Helsinki. The participation was voluntary and all patients gave their informed consent to this study.

Population

This study includes 33 knees with a severe trochlear dysplasia in 30 patients (m/f = 12/21, mean age 24 ± 9 years) who underwent surgery with a combination of trochleoplasty and MPFL reconstruction as described

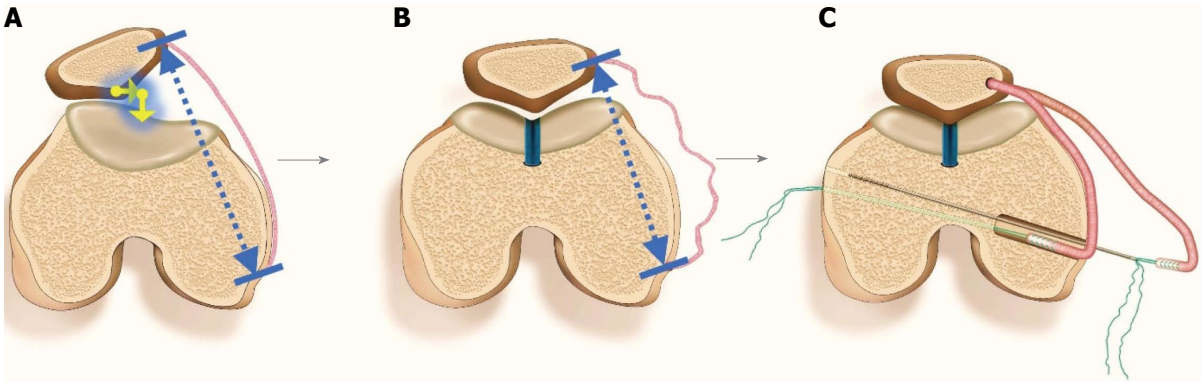

Figure 1 Drawings of the preoperative situation and the biomechanical changes during surgery. A: Drawing of a type C dysplasia showing a too high lateral facet with a bump in the superolateral aspect and a trochlear facet asymmetry with hypoplastic medial facet. This trochlea is not effective in constraining a patellar displacement; B: After mobilization of a thin osteochondral flap off the medial and lateral trochlea, the trochlear bone is deepened. The lateral edge of the trochlea is not lowered to obtain a raised lateral inclination. This way, a recentralized groove is created. The flexible osteochondral flap is fixed into the new formed groove with a transosseous resorbable 3 mm Vicryl band. As depicted, a trochleoplasty leads to a more medial and dorsal biomechanical position of the patella with a reduced distance between the femoral and patellar insertions of the medial soft tissue restraints. As a consequence, a preexisting insufficiency of the medial patellofemoral ligament (MPFL) might be aggravated by these biomechanical changes; C: Hardware-free MPFL reconstruction technique for the alignment of the medial soft tissue restraints during a trochleoplasty.

below. The estimated mean number of dislocations before surgery was 35 ± 24 (range: 1-250). Before surgery, all patients had a clear positive patella apprehension sign. Exclusion criteria were additional surgeries such as corrections of the knee rotation and/or axis, tibial tuberosity transfers, *etc*. Moreover, patients with advanced osteoarthritic changes or previous fractures of the knee were not included in this study. Factors of patellar instability were measured on preoperative radiographs and magnetic resonance imagings (MRIs) or CT scans[4]. In our series, the mean Caton-Deschamps index was 1.09 ± 0.09 and the tibial tubercle-trochlear groove distance was 16 mm ± 3 mm. The lateral trochlea inclination (LTI) angle was measured on the most superior MRI slice depicting the cartilage of the trochlear surface using the method described by Carrillon *et al*[17]. In our patients, the mean angle between the posterior contours of the condyles and the lateral facet of the trochlear groove was -9° ± 6°. Trochlear dysplasia was graded using the Dejour classification. Nine knees showed a type B, ten a type C and 14 a type D trochlear dysplasia.

Assessment and evaluation

The mean follow-up period was 29 ± 23 mo. Possible complications such as recurrent dislocations, fractures, knee stiffness, *etc*. were registered. In addition to a routinely performed clinical examination, the knee function was assessed with different scoring scales. In this study, the Kujala anterior knee pain scoring, the knee-specific outcome measure of the International Knee Documentation Committee (IKDC) and the Lysholm knee scale was used. Moreover, additional questionnaires and different visual analog scales were used to assess the general satisfaction of the patients, the satisfaction with the cosmetic outcome, the return to sports, a potential avoidance behaviour, different sports activities as well as a potential anterior knee pain.

Surgical technique

The gracilis tendon is harvested through a minimal invasive posterior or anterior harvest over the pes anserinus. After whip-stitching the armed graft has been given in a Vancomycin solution for presoaking in most cases. In contrast to the Bereiter technique, which describes a lateral parapatellar approach, we prefer a short medial parapatellar access to expose the trochlea. A seven to 10 cm long skin incision running from the medial part of the patella to the distal part of the quadriceps tendon is made (Figure 2A). The medial patellar retinaculum is divided by leaving enough tissue near the patella for later reattachment. The proximal joint capsule is incised between the superomedial pole of the patella and the vastus medialis obliquus muscle. Finally, the distal quadriceps tendon is split. Using this distally shortened medial parapatellar approach, the saphenous nerve with its infrapatellar branch is usually not affected. With this simple arthrotomy and a dislocation of the patella towards lateral, the trochlea can be completely exposed (Figure 2B). A soft tissue tunnel between both layers and running down from medial patella to the femoral MPFL insertion can be created easily by using this approach. After exposure of the trochlea, the articular cartilage is separated from the synovium. Using a curved osteotome, a thin osteochondral flap, leaving 2 mm of subchondral bone, is very carefully chiselled off the medial and lateral trochlea (Figure 2B). The flap is extended down to the intercondylar notch. The trochlear bone is then deepened using chisels and a high-speed diamond burr (Figure 2C). The lateral edge of the trochlea is not lowered to obtain a raised lateral inclination angle with an effective bony stabilization. This way, a recentralized groove is created. In cases with an increased TT-TG distance, the groove can also

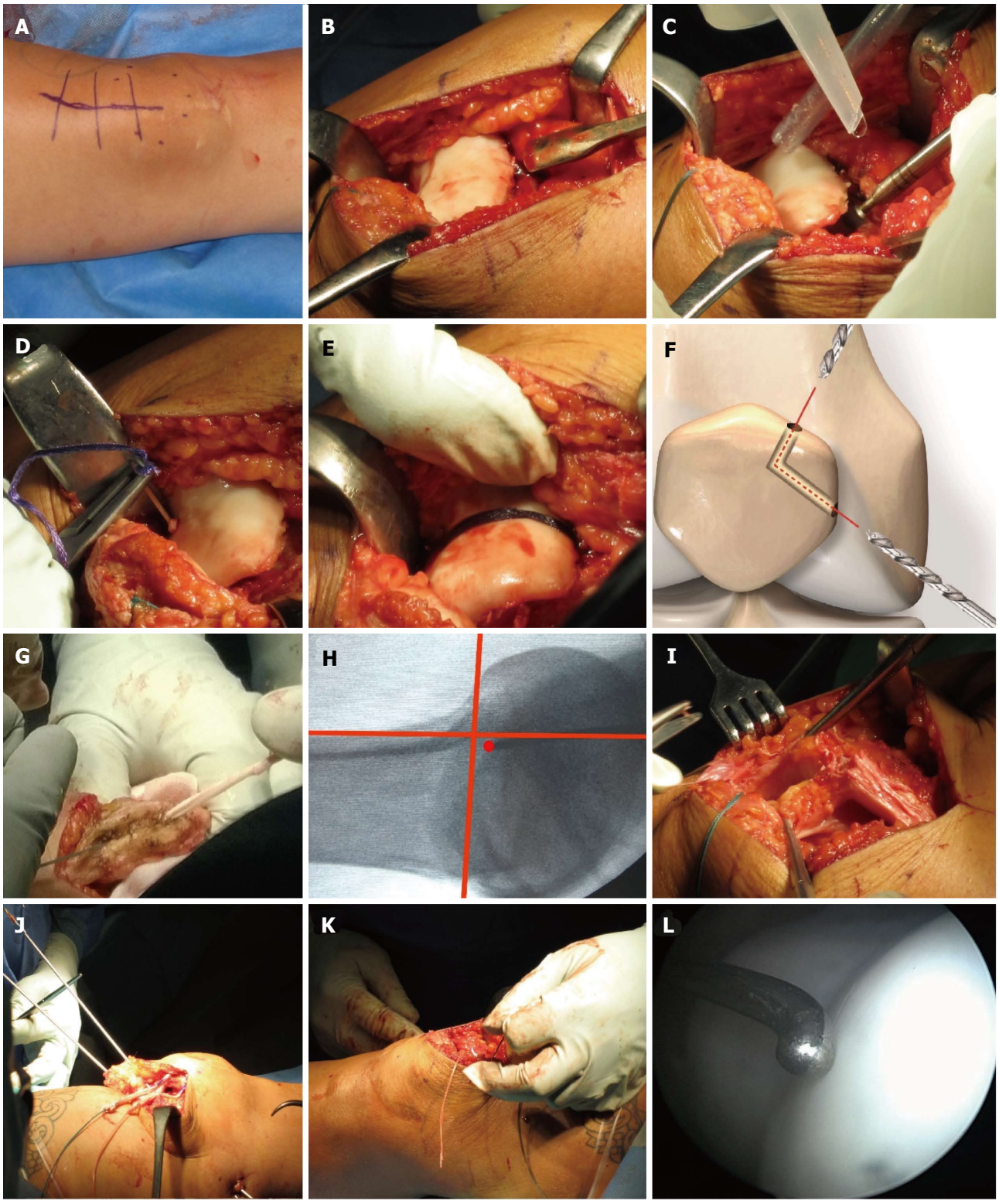

Figure 2 Step-by-step description of the combined surgical procedure. A: Short skin incision running from the medial part of the patella to the distal part of the quadriceps tendon; B: Using a curved osteotome, a thin osteochondral flap is chiselled off the trochlea; C: Trochlear bone is deepened using chisels and a high-speed burr; D: Vicryl band is passed from the distal beginning of the formed groove through the condyle using a curved needle; E: Starting at the junction between the trochlear cartilage and the anterior femoral bone, the other end of the band is passed through the femur. After pressing the flap onto the bone, the band is fastened; F: Drilling of a V-shaped tunnel coming from the superomedial pole and from the middle of the medial facet of the patella; G: Gracilis tendon is passed through the drill holes; H: Femoral medial patellofemoral ligament (MPFL) insertion side is marked with a K wire under fluoroscopic guidance; I: Prepared soft tissue tunnel between both layers of the medial retinaculum is running down to the femoral MPFL insertion; J: Two divergent beath pins are passed from the blind ending tunnel through the lateral femoral cortex; K: After passing the strands to the lateral femur, a temporary knot is tied down in approximately 30° knee flexion; L: Arthroscopy of the trochlear groove after trochleoplasty.

be deepened in a lateralized position. Then, the thin and flexible osteochondral flap is pressed into the newly formed groove. When the flap is not flexible enough, it should be thinned with the high-speed burr. The osteochondral flap is fixed into the new formed groove with a transosseous resorbable 3 mm Vicryl band (Ethicon Products, Norderstedt, Germany). For this step, the Vicryl band is passed from the distal start of the formed groove, which is usually a couple of millimeters above the intercondylar notch, through the femoral condyle using a big and eyed curved needle (Figure 2D). A second, proximal transosseous passage through the femoral condyle is performed starting exactly at the proximal end of the new groove. After pressing the flap onto the femoral bone, the Vicryl band is tightened and fastened (Figure 2E). If needed, a second Vicryl band, running from the distal part of the sulcus to the craniolateral edge of the trochlea, can be used to press the flap more firmly to the bone. After preparation of the medial patella facet and a debridement of the bone between both layers, two guide wires, coming from the middle of the medial edge of the patella and the superomedial pole, are advanced into the bone. Using a 4.5 mm cannulated drill bit, a V-shaped tunnel with an angulation of around 120° is created. The drillings should run as vertically as possible and leave a bone bridge between both ends of at least 15 mm (Figure 2F). The starting points of both patellar tunnels may correspond to a recent anatomic study on the MPFL, where the attachment spreads out along the upper and middle third of the medial patella edge[18]. Using a curved needle, the graft is passed through the tunnel (Figure 2G). After palpation of the bony femoral MPFL insertion, the origin is marked with a K wire under fluoroscopic guidance. As described by Schöttle *et al*[19], the radiographic landmark of the femoral attachment is located 2.5 mm distal to the posterior origin of the femoral condyle and 1.3 mm anterior to a line at the posterior cortical bone of the femur (Figure 2H). After a stab incision, the guide wire is advanced to the opposite cortical bone of the femur and overreamed to a depth of at least 4 cm. Then the medial capsule is exposed and a soft tissue tunnel between both layers of the capsule is extended down to the femoral insertion of the MPFL graft (Figure 2I). Two beath pins are introduced into the femoral bone tunnel. From the end of this blind-ending tunnel, both pins are advanced in divergent directions and passed through the lateral cortical bone of the femur (Figure 2J). Using the prepared soft tissue tunnel between both layers of the medial capsule, both armed ends of the graft loop are shuttled from the patella down to the femoral bone tunnel. Each strand of the whipstitch sutures at both ends of the graft is passed through the eyelets of the beath pins. By passing the pins through the femur, the ends of the whipstitch sutures are passed through the lateral femoral cortex. By pulling on each suture pair, both armed ends of graft are introduced into the tunnel (Figure 2K). On the lateral femur, a temporary knot is tied down to the lateral femoral cortex in approximately 30° knee flexion. This knot is temporarily fastened with a needle driver or by hand. The tension of the MPFL graft and the achieved motion of the patella is assessed by knee flexion and lateral translation of the patella. If necessary, the tension of the double limbed graft can be adjusted and functionally tested again. Finally, the knot is permanently tied up by using a series of half hitches. The inner layer of the capsule underneath the graft and the thicker superior layer which lies above the graft are closed separately and right up to both layers at the patellar margin (Figure 2G and I). The tendon of the vastus medialis obliquus muscle can be tightened medially to the patella if needed. Finally, the longitudinal incision within the distal part of the quadriceps tendon is closed up.

Rehabilitation

In the first two post-operative weeks, a partial load was recommended. In the first six weeks, an adjustable knee brace was prescribed. During the first two weeks, the motion was restricted to a knee flexion between 0° and 30°. During the third and fourth weeks, the flexion was limited to 60° and to 90° within the fifth and sixth weeks. In this context, we have to amend that we do not recommend these limitations any more (please see discussion). A rehabilitation of 12 wk was recommended before starting with sporting activities.

Statistical analysis

The statistical analyses in this study were done by using the SPSS statistics 22.0 software (SPSS Inc, Chicago, IL, United States). A statistical review of the study was performed by a biomedical statistician. The Wilcoxon signed-rank test was used to compare the pre- and postoperative clinical scores. For the comparison of the scoring between different groups within this study we used the Mann-Whitney-*U* test.

RESULTS

Stabilization of the patellofemoral joint

No patients showed signs of a persistent instability. Thus, persistent postoperative instabilities from subtle instability with anamnestic subluxations to frank dislocations were not reported. The apprehension tests were negative in all patients. Two patients reported a persistent avoidance behavior. Even if they had already mastered typical stress situations with experienced luxations in the past, they continued a slight avoidance behavior. Both patients reported that this behaviour was caused psychologically and not instability- and/or pain-related. All other patients reported being able to fully load their knee without anxiety.

Patient satisfaction with the clinical results

In 31 of the 33 cases (94%) the patients were very satisfied with the clinical outcome of the surgery. All of them would again decide for the same procedure.

Two patients (6%) were dissatisfied. Both patients had a flexion deficit between 20° and 30°. One of these patients also reported an anterior knee pain. However, the main reason for her disappointment was that she was not able to play and to crawl an all fours with her toddler.

Patient satisfaction with the cosmetic results

Regarding the cosmetic outcome, all patients were satisfied with the outcome. Thus, no patients felt impaired in their self-confidence and/or in their clothing choices such as skirts or trousers. Two patients were only partially satisfied because they would have preferred a shorter and narrower scar. On the other hand, they would not decide for an aesthetic correction operation assuming that this would be most likely successful.

Pain

Four patients (12%) reported no changes of their pain symptoms, which could be described in all of these cases as a slight anterior knee pain occurring occasional during exercise and/or longer runs. A further four patients (12%) reported an increase of pain at the last follow-up. Further six patients (18%) reported a severe knee pain before surgery which improved almost completely at the last follow-up. Further 14 patients (42%), who mainly showed severe pain symptoms before surgery, became completely pain-free. Further five patients (15%) had no knee pain before surgery as well as at the last follow-up. Taken together, in 29 of 33 cases (89%), the patients either remained unchanged with mild symptoms or no pain, or showed a notable improvement to an almost or completely pain-free situation. The assessment of pain using a visual analog scale showed a significant pain reduction from a mean of 4.8 ± 2.0 to 1.3 ± 3.4 points ($P < 0.0001$).

Return to sports

In 25 of the 33 cases, patients were engaged in regular physical activity before surgery. After surgery, two of these did not return to full sporting activities. Both did not have any complaints. One patient reported an anxiety or avoidance behaviour for typical stress situations as a reason for not returning to his full sporting activities. He played soccer and he felt that this sport is too strenuous or risky for his knee. The other patient preferred to wait for the surgery of her contralateral knee. Of the eight patients who were not engaged in sporting activities before surgery, three moved to the group of patients engaging in regular physical activity. The remaining five patients were very satisfied with their knee function during daily activities and none of them reported any complaints or recurrent luxations. Nevertheless, four of them still had no interest in sporting activities. One of the five patients who remained uninvolved in sports reported a continuing avoidance behavior in her daily activities. Although she had already mastered typical stress situations with previously experienced dislocations, she reported persistent avoidance behavior.

Complications

No deep infection or wound infection occurred. Recurrent dislocations, patella fractures, breakages of the osteochondral flap during surgery *etc,* were not registered. The re-operation rate in our study was 6% (2/33). In both cases, an early postoperative motion deficit with a markedly reduced flexion between 70° and 90° was treated. After the hospital stay, both patients did not attend the recommended physiotherapy. In both cases, arthroscopy with an arthrolysis and a mobilization was performed around three months after the initial surgery. During arthroscopy, adhesions within the joint were removed. Arthroscopy of the trochlear groove and the cartilage of the patellofemoral joint showed regular findings, the vicryl fiber was fully resorbed (Figure 2L). Subsequently, both patients had better motion and decreased pain during motion. At the final follow-up, they showed an unlimited motion and no anterior knee pain. Furthermore, we have to report three patients with a slight flexion deficit at the last follow-up. Two showed a deficit of around 20°. Both patients reported a slight anterior knee pain occurring after prolonged load during physical exercise such as longer runs, *etc.* A persistent and/or severe anterior knee pain was denied. The third patient showed a flexion deficit of 35° compared to the contralateral side. He was pain-free.

Functional outcome at the scoring

As depicted in Figure 4, the Kujala score improved significantly from a mean of 64 ± 16 points preoperatively to 94 ± 9 points postoperatively ($P < 0.0001$). The Lysholm score improved significantly from a mean of 63 ± 17 to 95 ± 6 points and the IKDC score from 58 ± 11 to 85 ± 12 points, $P < 0.0001$, respectively. There were no significant differences regarding age, sex, BMI and affected side of the knee ($P > 0.05$).

DISCUSSION

Different deepening trochleoplasty techniques are currently performed in a symptomatic dysplasia[20]. Dejour *et al*[21] describes an osteotomy and bone removal at both femoral condyles to create a V-shaped trochlear groove. Both trochlear fragments are refixed with metallic staples. Goutallier *et al*[22,23] described the recession trochleoplasty, where the trochlear bump is settled into a deeper position after the removal of a wedge at the lateral femoral condyle. The Bereiter *et al*[24]'s technique describes a lateral parapatellar approach to raise an osteochondral flap from the anterior aspect of the femur. After remodeling the trochlear groove, the flap is seated and pressed into the deepened trochlea. A histological follow-up study reported no further cartilaginous damage or degeneration for this "thin flap technique"

[25]. This corresponds to our findings of an intact and stable cartilage in two patients who underwent an arthroscopic arthrolysis (Figure 2L). All authors who use the Bereiter trochleoplasty describe a lateral parapatellar approach[26-32]. In contrast, the Dejours' Lyons' procedure uses a modified midvastus approach with a dissection of the vastus medialis muscle fibers extending around 4 cm into the muscle belly[21]. As described above, we routinely use a shortened medial parapatellar approach (Figure 2A). This approach provides a good exposure of the medial edge of the patella to create our bony tunnel for the graft loop (Figure 2G). Furthermore, it provides a good access to the medial capsule for the preparation of a soft tissue tunnel between both layers going down to the femoral insertion of the MPFL graft (Figure 2I). An extensive skin mobilization or a further skin incision to expose the medial edge of the patella is not needed for the MPFL reconstruction. Moreover, we feel that this approach provides a much easier access to the trochlear groove (Figure 2B). After the closure of both capsular layers, the tendon of the vastus medialis obliquus muscle can be tightened medially to the patella if needed. Taken together, this medial parapatellar approach might have several advantages.

Even if MPFL reconstruction is a proven method, an optimized tensioning of the graft should not be taken for granted. Regarding the literature, an excessive graft tension is one of the most common complications during MPFL reconstruction[10,33]. This might lead to stiffness, pain, cartilage degradation, arthrosis and patella fractures[10,33,34]. Thus, techniques which provide an adequate tensioning might help to achieve a sufficient stabilization with a minimized risk of an overtightened graft. Regarding the literature, a variety of techniques are described to get an appropriate amount of graft tension. Thaunat and Erasmus[35] recommend a full extension and the use of a hook to pull the patella proximal to avoid an overtensioning. Feller *et al*[36] tension the graft with one quadrant of lateral translation in knee extension, then the knee is flexed to 20° for permanent fixation. Other authors prefer techniques with the use of 30° of knee flexion for graft fixation[8,26,28] and some prefer a position between 60° and 90° of flexion because this might allow a more precise settling of the patella within the deeper, more inferior parts of the trochlear groove[37]. Therefore, finding the most appropriate technique for graft fixation seems quite confusing. Furthermore, there is currently no consensus on the question of how many degrees the knee should be flexed when the graft is secured to its insertion points. Therefore, our technique to simply test and balance the tension during knee motion before permanent fixation might be a feasible and satisfying solution. Considering that 30° of knee flexion seems to be recommended most frequently in the literature[8,26,28], we begin with a temporary graft fixation at 30° of flexion. Only after testing and balancing the tension is the graft permanently fastened[14]. Because our technique uses nearly the entire length of the gracilis tendon with a loop through the patella, this construct appears less rigid (Figure 1C). This might additionally reduce the risk of an overloading. Besides the advantage to reach a balanced and less rigid construct, the avoidance of hardware such as screws and/or anchors might be another benefit of our technique. This does not only save money, it also reduces possible implant specific complications such as an implant loosening and/or discomfort with the anchoring material[6,16,28].

An important finding of the present study is that the combination of a modified Bereiter trochleoplasty and our hardware-free, balanced MPFL reconstruction technique, provides a sufficient and reliable stabilization of the patellofemoral joint. Thus, the apprehension tests were negative in all cases and no subluxations or recurrent dislocations were reported at the last follow-up. This is in accordance to a recent systematic review, where the overall rate of recurrent dislocations after different trochleoplasty techniques was 2%[20]. The highest rate for recurrent dislocations was reported for the recession type trochleoplasty (10.5%), followed by the Dejour (3.2%) and Bereiter (0.8%) techniques[20]. Interestingly, all studies on the combination of a Bereiter trochleoplasty and a MPFL reconstruction describe a 0% rate for recurrent dislocations[26,28,38]. Regarding a residual apprehensiveness, studies on a Bereiter or Dejour throcheloplasty without a routinely added MPFL reconstruction might be of interest. These studies reported a residual apprehensiveness in 16%[39], 20%[31], 21%[32] and 47%[40] of cases. In contrast, in studies where a MPFL reconstruction was routinely performed in combination with a trochleoplasty, the apprehension sign was eliminated in all patients[26,28,38]. These data imply that a MPFL reconstruction seems to be a useful addition to a trochleoplasty. Regarding the clinical outcome, studies on trochleoplasties which were routinely combined with a MPFL reconstruction demonstrate similar postoperative Kujala scores of 96[26], 88[28] and 95[38] points, respectively. In comparison, studies on trochleoplasties which were not routinely combined with a MPFL reconstruction showed Kujala scores of 76[31], 80[32], 75[40] and 71 points[27], respectively. At this point, we would like to mention that we did not consider all studies with different types of trochleoplasty techniques, soft tissue procedures, additional procedures, *etc.* Rather, we aim to highlight possible tendencies. Thus, differences that are apparent at first sight might not be substantial or at least statistically significant. However, the superior results of a combined surgery in terms of a persisting apprehensiveness, recurrent dislocations, as well as in terms of the clinical outcome scoring can also be explained by the pathophysiology of the patient cohort. Thus, in more than 90% of cases, a dislocation of the patella results in a traumatic disruption and insufficiency of the MPFL[1,11,12]. Moreover, a trochleoplasty changes the articulation of the patella to a more medial and dorsal biomechanical position (Figure 1A). These changes, measuring at least 5 mm in each direction, have been nicely shown in this series with pre- and postoperative CT scans after a Bereiter trochleoplasty[13]. This might lead

to a reduced distance between the femoral and patellar insertions of the medial soft tissue restraints (Figure 1B). Thus, a preexisting insufficiency of the MPFL might be aggravated by the biomechanical changes following a trochleoplasty. As a consequence, a balanced alignment of the medial soft tissue restraints, such as an adequately tensioned MPFL reconstruction (Figure 1C), seems very reasonable during a trochleoplasty.

Another additional surgery, which is not so rarely combined with a trochleoplasty, is a tibial tuberosity transfer to reduce an elevated TT-TG as a further instability factor [27,40-42]. During a trochleoplasty we normally prefer to deepen and set the created trochlear groove more laterally to tendentially correct an asymmetry of the trochlear facets (Figure 1A and B). This possibility to address an elevated TT-TG distance has already been described by several authors for both the Dejour and the Bereiter technique[29,41,42]. Fucentese *et al*[13] demonstrated a case series with pre- and postoperative CT scans showing a successful lateralized trochlear groove after trochleoplasty. This possibility might influence the decision to perform an additional medialization osteotomy of the tuberosity. Considering this, we perform this additional procedure only in cases with an excessive TT-TG distance.

Showing an overall rate of 6.7%, a significant motion deficit is the second most common complication in trochleoplasty procedures[20]. In our series, at the last follow-up, three patients (9.1%) showed a slight flexion deficit compared to the contralateral side. Two had a deficit of 20° and one patient had a deficit of 30°. In regard to these data, we reconsidered our rehabilitation protocol, which limited the flexion to 30° for the first two weeks, to 60° in the third and fourth weeks and to 90° in the fifth and sixth weeks. The rationale behind these limitations was to avoid a shearing of the osteochondral flap. Reviewing the literature, we had to recognize that the majority of authors are much more progressive. Thus, most of them use protocols without a postoperative flexion limitation[26,27,30,31,38,40]. Other authors limit the flexion to 100°[21], 90°[28] or 60°[23,29]. Interestingly, some authors recommend a 20° or 30° block to full extension[30,31,38]. The idea of this protocol is to centralize the patella within the remodeled groove and to facilitate a healing of the trochlear osteotomy[30]. However, considering our results we do not use or recommend the protocol previously described in the methods section any more. Currently, we do not limit the flexion after trochleoplasty. Moreover, the two patients who needed an early arthroscopic arthrolysis as a result of a failed physiotherapy emphasize the importance of motion exercises. Therefore, physiotherapy including a continuous passive motion (CPM) is performed immediately after surgery. Moreover, each patient receives a knee CPM machine as a loan for at least four weeks after surgery. Regarding the return to sports rates, we had two patients who did not return to full sporting activities. One of these was in the group which was engaged in sports before surgery, the other patient did not in participate in regular physical activity before surgery. Neither patient had complaints or an ongoing instability. However, even if they had already mastered situations with experienced luxations in the past, both reported an ongoing anxiety for typical stress situations. Both reported that this behavior was psychologically caused and not instability- and/or pain-related. Thus, despite a sufficient stabilization, an unlearning process of such an acquired avoidance behavior should not be taken for granted. This study result is important to us because it highlights the need for a prolonged postoperative physiotherapy according to the individual need of the patient. This might minimize the reported avoidance behaviour.

The major limitations of this study are the short mean follow-up of 29 mo and the lack of a direct comparison to other surgical techniques. A larger clinical outcome study is needed to ensure the efficacy of our method. Therefore, the outcome results should be regarded cautiously. Being able to present only short-term results, data on the prevention of a secondary arthritis are lacking. However, the study presented here was a necessary first step in exploring our modified method, which seems to provide reasonable advantages. The preliminary clinical results demonstrate a good efficiency in relieving the symptoms and improving the function of the affected knee.

Our modified technique shows encouraging results in terms of a sufficient stabilization of the patellofemoral joint, a low incidence of complications and a good outcome in terms of pain, cosmetic results and return to sports. In accordance to these results, a significant improvement in all evaluated scores was achieved and a high patient satisfaction was demonstrated. These findings correlate with the literature on similar techniques, which combine a trochleoplasty with an alignment of the medial soft tissue restraints. Nevertheless, the good outcome in our case series and in previous studies should not be taken for granted. The need for an individual postoperative physio- and sports therapy is also outlined in this study.

ARTICLE HIGHLIGHTS

Research background

Trochlear dysplasia is an important and frequent instability factor in patients with recurrent patella dislocations. These patients typically have an insufficiency of the medial patellofemoral ligament (MPFL), which is an additional instability factor. During a trochleoplasty, the articulation of the patella is changed to a more dorsomedial position, which might worsen the insufficiency of the medial soft tissue restraints. All these patho-biomechanical conditions are relevant for a symptomatic instability and should therefore be addressed during surgery. Despite its relevance, studies on combined concepts to address all pathological conditions are rare.

Research motivation

Regardless of whether a MPFL reconstruction is performed as an isolated surgery or as in combination with a trochleoplasty, an adequate tensioning of the graft is a key problem during these surgical procedures. Thus, an overtensioning might lead to stiffness, pain, cartilage degradation, arthrosis and patella fractures, whereas an undertensioning leads to persistent instability

complaints. Authors' technique, which provides an adequate graft tensioning, appears to be helpful to solve these problems. Thus, the study presented here was a necessary first step in exploring authors' method, which seems to provide reasonable advantages.

Research objectives

To realize a combination of authors' technique of a balanced MPFL reconstruction to the bony alignment procedure, authors modified both, the technique and especially the approach of the Bereiter trochleoplasty as well as authors' recently published technique of a balanced MPFL reconstruction. To evaluate authors' method, 33 knees with with recurrent patellar dislocations and a trochlear dysplasia were evaluated after a mean follow-up of 29 mo.

Research methods

To assess the outcome of authors' modified technique, the Kujala, IKDC and Lysholm scoring were evaluated. Moreover, patients' satisfaction with the general outcome, the return to sports, the cosmetic outcome, the pre- and postoperative pain and a potential avoidance behaviour were assessed.

Research results

The preliminary clinical results of this technique demonstrate a good efficiency in relieving the symptoms and improving the function of the affected knee. There were no signs of a persistent instability. A significant pain reduction and a significant improvement at the Kujala, Lysholm and IKDC scoring is demonstrated. 94% of the patients were very satisfied with the clinical and cosmetic outcome of the surgery. 92% of the patients who were engaged in regular physical activity before surgery returned to full sporting activities. In regard to three patients showing a slight flexion deficit compared to the contralateral side at the last follow-up, authors changed the postoperative treatment protocol. Thus, authors do not limit the flexion any more post-operatively and authors try to ensure intensive motion exercises. One patient did not return to sports and another patient, who was not active in sports before surgery, still did not participate in regular physical activity after surgery. Both reported that this was related to a persistent avoidance behavior and not instability- and/or pain-related. This specific problem, which reduced authors' return to sports rate, might highlight the need for an intensive individual sports therapy.

Research conclusions

In patients with a symptomatic patellar instability, both a trochlear dysplasia and an insufficiency of the MPFL should be addressed during surgery. Regarding the literature, an inadequate graft tensioning is one of the most important reasons for complications during MPFL reconstruction such as stiffness, pain, cartilage degradation, arthrosis, patella fractures, *etc*. Therefore, authors' balanced MPFL reconstruction technique might optimize the alignment of the medial soft tissue restraints with a correspondingly low incidence of complications. The authors technique is a practicable solution to achieve a feasible correction of the bony dysplasia combined with a balanced alignment of the medial soft tissue restraints. Thus, authors' technique shows a reliable stabilization of the patellofemoral joint and a low incidence of complications. The results in common clinical outcome scorings as well as in terms of pain, return to sports and patient satisfaction are encouraging. To realize a simple combination of authors' recently published techniques of a balanced MPFL reconstruction with sulcus deepening trocheloplasty, authors modified both techniques. Especially the described approach to the medial margin of the patella, the medial retinaculum and to the trochlear groove appears very feasible. On the one hand, the study presented here was a necessary first step in exploring authors' modified method, which seems to provide reasonable advantages. On the other hand, this study gives an original insight to the patients' outcome. Besides the assessment of the commonly used scorings and the incidence of complications, this investigation gives a deeper insight to understand the outcome in terms of pain, cosmetic results, patient satisfaction and the return to sports. This might give us a better understanding of the patients' expectations and the role of physio- as well as an individual sports therapy. Because both trochlear dysplasia and an insufficiency of the medial soft tissue restraints are relevant for a symptomatic patellar instability, a method which addresses both patho-biomechanical conditions might be a good solution. A balanced medial soft tissue reconstruction might optimize the procedure. To combine authors' technique of a balanced MPFL reconstruction to the bony alignment procedure, authors modified both the technique and especially the approach of the Bereiter trochleoplasty as well as authors' MPFL reconstruction technique. Authors' balanced MPFL reconstruction technique might help to get an adequate alignment of the medial soft tissue restraints. Besides the assessment of the commonly used outcome scorings, this study gives a better understanding of the outcome in terms of pain, cosmetic results, patient satisfaction and the return to sports. A new phenomenon author noticed in two patients was a persistent avoidance behaviour for typical stress situations during sports. Even if both patients reported that this was not instability- and/or pain-related, this behaviour interfered with their return to sports. Even if this phenomenon was seldom, these findings might highlight the need for an intensive physiotherapy as well as the need of an individual sports therapy. The modified technique shows encouraging results in terms of a sufficient stabilization of the patellofemoral joint, a low incidence of complications and a good outcome in terms of pain, cosmetic results and return to sports. The preliminary clinical results of authors' technique demonstrate a good efficiency in relieving the symptoms and improving the function of the affected knee. Therefore, authors will continue this method in the future when indicated. In three patients, authors noticed a slight flexion deficit at the last follow-up. Considering this phenomenon, authors changed the postoperative treatment schedule to a protocol without any postoperative limitations of flexion. Furthermore, authors will try to ensure intensive postoperative motion exercises by using continuous passive motion devices, *etc*.

Research perspectives

The comparatively good outcome presented in authors' study should not be taken for granted. The need for an individual postoperative physio- and sports therapy is also outlined in this study. A larger clinical outcome study with longer follow-up periods is needed to investigate long-term outcome results of authors' methods. This will assess the durability of the clinical results. Furthermore, data on the prevention of a secondary arthritis are of interest in this patient group, which normally shows high rates of osteoarthritis development. Besides further improvements of the surgical technique, the questions of how to optimize and individualize the postoperative physio- and sports therapy will be of interest. A larger long-term clinical outcome study on the clinical results and the prevention of secondary arthritis will be a useful method for the future research.

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SYSTEMATIC REVIEWS

Antibiotic bone cement's effect on infection rates in primary and revision total knee arthroplasties

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Abstract

AIM

To compare infection rates in primary and revision total knee arthroplasty (TKA) procedures using antibiotic impregnated bone cement (AIBC) to those rates in procedures not using AIBC.

METHODS

A systematic review and meta-analysis was conducted in search for randomized controlled trials/studies (RCTs) pertaining to the field of antibiotic AIBC *vs* non-AIBC groups in both primary and revision TKA procedures. The primary literature search performed was to identify all RCTs that assessed AIBC in primary and revision TKA procedures. This search was done strictly through the PubMed database using the article "filters" setting that identified and separated all RCTs from the overall search. The original search was "Primary/revision total knee arthroplasty using AIBC". Other key terms and phrases were included in the search as well. Eligible articles that were used in the "results" of this review met the following criteria: (1) Involved primary or revision TKA procedures (for any reason); (2) included TKA outcome infection rate information; (3) analyzed an AIBC group *vs* a non-AIBC control group; (4) were found through the RCT filter or hand search in PubMed; and (5) published 1985-2017. Exclusion criteria was as follows: (1) Patients that were not undergoing primary or revision TKA procedures; (2) articles that did not separate total hip arthroplasity (THA) *vs* TKA results if both hip and knee revisions were evaluated; (3) papers that did not follow up on clinical outcomes of the procedure; (4) extrapolation of data was not possible given published results; (5) knee revisions not done on human patients; (6) studies that were strictly done on THAs; (7) articles that were not found through the RCT filter or through hand search in PubMed; (8) articles that did not evaluate AIBC used in a prosthesis or a spacer during revision; (9) articles that did not compare an AIBC group *vs* a non-AIBC control group; and (10) articles that were published before 1985.

RESULTS

In total, 11 articles were deemed eligible for this analysis. Nine of the 11 studies dealt with primary TKA procedures comparing AIBC to non-AIBC treatment. The other two studies dealt with revision TKA procedures that compared such groups. From these papers, 4092 TKA procedures were found. 3903 of these were primary TKAs, while 189 were revision TKAs. Of the 3903 primary TKAs, 1979 of these used some form of AIBC while 1924 were part of a non-AIBC control group. Of the 189 revision TKAs, 96 of these used some form of AIBC while 93 were part of a non-AIBC control group. Average follow-up times of 47.2 mo and 62.5 mo were found in primary and revision groups respectively. A two-tailed Fisher's exact test was done to check if infection rates differed significantly between the groups. In the primary TKA group, a statistically significant difference between AIBC and non-AIBC groups was not found (AIBC infection rate = 23/1979, non-AIBC infection rate = 35/1924, P = 0.1132). In the revision TKA group, a statistically significant difference between the groups was found (AIBC infection rate = 0/96, non-AIBC infection rate = 7/93, P = 0.0062). No statistically significant differences existed in Knee Society Scores, Hospital for Special Surgery Scores, or Loosening Rates.

CONCLUSION

AIBC did not have a significant effect on primary TKA infection rates. AIBC did have a significant effect on revision TKA infection rates.

Key words: Total knee arthroplasty; Knee revision; Antibiotic impregnated/laden/infused bone cement; Bone cement; Knee arthroplasty; Primary/revision total knee arthroplasties infection

Core tip: A systematic review and meta-analysis of randomized controlled trials/studies on primary and revision total knee arthroplasties (TKA) using antibiotic impregnated bone cement (AIBC). AIBC was found to lower infection rates in revision TKA procedures, but not in primary TKA procedures.

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INTRODUCTION

The use of antibiotic impregnated bone cement (AIBC) was first described by Buchholz and Englebrecht[1] in 1970. Throughout the years since, AIBC's mechanical properties and use in a clinical setting have been expounded upon greatly. In as early as 1981, Buchholz *et al*[2] reported up to a 77% success rate using AIBC, many times without systemic antibiotics, in primary total hip arthroplasity (THA) and total knee arthroplasty (TKA) procedures. More recently, antibiotic infused spacers have also been described in two stage joint knee revision procedures to reduce the rate of infection during and after revision.

Since AIBC was first introduced into the field of orthopedics there has been controversy over its safety and how antibiotics affect the bone cement. In addition to the problem of organism specific antibiotic resistance, mechanical loosening may also result from antibiotic combination. One study[3] found that in low doses ($\leqslant$ 2 g of antibiotic powder per 40 g cement) AIBC does not lead to an increased rate of mechanical loosening. However, other studies[3-5] have indicated that in much higher doses (> 4.5 g of antibiotic powder per 40 g cement) or with usage of liquefied antibiotics in bone cement, mechanical problems such as loosening in the prosthesis can occur more frequently. Adalberth *et al*[6] performed a study demonstrating that antibiotics added to bone cements had similar fixation, extent of radiolucent lines, and clinical outcomes as compared to plain bone cement (PBC). Moreover, in a recent systematic review and meta-analysis published in 2013 inspecting eight randomized controlled trials/studies (RCTs) comparing AIBC and non-AIBC primary TKA and THA procedures, there was shown to be no difference in rate of aseptic loosening when antibiotics were added to the cement as compared to the control[7].

Much of the information published and reviewed on antibiotic and antiseptic usage thus far has focused on primary total joint arthroplasty (TJA) procedures. Nevertheless, promise has been shown using AIBC in revision procedures. Clinically, AIBC is widely accepted to cure surgical site infections during revision procedures[8,9]. Peersman *et al*[10] noted that rates of infection following revisions are approximately 2-3 times higher than rates following primary procedures. In 2015, Bini *et al*[11] published that AIBC used in revision TKA procedures nearly halved the risk of re-revision suggesting AIBC's potentially crucial role in infection prevention during revision procedures. Furthermore, the planet is experiencing a large increase in elderly populations, which will most likely increase the need for TKA procedures in the near future. Kurtz *et al*[12] demonstrated that with this increase in age, there will also be an increase in deep infection rates following primary TKA. These rates are expected to rise up to 6.8% within the next 15 years. These statistics portray how important AIBC will be in the future of both primary and revision TKA procedures.

In recent years, the use of prophylactic antibiotics and antiseptics in both primary and revision TJA have been explored through systematic reviews found on PubMed[7,13-15]. Although interest in the area of antibiotics and antiseptics on infection rates in both primary and revision TKA and THA procedures has increased, there has been a lack of high quality information published in systematic reviews to draw relevant conclusions

from[13].

Not only has there been a shortage of studies that have explored this field, but many of the studies done have shown variable and inconclusive data. In a more detailed look at these studies, there was one systematic review that analyzed over 6300 primary TKAs and THAs that showed no statistically significant differences in the rates of deep infection or superficial infection between the group that used AIBC and the group that used PBC[7]. Similar results were found in two other systematic reviews published in 2015 and 2016 as well[14,15]. However, these studies did not include the most up-to-date articles on primary and revision TKA procedures. These reviews were not limited to RCTs and therefore did not consider the most credible sources for data collection in the field. Past reviews have not included information on TKA revisions, which is an overly unexplored field that will be considered in this systematic review.

The inconsistencies in search criteria and evaluations reported in most of these studies reveal the importance of a systematic review and meta-analysis on this topic. As shown from the search conducted on this topic in PubMed, there has not been an up-to-date systematic review evaluating both primary and revision TKA procedures with AIBC *vs* non-AIBC control groups strictly in randomized controlled trials/studies in the current literature. As agreed upon in multiple studies[16,17], periprosthetic joint infections are some of the most devastating complications of TKA procedures and the importance of their prevention is of great value to the field of orthopedics. It is hypothesized that AIBC will result in lower infection rates amongst primary and revision TKA procedures. Therefore, the purpose of this review and analysis was to combine the most up-to-date and relevant data from RCTs focusing on primary and revision TKA procedures using AIBC *vs* not using AIBC. This study aimed to primarily analyze and compare infection rates in primary and revision AIBC procedures to those rates in procedures not using AIBC. A secondary aim was to examine other clinically significant differences between groups using and not using AIBC during primary and revision TKAs.

MATERIALS AND METHODS

Study design

A systematic review and meta-analysis was conducted in search for randomized controlled trials/studies (RCTs) pertaining to the field of AIBC *vs* non-AIBC groups in both primary and revision total knee arthroplasty procedures.

Literature search

The primary literature search performed was to identify all randomized controlled trials/studies that assessed antibiotic impregnated bone cement in primary and revision TKA procedures. This search was done strictly through the PubMed database using the article "filters" setting that identified and separated all RCTs from the overall search. The original search was "Primary/revision total knee arthroplasty using AIBC".

Other key terms and phrases in the search included "primary TKA infection", "primary knee infection", "knee revision infection", "knee revision failure", "revision TKA infection", "antibiotic impregnated/ laden/ infused bone cement", "2 stage knee revision", and "1 stage knee revision". In addition, search terms such as "gentamicin", "tobramycin", "cefuroxime", "cefazolin", and "vancomycin" were used in conjunction with the phrases above. After the primary literature search was conducted, articles that met relevant criteria were further scanned in their titles and abstracts for inclusion. Once articles' titles and abstracts were scanned, the articles were hand-searched for other sources that could be of relevance to the topic. PubMed articles that did not initially show full text access were searched in Ovid, MEDLINE database as well as in the Journal of Bone and Joint Surgery (American volume), and Clinical Orthopedics and Related Research. During the screening process all titles and abstracts were inspected for the key search terms mentioned. This search was conducted up until July 2017.

Inclusion and exclusion criteria

Eligible articles that were used in the "results" of this review met the following criteria: (1) Involved primary or revision TKA procedures (for any reason); (2) included TKA outcome infection rate information; (3) analyzed an AIBC group *vs* a non-AIBC control group (4) were found through the RCT filter or hand search in PubMed; and (5) published 1985-2017.

Exclusion criteria was as follows: (1) Patients that were not undergoing primary or revision TKA procedures; (2) articles that did not separate THA *vs* TKA results if both hip and knee revisions were evaluated; (3) papers that did not follow up on clinical outcomes of the procedure; (4) extrapolation of data was not possible given published results; (5) knee revisions not done on human patients; (6) studies that were strictly done on THAs; (7) articles that were not found through the RCT filter or through hand search in PubMed; (8) articles that did not evaluate AIBC used in a prosthesis or a spacer during revision; (9) articles that did not compare an AIBC group *vs* a non-AIBC control group; and (10) articles that were published before 1985.

Exclusion criteria were limited to studies evaluated in the results of this paper. Multiple studies were used as references in this paper that did not meet the inclusion criteria or that did meet the exclusion criteria. However, these articles were used only in the introduction and discussion sections of this review to bring other relevant data on this topic into light. It is important to note that data from these articles may still be relevant to the topic, but do not meet inclusion criteria for analysis in this paper. Inclusion criteria were selected in order to set a standard for comparison amongst the RCTs discovered upon the systematic search. If study information was unclear, authors were contacted requesting the relevant

Table 1 Data from primary total knee arthroplasty randomized controlled trials

Paper	AIBC group number of TKAs infected	Infection rate of AIBC group	Non-AIBC number of TKAs infected	Infection rate of non-AIBC group	Reason for procedure	Follow-up (mo)
Chiu *et al*[18], 2001	0/41	0	5/37	0.13514	Osteoarthritis	50
Vrabec *et al*[23], 2016	0/10	0	0/5	0	N/A	12
Chiu *et al*[19], 2002	0/178	0	5/162	0.03086	N/A	49
Lizaur-Utrilla *et al*[24], 2014	1/48	0.020833	0/45	0	Non-inflammatory arthritis	76.8
Nilsson *et al*[25], 1999	0/28	0	2/29	0.068966	Osteoarthritis and Rheumatoid arthritis	60
Bercovy *et al*[26], 2012	2/164	0.012195	1/157	0.006369	N/A	91.2
Hinarejos *et al*[20], 2013	20/1483	0.013486	20/1465	0.013652	N/A	38
McQueen *et al*[22], 1987	0/13	0	1/13	0.076923	Osteoarthritis and rheumatoid arthritis	24
McQueen *et al*[21], 1990	0/14	0	1/11	0.090909	Osteoarthritis	24
	Total: 23/1979 (1.16%)		Total: 35/1924 (1.82%)			Average: 47.2

AIBC: Antibiotic impregnated bone cement; TKA: Total knee arthroplasty.

information to check eligibility of the article.

Outcome measures

The chief outcome evaluated in this analysis was infection rate following primary or revision TKA. Other factors were assessed and quantified including follow-up times, record of previous infection, whether or not systemic antibiotics were used to supplement AIBC, and publication year. Variables reported in more than one paper that were noted in this analysis included whether or not there was a statistically significant difference in deep infection rates, loosening rates, Knee Society Scores (KSS), and Hospital for Special Surgery Scores (HSS).

Article quality

Only randomized controlled trials were assessed. Articles were published in reputable journals including the Journal of Bone and Joint Surgery, Journal of Arthroplasty, Journal of Clinical Orthopaedics and Related Research, Journal of International Orthopaedics, and the Journal of Knee Surgery, Sports Traumatology, and Arthroscopy. All articles were deemed of high quality based on these factors.

Literature search results

After searching all key terms and phrases, a total of 176 RCTs were shown on the PubMed database. After initial screening of titles and abstracts, 148 articles were eliminated because they were deemed irrelevant to this study for various reasons (Figure 1). The 28 remaining articles were full-text hand searched in order to identify if they were appropriate for this study. Of the 28 articles, six were found to fit inclusion criteria. Five more articles were also found to fit inclusion criteria through the full-text hand search of the 28 articles. Therefore, 11 articles in total were found in the initial screening and secondary hand search. Further details of this search and screening procedure using inclusion and exclusion criteria were found in a flow chart (Figure 1). Further information from the articles including first author, year published, number of TKAs studied, infection rates, follow-up times, and reason for the TKA procedures was noted in Tables 1 and 2. RCTs' individual comparisons were shown in Tables 3 and 4. Information on loosening rates, statistically significant differences in deep infection found in individual articles, and KSS and HSS knee scores were described in Table 5.

Statistical analysis

From the studies searched, important statistics were extracted and compiled into Excel documents for analysis. Averages and totals were calculated for relevant data sets as mentioned in the "outcome measures" section above. A two-tailed Fisher's exact test was used to calculate statistically significant differences in infection rates between groups. Differences in loosening rates were calculated using a two-tailed Fisher's exact test as well. Differences in KSS/HSS knee scores were calculated using a two-tailed, type-3 *t*-test (95%CI).

RESULTS

General study characteristics

In total, 11 articles were deemed eligible for this analysis. Nine of the 11 studies dealt with primary TKA procedures comparing AIBC to non-AIBC treatment[18-26]. The other two studies dealt with revision TKA procedures that compared such groups[17,27]. From these papers, 4092 TKA procedures were found. 3903 of these were primary TKAs, while 189 were revision TKAs. Of the 3903 primary TKAs, 1979 of these used some form of AIBC while 1924 were part of a non-AIBC control group. Of the 189 revision TKAs, 96 of these used some form of AIBC while 93 were part of a non-AIBC control group. Average follow-up times of 47.2 mo and 62.5 mo were found in primary and revision groups respectively. In six of the studies, the TKA procedures were conducted after a diagnosis of some form of arthritis[17,18,21,22,24,25]. In one study[27], the revision TKAs were done because of previous infection. Four of the studies did not report such data on the patient population used[19,20,23,26]. In all of the studies, systemic antibiotics were used in conjunction with AIBC to facilitate recovery and prevent reinfection.

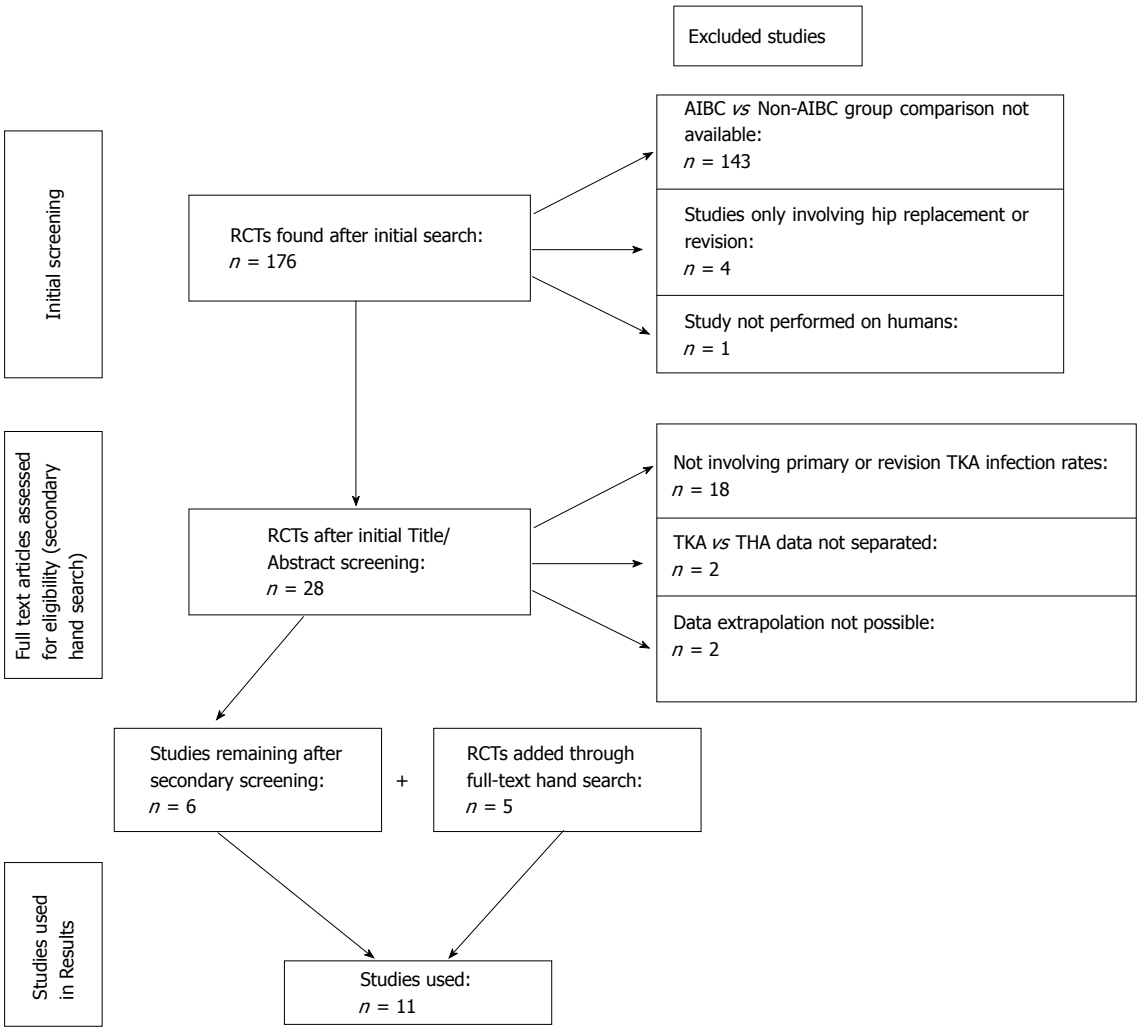

Figure 1 Flow diagram for studies included in result analysis. This flow chart describes the articles that were included and excluded in the analysis based on the initial screening and further full-text assessment. Articles that were assessed and screened are shown to the left. Articles that were excluded are shown to the right. Right pointing arrows lead to excluded articles in different parts of the screening and evaluation processes. Downward pointing arrows show points from one set of screenings to the next, displaying how many articles were left after exclusion criteria had been considered. Reasons for exclusion were also shown in the right column. AIBC: Antibiotic impregnated bone cement; TKA: Total knee arthroplasty; THA: Total hip arthroplasity; RCTs: Randomized controlled trials /studies.

Table 2 Data from revision TKA RCTs

Paper	AIBC group number of TKAs infected	Infection rate of AIBC group	Non-AIBC number of TKAs infected	Infection rate of non-AIBC group	Reason for procedure	Follow-up (mo)
Nelson *et al*[27], 1993	0/3	0	0/3	0	Previous infection	36
Chiu *et al*[17], 2009	0/93	0	7/90	7.78%	Osteoarthritis	89
	Total: 0/96 (0.00%)		Total: 7/93 (7.53%)			Average: 62.5

RCTs: Randomized controlled trials/studies; AIBC: Antibiotic impregnated bone cement; TKA: Total knee arthroplasty.

Also, eight of the 11 studies had an infection rate of 0.0% when AIBC was used, even with an average follow up of over 47 mo amongst those studies. However, only three of the 11 studies found a 0.0% infection rate when AIBC was not used. These differences were not large enough in the primary TKA group to indicate statistical significance, but did indicate AIBCs crucial role in preventing infection post-revision. Overall, AIBC groups were compared to PBC groups, systemic antibiotic groups, and hydroxyapatite coated prostheses groups. All studies used in the results/analysis were published between 1987-2016 with an average publication year of 2003.

Infection rates

A two-tailed Fisher's exact test was done to check if infection rates differed significantly between the groups. Deep infection rates were analyzed in this review because superficial infection rates were not reported to be statistically significant in any of the articles. In the primary TKA group, a statistically significant difference between AIBC and non-AIBC groups' infection rates

Table 3 Comparisons made between groups in primary TKA RCTs

Paper	Comparison
Chiu *et al*[18], 2001	Cefuroxime-impregnated cement *vs* PBC
Vrabec *et al*[23], 2016	Intravenous tobramycin *vs* AIBC with tobramycin
Chiu *et al*[19], 2002	Cefuroxime-impregnated cement *vs* PBC
Lizaur-Utrilla *et al*[24], 2014	Tibial fixation with either a cemented (Palacos with Gentamicin) *vs* cementless with screw augmentation (systemic antibiotics only)
Nilsson *et al*[25], 1999	Vacuum mixed bone cement (Palacos–Gentamicin) *vs* hydroxyapatite-coated prostheses
Bercovy *et al*[26], 2012	Hydroxyapatite-coated prostheses *vs* cemented (Refobacin) tibial components
Hinarejos *et al*[20], 2013	Simplex P cement loaded with 0.5 g of erythromycin and three million units of colistin in 40 g of cement (Stryker) *vs* simplex cement without antibiotic
McQueen *et al*[22], 1987	Cefuroxime in bone cement (1.5 g of cefuroxime powder was added to 40 g of CMW cement powder) *vs* systemic (1.5 g) cefuroxime
McQueen *et al*[21], 1990	Cefuroxime in bone cement (1.5 g of cefuroxime powder was added to 40 g of CMW cement powder) *vs* systemic (1.5 g) cefuroxime

CMW: A kind of bone cement made by CMW laboratories of DePuy Synthes Companies; RCTs: Randomized controlled trials/studies; PBC: Plain bone cement; AIBC: Antibiotic impregnated bone cement.

Table 4 Comparisons made between groups in revision TKA RCTs

Paper	Comparison
Nelson *et al*[27], 1993	Gentamicin-PMMA beads *vs* conventional systemic antibiotics
Chiu *et al*[17], 2009	AIBC (vancomycin-impregnated) *vs* PBC in TKA Revision

RCTs: Randomized controlled trials/studies; PMMA: Polymethyl methacrylate; AIBC: Antibiotic impregnated bone cement; TKA: Total knee arthroplasty; PBC: Plain bone cement.

was not found (AIBC infection rate = 23/1979, non-AIBC infection rate = 35/1924, P = 0.1132). In the revision TKA group, a statistically significant difference between the groups' infection rates was found (AIBC infection rate = 0/96, non-AIBC infection rate = 7/93, P = 0.0062). AIBC used directly in the revision prosthesis benefitted patients and helped prevent infection. Further information for individual articles having to do with the items mentioned in this paragraph was noted in Tables 1 and 2.

Other quantifiable variables reported

Other variables reported in more than one study were loosening rates[17,18,24,26,29], postoperative KSS scores[24-26], and postoperative HSS scores[17-19]. Loosening rates did not significantly differ between groups (P = 1.00). Postoperative HSS and KSS scores also did not differ significantly between groups (P = 0.1208 and P = 0.38496 respectively). Tables 1 and 2 reported numbers of TKA procedures and rates of infection for each paper. Table 5 supplied additional information on loosening rates and KSS/HSS scores.

In all studies that reported superficial infection rates, there were no statistically significant differences between AIBC and non-AIBC groups. Superficial infection rates were almost always higher than deep infection rates in both groups. Three papers reported having statistical significance when comparing deep infection rates amongst groups[17-19]. More than half of the studies reported deep infections to occur in an early to moderate time period after the operation, while none of the studies reported chronic deep infection to be the most common type of infection after procedures.

Significant results from individual papers

Vrabec *et al*[23] described that local concentrations of antibiotics from AIBC not only had supratherapeutic concentrations in the joint fluid, but also achieved therapeutic concentrations locally within the first 48 h postoperatively. Systemic antibiotics, on the other hand, only achieved subtherapeutic levels locally, not in the joint fluid.

In Lizaur-Utrilla *et al*[24], statistically significant differences were found in clinical outcomes such as knee score (P = 0.022), range of motion (P = 0.042), and WOMAC (P = 0.036) between groups, all favoring cementless components. Lizaur-Utrilla *et al*[24] also reported that cementless TKA was the better option for younger patients with osteoarthritis even though revision rates and survival rates were similar between cemented and cementless groups.

Results from three different studies found Staphylococcus aureus, Staphylococcus epidermidis, coagulase-negative Staphylococcus, and group-B Streptococcus to be the most common organisms found in TKA deep infection cultures[17,18,21]. Also, Chiu *et al*[17] reported that those organisms identified through culture in revision infections are more virulent and less sensitive to certain cephalosporin antibiotics than those found in primary TKA infections.

All studies done by Chiu *et al*[17-19] were conducted in a country outside of the United States, where operating room standards are unequivocal to more medically advanced nations. Their results were therefore most relevant for TKAs performed in an operative setting lacking "clean-air measures" such as ultraviolet light, laminar flow, and body exhaust systems. Chiu *et al*[18] 2001 and Chiu *et al*[17] 2009 reported that adding certain antibiotics such as cefuroxime or vancomycin only cost

Table 5 HSS, KSS knee scores, and loosening rates

Paper	Statistically significant differences in deep infection rate	HSS knee score AIBC	HSS knee score non-AIBC	KSS score AIBC	KSS score non-AIBC	Loosening AIBC	Loosening non-AIBC
Chiu *et al*[18], 2001	Yes (P = 0.021)	91	86	-	-	0/41	2/37
Vrabec *et al*[23], 2016	No (P value not reported)	-	-	-	-	-	-
Chiu *et al*[19], 2002	Yes (P = 0.0238)	90	88	-	-	1/178	0/162
Lizaur-Utrilla *et al*[24], 2014	No (P value not reported)	-	-	89	94	4/48	1/45
Nilsson *et al*[25], 1999	No (P value not reported)	-	-	93	93	0/28	1/29
Bercovy *et al*[26], 2012	No (P value not reported)	-	-	94.3	94.6	1/164	1/157
Hinarejos *et al*[20], 2013	No (P = 0.96)	-	-	-	-	-	-
McQueen *et al*[22], 1987	No (P value not reported)	-	-	-	-	-	-
McQueen *et al*[21], 1990	No (P value not reported)	-	-	-	-	-	-
Nelson *et al*[27], 1993	No (P value not reported)	-	-	-	-	-	-
Chiu *et al*[17], 2009	Yes (P = 0.0130)	87	85	-	-	0/93	0/90

AIBC: Antibiotic impregnated bone cement; HSS: Hospital for special surgery scores; KSS: Knee society scores.

$ 10-15 in Taiwan, where their studies were conducted. The price for adding antibiotics to bone cement was reported to cost much less than having to do a possible re-revision due to infection if antibiotics were not added to the cement. Chiu *et al*[18] 2001, Chiu *et al*[17] 2009, and Hinarejos *et al*[20] 2013 considered other factors that could correlate with the development of infection such as age, sex, side of the lesion, reason for the revision, time between the primary and revision procedures, body mass index, ASA grade, tourniquet time, operative time, hospital stay, HSS score, and period of follow-up. None of these factors were significant in the development of infections in any of these studies.

Hinarejos *et al*[20] did not report erythromycin and colistin-loaded cements to significantly impact infection rates in primary TKAs. In Hinarejos *et al*[20] study, there was an average operation time 4.4 min longer in the group with an infection and the group with deep infections had significantly higher percentages of procedures over 125 min. With this data, Hinarejos *et al*[20] found that male sex and an operating time of > 125 min were factors related to a higher rate of deep infection.

McQueen *et al*[22] 1987 detailed that the knee arthroplasty that had been diagnosed with a deep infection in the group not using AIBC had previously undergone a medial meniscectomy and a proximal tibial osteotomy, which accounted for higher chances of infection following that operation.

When looking at hydroxyapatite (HA) coating *vs* cemented TKA components, Nilsson *et al*[25] and Bercovy *et al*[26] both found that HA-coated implants were more stable than cemented implants. Bercovy *et al*[26] noted that HA-coated components performed similarly to cemented components and both Bercovy *et al*[26] and Nilsson *et al*[25] reported HA-coated implants to be a reliable option in primary TKA procedures. Other various elements were described in all of the studies, however, only the most frequent were reported in this analysis. More information on comparison details from individual articles was noted in Tables 3 and 4.

Bone cements and antibiotics

Different types of antibiotics added to bone cements involved in this analysis included cefuroxime, vancomycin, tobramycin, gentamicin, refobacin, colistin, and erythromycin. Cefuroxime and vancomycin were the antibiotics used in studies with significant differences in infection rates. More information about types and amounts of bone cements/antibiotics used in these papers was presented in Tables 3 and 4.

DISCUSSION

Overall analysis displayed AIBC's potential as an infection prevention tool. It was found that the use of AIBC did not reduce the infection rates in primary TKAs. A possible explanation for this insignificant difference could be that primary TKA procedures are 2-3 times less susceptible to infection[10] than TKA revisions, making AIBC less relevant in the prevention of infection outcomes in primary *vs* revision TKA procedures. In primary TKA procedures, both AIBC and other forms of systemic antibiotics have been proven to be equally effective in infection prevention[7]. However, the opposite is true for revision TKA. With revision TKAs, the only outcome found to vary significantly between AIBC and non-AIBC groups was infection rates. Since revision TKAs have higher chances of infection and are oftentimes undergone because of previous infection, the added benefits of AIBC during the revision procedure could significantly decrease infection post-revision. With this data, the hypothesis that AIBC would lower infection rates in TKA revisions was supported. The hypothesis that AIBC would lower infection rates in primary TKAs was not supported.

Some individual papers noted significant differences between groups in multiple ways, but with the strict inclusion criteria used in this paper, perhaps not enough papers were included to obtain significant results for variables besides infection rates. There were no differences in clinical knee scores found in this study or in the systematic review done by Wang *et al*[7]. None of the studies noted differences in superficial infection rates. Josefsson *et al*[28] proposed that the antibiotics from loaded cement do not reach the superficial parts of the wound in a sufficient concentration to prevent infection. This gave one explanation for the lack of

statistical significance in superficial infection rates found throughout literature reviews as well[7,13-15].

This systematic review differed from other systematic reviews in multiple ways. The systematic review and meta-analysis done previously on primary TKA and THA AIBC *vs* non-AIBC groups was published in 2013[7]. That systematic review had articles published up until 2013 and used four RCTs[19-22] that were used in this analysis paper. With the goal of including the most recent published results in the field, this study included two papers[23,24] published after 2013. This study also included seven other RCTs that the previous meta-analysis[7] did not (five extra primary TKA RCTs and two revision TKA RCTs). In that systematic review[7], there were also no significant differences in infection rates in the TKA group found. Other reviews[14,15] published with similar search criteria as Wang *et al*[7] found insignificant results as well. However, these reviews did not include similar search criteria and were not limited to RCTs only. None of these reviews considered TKA revisions.

Even though this study sought to include a large number of revision TKA procedures, there were a limited number of patients found that were evaluated in revision TKAs. As noted in the limitations section, this was a drawback to this study. If a larger sample size in the revision TKA group were possible, this data would be even more clinically significant. Without such additional data, conclusions would be hard to make, but considering data from this study it is speculated that revision TKA procedures would continue to show significant differences in AIBC *vs* non-AIBC infection rates.

Most studies suggest that both systemic antibiotics and AIBC be used when treating septic patients. In the results of this analysis, it was found that the use of systemic antibiotics in conjunction with AIBC was the standard in all 11 articles. One comprehensive literature review[29] recommended that for best results prophylactic antibiotics be used before revision TKA, AIBC used during the procedure, and the surgery should also be followed with systemic antibiotics.

The primary advantage of preventing deep periprosthetic joint infection often outweighs the minor shortcoming of AIBC. According to Chiu *et al*[17], there is a significant cost benefit to adding antibiotics to bone cement. Chiu *et al*[17] stated that adding antibiotics to bone cement in revision procedures would cost much less than having a re-revision performed. The reality is that most surgical revisions use AIBC with antibiotics and bone cements in various combinations. It is evident that standards for safe use of AIBC must be followed for successful clinical results.

Even though the data suggests that AIBC significantly reduces the risk of infection in revision, there is clearly a shortage of high quality randomized controlled studies comparing AIBC to non-AIBC use in knee revision procedures. Furthermore, only two of the RCTs[17,27] meeting criteria in the study had data comparing an AIBC group with a group not using AIBC during revision. This could be explained by the strict inclusion and exclusion criteria set for this literature search. In the future, a literature search encompassing a more broad scope of papers that fit a different set of criteria could be done to get a larger sample size and more significant results from analysis. In order to have more significant results for AIBC in TKA procedures, more RCTs also need to be conducted with the specific aim of comparing AIBC use in TKA procedures *vs* procedures not using AIBC or some other form of antibiotic therapy. Although this study was limited to primary and revision TKAs, even more possibilities exist with AIBC in other joint reconstructive surgeries. With an increasing population, numbers of primary TKA and TKA revisions are bound to increase in the near future[12]. The availability of potential patients needing TKA procedures that can be used in studies will therefore soon also be increasing. With this increase, hopefully more high quality studies and data can be accumulated on this topic.

Limitations

In spite of the fact that strong efforts were made to create a well-designed study, there were some intrinsic limitations in this review. One of the first limiting factors of note came about in the literature search. After some time searching for RCTs based through PubMed on this topic, it was clear that not many were available for use that met inclusion criteria. It was especially difficult to find RCTs that compared AIBC to a non-AIBC control in total knee revisions (only two studies found on this). Upon search, more articles were found pertaining to primary TKA/THA with AIBC. Revision procedures were seen to a much smaller extent. For these reasons, the sample size was relatively small and could potentially be expanded if studies outside of RCTs found using only the PubMed "filters" setting were included. Another limitation was that not all studies were held to the same standard of evaluation during patient follow up. Due to the fact that some studies were only focused on infection rates while others were focused on clinical knee scores and patient satisfaction, there was not a standard of comparison across each and every study evaluated. Along those same lines, knee scores were reported in two different ways (Knee Society Score and Hospital for Special Surgery Score), making them difficult to compare amongst papers. As expected, not all studies had the same follow up times, which made comparison between short, intermediate, and long term results more difficult. Also, not all revisions were done for the same purposes. Also, eligible studies came from hospitals located across many different countries, which have different populations of patients and populations of bacteria. Since we did not restrict our study to a certain type of bone cement or prostheses, many types of bone cements and implants were used across articles. All of these limitations may affect outcomes of this review and meta-analysis in some way.

AIBC did not have a significant effect on primary TKA infection rates. AIBC did have a significant effect on

revision TKA infection rates.

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SYSTEMATIC REVIEWS

Systematic review of bone marrow stimulation for osteochondral lesion of talus - evaluation for level and quality of clinical studies

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

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Abstract

AIM

To clarify the quality of the studies indicating lesion size and/or containment as prognostic indicators of bone marrow stimulation (BMS) for osteochondral lesions of the talus (OLT).

METHODS

Two reviewers searched the PubMed/MEDLINE and EMBASE databases using specific terms on March 2015 in accordance with the Preferred Reporting Items for Systemic Reviews and Meta-Analyses guidelines. Predetermined variables were extracted for all the included studies. Level of evidence (LOE) was determined using previously published criteria by the Journal of Bone and Joint Surgery and methodological quality of evidence (MQOE) was evaluated

using the Modified Coleman Methodology Score.

RESULTS

This review included 22 studies. Overall, 21 of the 22 (95.5%) included studies were level Ⅳ or level Ⅲ evidences. The remaining study was a level Ⅱ evidence. MQOE analysis revealed 14 of the 22 (63.6%) included studies having fair quality, 7 (31.8%) studies having poor quality and only 1 study having excellent quality.

CONCLUSION

The evidence supporting the use of lesion size and containment as prognostic indicators of BMS for OLTs has been shown to be of low quality.

Key words: Osteochondral lesion of talus; Arthroscopy; Bone marrow stimulation; Systematic review

Core tip: Bone marrow stimulation (BMS) is a reparative procedure for osteochondral lesions of the talus, promising approximately 85% success rates in the short- and mid-term. To date, the prognostic factors for BMS are lesion size and containment of the lesion. No other factors have been shown to be universal predictors. However, the level of evidence and methodological quality of evidence for clinical studies accompanying both the lesion sizes and containment are low. Overall, 95.5% of the studies included in the analysis are level Ⅳ or level Ⅲ. No level Ⅰ study was identified. The methodological qualities of the included studies were not strong. In particular, the scores of "primarily evaluates outcome criteria and recruitment rates" were low.

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INTRODUCTION

Bone marrow stimulation (BMS) is a reparative procedure for osteochondral lesions of the talus (OLT)[1]. The aim of this arthroscopic procedure is to stimulate mesenchymal stem cells (MSCs) to promote fibrous cartilage tissue by breaching the subchondral bone plate (SBP) using an awl or wire[1]. Several investigators have demonstrated good to excellent clinical outcomes in around 85% of patients, treated with BMS for OLT, for the short to medium term[2].

The main prognostic factor in the treatment of OLT has been regarded as the lesion size[1,3,4]. The maximum size for BMS treatment is generally accepted as less than 15 mm in diameter or 150 mm^2 in area. Chuckpaiwong *et al*[4] found that smaller than 15 mm in diameter was the critical cut-off value to obtain a successful outcome following BMS. Choi *et al*[5] concluded that 150 mm^2 is the critical defect area beyond clinical outcomes following BMS for OLT decreased significantly. However, a recent systematic review by Ramponi *et al*[6] showed the critical lesion size to be 107.4 mm^2 in area and/or 10.2 mm in diameter, for BMS. Containment of the lesion has also been demonstrated as a universally accepted prognostic factor for good clinical outcomes following BMS for OLT[3,7].

Recently, level of evidence (LOE) and methodological quality of evidence (MQOE) have been used to assess relative value of outcomes reported in the clinical studies[8-11]. Despite the widespread clinical use of lesion size as a cut-off value for BMS in OLT, there has been no comprehensive assessment of LOE and QOE for clinical studies accompanying both the lesion size and clinical outcomes. The same can be said for the presence or absence of containment of OLT.

The purpose of this systematic review was to clarify the LOE and MQOE of for the published literature investigating clinical outcome following BMS for OLT, with special emphasis on studies investigating lesion size and containment as predictors.

MATERIALS AND METHODS

Search strategy

A systematic literature search of the PubMed/MEDLINE and EMBASE databases was performed in March 2015 in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[12]. Each database was searched using the following key words, (microfracture OR microdrilling OR drilling OR drill OR bone marrow stimulation OR marrow stimulation OR BMS OR abrasion chondroplasty OR arthroscopy OR arthroscopic) AND (talus OR talar OR ankle) AND (cartilage OR osteochondritis dissecans OR chondral OR osteochondral OR transchondral OR osteochondral lesion OR OCL OR OCD).

Titles and abstracts were screened using specific inclusion and exclusion criteria. Full texts of potentially relevant studies were then reviewed. Citations and references of all articles and relevant studies were manually assessed. Studies were searched and independently assessed by two independent reviewers. Differences between reviewers were discussed together and resolved by consensus or if a persistent disagreement occurred, a senior author was consulted.

Inclusion and exclusion criteria

Currently BMS is defined as microfracture, drilling, or abrasion. The inclusion criteria of the current systematic review was the following: (1) therapeutic clinical studies evaluating both lesion size of OLT and outcomes in patients who underwent BMS; (2) all patients included had more than a 24 mo follow up; (3) published in a

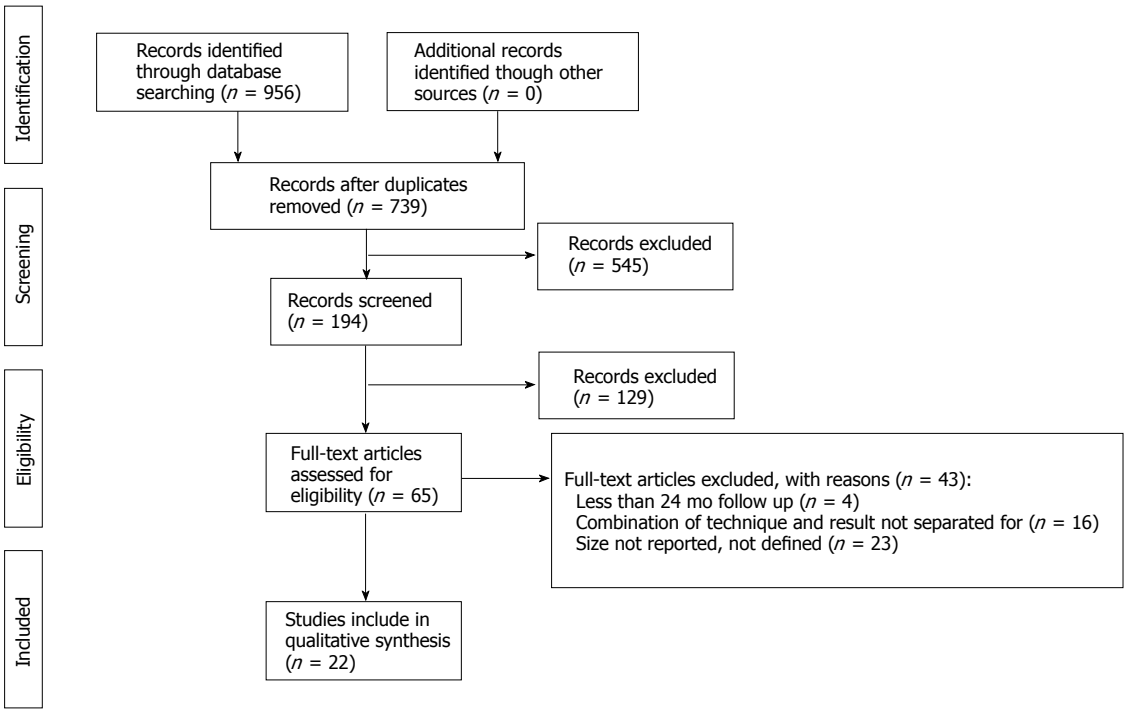

Figure 1 PRISMA study selection flow diagram.

peer-review journal; (4) published in English; and (5) full text of studies available. Exclusion criteria was the following: (1) cadaveric studies; (2) animal studies; (3) case reports; (4) review articles; (5) technique articles; (6) articles with unseparated results if more than one technique is described; (7) inadequately surgical technique description; (8) use of scaffolds; and (9) errors in reported data.

Data extraction and analysis

Two independent reviewers performed data extraction for each study. If any discrepancy existed, the senior author evaluated all available data and a consensus was reached. Studies that included more than one surgical procedure or a subgroup of patients with different follow-up times were included in the data for analysis[13,14].

The primary outcome of current study was LOE and MQOE of included studies. LOE of each study was graded based on the previously published criteria[15]. MQOE was assessed using the Modified Coleman Methodology Score (MCMS) (Table 1)[6]. This score consists of 2 parts, Part A (primarily evaluates baseline study characteristics; 0-60) and Part B (primarily evaluates outcome criteria and recruitment rates; 0-40). According to Jakobsen's CMS, the score of excellent studies are between 85 to 100 points; good studies 70 to 84 points, fair studies 55 to 69 points and poor studies scored under 55 points[9].

Statistical analysis

The statistical analysis was performed using a commercially available contemporary statistical software package (SAS 9.3; SAS Institute, Cary, NC, United States). In CMMS, all obtained scores were adjusted to percentage (each score/total score), the adjusted scores of CMMS were compared between Part A and Part B to determine statistical significance. As a Shapiro-Wilk's *W* test showed non-normal distributed data, the Mann-Whitney *U* test was performed for this. Additionally, the adjusted score of each parameter were compared to investigate any difference using the Kruskal-Wallis test and Steel-Dwass test for data obtained without standard Gaussian distribution. A *P*-value < 0.05 was considered statistically significant.

RESULTS

The flow diagram is shown in Figure 1. After full texts articles were assessed based on the inclusion/exclusion criteria. There were 22 clinical studies included in the current systematic review[3-5,7,13,16-32].

Demographics

Summary of the demographic data was shown in Table 2: 1.879 ankles were identified (931 males; 545 females)[3-5,7,13,16-32]. The mean lesion area was 111.9 mm^2 and the mean diameter was 9.5 mm. The mean follow-up was 48.5 (range 24-146) mo.

LOE

Overall, 95.5% of the studies included were level Ⅳ[4,7,17,18,20,22,25-29,31] or level Ⅲ[3,5,16,19,21,23,30,32]. No level Ⅰ studies were included in the current review. Gobbi *et al*[13], was described as LOE Ⅰ in the published journal, however, this study was re-assigned as LOE Ⅱ (prospective cohort

Table 1 Modified Coleman Methodology Score[6]

Section	No. or factor	Score
Part A: Only one score to be given for each section		
1 Study size - number of patients		
	> 60	10
	41-60	7
	20-40	4
	< 20, not stated	0
2 Mean follow up (mo)		
	> 24	5
	12-24	2
	< 12, not stated or unclear	0
3 Number of different surgical procedures included in each reported outcome. More than one surgical technique may beassessed but separate outcomes should be reported		
	One surgical procedure	10
	More than one surgical procedure, but > 90% of subjects undergoing the one procedure	7
	Not stated, unclear, or < 90% of subjects undergoing the one procedure	0
4 Type of study		
	Randomized controlled trial	15
	Prospective cohort study	10
	Retrospective cohort study	0
5 Diagnostic certainty (MRI)		
	In all	5
	In > 80%	3
	In < 80%	0
6 Description of surgical procedure given		
	Adequate (technique stated and necessary details of that type of procedure given)	5
	Fair (technique only stated without elaboration)	3
	Inadequate, not stated, or unclear	0
7 Description of postoperative rehabilitation		
	Well described (ROM, WB and sport)	10
	Not adequately described (2 items between ROM and WB and sport)	5
	Protocol not reported	0
Part B: Scores may be given for each option in each of the three sections if applicable		
1 Outcome criteria		
	Outcome measures clearly defined	2
	Timing of outcome assessment clearly stated (*e.g.*, at best outcome after surgery or follow-up)	2
	Objective, subjective and imaging criteria	6
	2 items between objective, subjective and imaging criteria	4
	Objective or subjective or radiological criteria	2
2 Procedure for assessing outcomes		
	Subjects recruited (results not taken from surgeons files)	5
	Investigator independent of surgeon	4
	Written assessment	3
	Completion of assessment by subjects themselves with minimal investigator assistance	3
3 Description of subject selection process		
	Selection criteria reported and unbiased	5
	Recruitment rate reported	
	> 80% or	5
	< 80%	3
	Eligible subjects not included in the study satisfactorily accounted for, or 100% recruitment	5

MRI: Magnetic resonance imaging; ROM: Range of motion; WB: Weight bearing.

study). Table 2 shows information about LOE (Table 2).

MQOE

The mean MCMS was 57.5 ± 10.2 out of 100 points (range 38-89) (Table 3). Part A was 38.1 ± 8.1 (range 22-60; percentage: 63.5%) and Part B was 19.2 ± 5.5 (range 11-29; percentage: 48.0%), respectively. The adjusted MCMS of Part A were significantly higher than that of Part B ($P < 0.05$). In the part A, the adjusted MCMS of "Type of study" were significantly lower among all the parameters ($P < 0.05$). With regard to Part B, "Outcome criteria" had significantly higher scores compared with the others ($P < 0.05$). Of the 22 included studies, 14 studies (63.6%) were of fair quality[3-5,13,19,20,23-25,27,28,30-32], 7 (31.7%) of poor

Table 2 Studies included and demographic datas

Ref.	Year	No. of ankles	No. of males	No. of females	Follow -up (mo)	Lesion area (mm^2)	Lesion diameter (mm)	Prognostic factors	LOE	MCMS (points)
[23]	2013	50	20	30	35.5	61.7	8.8	Lesion size	Ⅲ	58
[29]	2015	15	7	8	94.8	87		Lesion size	Ⅳ	50
[5]	2009	120	80	37	35.6	111.7	11.4	Lesion size	Ⅲ	56
[3]	2013	399			74	111.3		Lesion size, contained	Ⅲ	61
[32]	2015	90	68	22	38.3	100		Lesion size	Ⅲ	67
[24]	2013	298	184	114	52	98.5		Lesion size	Ⅲ	57
[19]	2012	173	121	52	70.3	95.4		Lesion size	Ⅲ	54
[4]	2008	105	73	32	31.6		8.84	Lesion size	Ⅳ	57
[16]	2000	17	13	4	84	85.2		Lesion size	Ⅲ	33
[13]	2006	10	6	4	53	450		Lesion size	Ⅲ	61
[18]	2011	22	16	6	32	76		Lesion size	Ⅳ	45
[30]	2014	50	28	22	27.1			Lesion size	Ⅲ	69
[20]	2012	22	12	10	24			Lesion size	Ⅳ	56
[21]	2012	81	64	17	37.4	100		Lesion size	Ⅲ	89
[17]	2010	35	27	8	33	90		Lesion size	Ⅳ	50
[31]	2014	58	37	21	35	124		Lesion size	Ⅳ	65
[25]	2013	50	30	20	141		8.8	Lesion size	Ⅳ	62
[26]	2013	38	23	15	52.8	100		Lesion size	Ⅳ	52
[27]	2013	50	22	28	36.3	62		Lesion size	Ⅳ	66
[28]	2015	41	17	24	42.5	67		Lesion size	Ⅳ	56
[22]	2012	25	19	5	32	110		Lesion size	Ⅳ	48
[7]	2011	130	64	66	37.2	84		Lesion size, contained	Ⅳ	50

LOE: Level of evidence; MCMS: Modified coleman methodology score.

quality[7,16-18,22,26,28] and only 1 (4.5%) study[21].

DISCUSSION

The aim of this systematic review is to clarify LOE and MQOE of published literature on BMS for OLT. Twenty-two studies with 1.879 patients were included, however, no level I study was identified in the study cohort. The result demonstrated that most of the studies reported the lesion sizes and the containment of the lesion were graded as low LOE. The quality of evidence in these studies demonstrated an average MCMS of 57.5 out of 100 points and only 4.5% of included studies were graded as excellent, which suggests that the methodological quality of the included studies was weak. In addition, scores of Part B (primarily evaluates outcome criteria and recruitment rates) was marked significantly lower than Part A (primarily evaluates baseline study characteristics. This systematic review has revealed that studies with low LOE and weak MQOE have supported this paradigm despite lesion size and the containment of the lesion being a common criteria value for the indication for BMS in treating OLT.

Lesion size and the containment of the lesion are accepted prognostic factors to use when making a decision in operative treatment for OLT[3,7]. In general, lesion size with less than 15 mm in diameter or less than 150 mm^2 are applied for BMS. It is also well known that a non-contained OLT have a worse outcome than a contained OLT[7]. However, this systematic review has revealed that most of these studies were of low LOE, and recently, several investigators evaluated the trend of LOE of published clinical studies in sport-related journals[33]. Unfortunately greater than 80% of studies in foot and ankle surgery remain to have low LOE despite increasing numbers of the LOE I and LOE II studies in the clinical sports medicine literature[9,10,33]. High-level clinical evidence can fundamentally provide adequate treatment for patients based on the principles of evidence-based medicine[34]. Additionally, Moher *et al*[35] described that non-blinded clinical studies without allocation concealment tended to describe an overestimated treatment effect than blinded clinical studies and well-designed blinded case control studies are required to establish prognostic factors in BMS for OLT.

The current systematic study revealed that the MQOE of the included 22 studies have been weak (Table 3)[9]. Of those clinical studies "Procedure for assessing outcomes" and "Description of subject selection process" in Part B (primarily evaluates outcome criteria and recruitment rates) were significantly low. These findings are consistent with the outcomes found by a recent systematic review that analyzed the outcome data following microfracture for OLT in 24 clinical studies[36]. The authors found that approximately half of included studies did not have a patient history or patient-reported outcome data, despite the presence of well described general demographics and study design. Additionally, clinical variables (48%) and imaging data (39%) has been the least reported in these studies. Poor methodological quality of the clinical study decreases the reliability of study's outcomes[37]. However, caution

Table 3 Outcome of modified Coleman methodology scores

Ref.	Part A							Part B			Total
	1 Study size - number of patients	2 Mean follow-up (mo)	3 No. of different surgical procedures included in each reported outcome	4 Type of study	5 Diagnostic certainty (MRI)	6 Description of surgical procedure given	7 Description of postoperative rehabilitation	1 Outcome criteria	2 Procedure for assessing outcomes	3 Description of subject selection process	
[23]	7	5	10	0	5	3	10	8	5	5	58
[29]	0	5	10	0	0	5	10	10	5	5	50
[5]	10	5	10	0	5	5	10	8	5	0	58
[3]	10	5	10	0	5	5	10	8	8	0	61
[32]	10	5	10	0	5	5	5	6	3	8	57
[24]	10	5	10	0	5	5	10	10	9	3	67
[18]	10	5	10	0	5	5	10	8	3	0	56
[4]	10	5	10	0	5	3	10	6	8	0	57
[16]	4	5	10	0	0	3	0	8	5	3	38
[13]	4	5	0	10	5	5	10	10	9	3	61
[18]	4	5	10	0	5	5	5	6	5	0	45
[30]	7	5	10	0	5	5	10	10	9	8	69
[20]	4	2	10	0	5	3	5	10	9	8	56
[21]	10	5	10	15	5	5	10	10	9	10	89
[17]	4	5	10	0	5	5	5	8	5	3	50
[31]	7	5	10	0	5	5	10	10	5	8	65
[25]	7	5	10	0	0	3	5	10	12	5	57
[26]	4	5	10	0	5	3	10	10	5	0	52
[27]	7	5	10	0	5	3	10	8	8	10	66
[28]	7	5	10	0	5	3	10	8	5	3	56
[22]	4	2	10	0	5	5	5	8	9	0	48
[7]	10	5	0	0	5	0	10	10	5	5	50
mean	6.8	4.7	9.1	1.1	4.3	4	8.2	8.6	6.6	4	57.5
SD	3	0.9	2.9	3.8	1.8	1.3	2.9	1.4	2.4	3.5	10.2

MRI: Magnetic resonance imaging.

should be taken when interrupting the outcomes of methodological quality. The methodological deficiencies have been reported using Coleman Methodological Score for tendinopathy[8,38], knee cartilage lesion[9], fracture[39], ligament injury[40-42] and OLT[43]. However, to our knowledge, the validity and reliability of this score for OLT is unknown. Nevertheless, we believe the outcome of the current study is important because the modification for MCMS in the current study could improve the validity and reliability of this score for OLT.

Several limitations of the current study exist mainly due to the inclusion criteria. Studies published in database other than MEDLINE and EMBASE were not included. Clinical studies not written in English were not evaluated. Nevertheless, this study does demonstrate important findings of that the LOE and QOE of published literature, on using BMS for OLT, are insufficient to produce any solid conclusion. A further limitation was that the current study focused only on the available clinical studies. As a result, the outcomes have addressed very little of the underlying mechanisms and intrinsic limitations of BMS for OLT. Currently, underlying biological aspects of cartilage regeneration has been well discussed due to low intrinsic activity of reparative cartilaginous tissue following BMS and potential ability of biological factors, although a recent systematic review has suggested a comprehensive assessment of the evidence behind the translation of basic science to the clinical practice[44,45]. Thus, the usefulness of the outcomes from the current study depends essentially on critical appraisal of the literature on the clinical application.

In conclusion, lesion size and the containment of OLT is a commonly used prognostic parameter in the treatment of osteochondral lesion of the talus However, this systematic review has revealed that low levels of evidence and weak quality of evidence in clinical studies need to be improved before this paradigm can be fully supported.

COMMENTS

Background

Lesion sizes and containment are commonly used in the orthopaedic community to predict the clinical outcomes of bone marrow stimulation for osteochondral lesion of talus.

Research frontiers

The widespread use of lesion size and containment as prognostic indicators prompts a much-needed comprehensive assessment of the studies supporting this data.

Innovations and breakthroughs

The evidence supporting the use of lesion size and containment as prognostic indicators of bone marrow stimulation (BMS) for osteochondral lesion of the talus (OLTs) have been revealed in this study to be of low level of evidence (LOE) and of weak methodological quality of evidence. Future studies with more robust study designs are warranted should the current paradigm ever need to be fully supported.

Applications
This systematic review has revealed that low levels of evidence and weak quality of evidence in clinical studies need to be improved before this paradigm can be fully supported.

Terminology
BMS: Bone marrow stimulation; LOE: Level of evidence; MCMS: Modified Coleman Methodology Score; MQOE: Methodological quality of evidence; OLT: Osteochondral lesion of the talus.

Peer-review
This is a timely, objective, well-written, well-conducted systematic review of a topic relevant to the field of orthopaedics.

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CASE REPORT

Acute compartment syndrome of the thigh following hip replacement by anterior approach in a patient using oral anticoagulants

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Abstract

Acute compartment syndrome (ACS) of the thigh following primary total hip arthroplasty (THA) is a highly uncommon complication and has not yet been reported before with regards to the anterior approach through the anterior supine interval. We present a case of a 69-year-old male patient with a history of stroke, who developed ACS of the thigh after elective THA while using therapeutic low molecular weight heparin as bridging for regular oral anticoagulation. ACS pathogenesis, diagnostic tools, treatment and relevant literature are discussed. The patient's ACS was recognized in time and treated by operative decompression with fasciotomy of the anterior compartment. Follow-up did not show any neurological deficit or soft-tissue damage.

Key words: Orthopedics; Total hip arthroplasty; Anterior supine intermuscular approach; Acute compartment syndrome; Anticoagulation therapy

Core tip: Acute compartment syndrome of the thigh is an uncommon complication following total hip arthroplasty, which has not yet been reported after hip replacement by anterior approach through the anterior supine interval. Global increase in venous thromboembolism chemoprophylaxis may lead to an increase in incidence of postoperative bleeding and with this an increase in acute compartment syndrome of the thigh following primary total hip arthroplasty. Onset of severe pain of the upper leg postoperatively should warrant a high index of suspicion of this condition. Diagnostic tools such as ultrasound, computed tomography or intra-compartmental pressure measurements can be useful but should not lead to any delay of treatment.

Hogerzeil DP, Muradin I, Zwitser EW, Jansen JA. Acute compartment syndrome of the thigh following hip replacement by anterior approach in a patient using oral anticoagulants. *World J Orthop* 2017; 8(12): 964-967 Available from: URL: http://www.wjgnet.com/2218-5836/full/v8/i12/964.htm DOI: http://dx.doi.org/10.5312/wjo.v8.i12.964

INTRODUCTION

Acute compartment syndrome (ACS) is a known complication often following trauma such as fractures or crush injuries. However, ACS of the thigh is an uncommon complication, which has not been reported before after hip replacement by anterior approach through the anterior supine interval. Known causes for ACS of the thigh include femoral fractures, acetabular or proximal femur surgery, tourniquet application and extensive deep vein thrombosis[1-4]. With the current trend of more oral anticoagulants being used and perioperative bridging therapy using LMWH it is noted that postoperative bleeding and the hereby possibly inferred ACS may be on the rise.

CASE REPORT

A 69-year-old male, using oral anticoagulation medication (Fenprocoumon 3 mg) due to a history of stroke, underwent total hip replacement of the right hip using the anterior approach through the anterior supine interval, as treatment for his end stage osteoarthritis. Only uncemented materials were used. Following hospital protocol, the administration of oral anticoagulation (OAC) medication was discontinued 5 d before surgery and the patient was bridged using LWMH (Tinzaparin 18.000 IE, subcutaneously) as venous thromboembolism (VTE) chemoprophylaxis. Preoperatively the patients' international normalized ratio was 1.3. Additionally, tranexamic acid, as part of hospital protocol regarding postoperative hemorrhage prophylaxis, was administered intraoperatively. THA was performed without any complications. However, total intraoperative blood loss was 600 cc, slightly higher than average. This was attributed to the patients' regular use of anticoagulation medication and current bridging therapy. The night following the operation the patient complained of pain in the ipsilateral leg which was interpreted as postoperative pain for which additional opioids were prescribed. One day following surgery hemoglobin levels were 7.0 g/dL (Preoperative Hemoglobin levels were 9.4 g/dL). During the course of the day the patient needed additional opioids to perform routine exercises. However, during the evening the pain aggravated and additional opioids could not suppress the pain with progressing symptoms of swelling, hematoma and paresthesia of the right leg.

Ultrasound of the thigh was performed which showed an intramuscular hematoma of the anterior compartment of 8.3 cm by 3.5 cm (Figure 1). Additional computed tomography (CT-scan) was performed which confirmed the diagnosis and showed 2 hematomas of the anterior compartment (Figures 2-4). No intra-compartmental pressure measurements were performed as the diagnosis had already been confirmed and would only have delayed treatment. Delay of diagnosis in this case can be attributed to the fact that the patients' need for additional opioids to perform routine exercises one day postoperatively is not an uncommon occurrence. Furthermore, the first postoperative Hemoglobin levels were slightly decreased (7.0 g/dL), however within acceptable postoperative range and thus warranted no further investigation at the time.

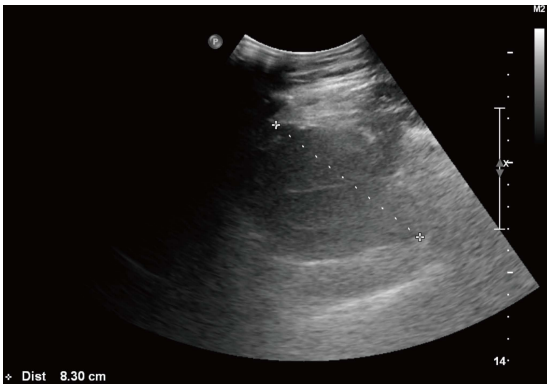

Figure 1 Ultrasound of the thigh showing an intramuscular hematoma of the anterior compartment.

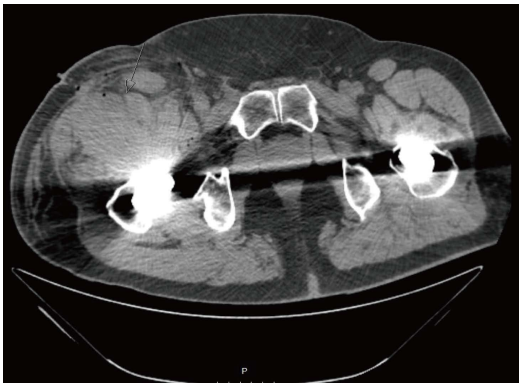

Figure 2 Transverse plane computed tomography scan showing a hematoma ventrally in the anterior compartment.

To prevent further expansion of the hematoma VTE prophylaxis was discontinued and an emergency fasciotomy through the anterior compartment of the thigh was performed. A large hematoma was evacuated, the surgical site was extensively irrigated with normal saline solution and tranexamic acid was administered topically in the wound. Cultures of the surgical site showed no infection. The following day postoperative hemoglobin levels were at 3.9 g/dL for which the patient received multiple 4 blood transfusions over the course of several days after which hemoglobin levels were normalized to 7.3 g/dL.

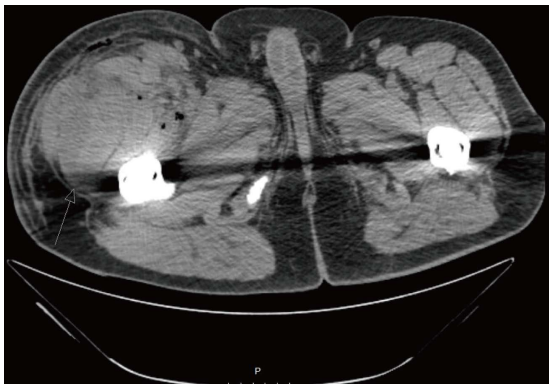

Figure 3 Transverse plane computed tomography scan showing a hematoma dorsally in the anterior compartment.

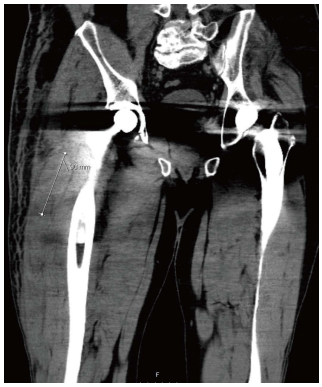

Figure 4 Coronal plane computed tomography scan showing a hematoma of the anterior compartment.

Directly after emergency fasciotomy the neurological deficit and the severe pain the patient had previously been experiencing, disappeared. Over the next few days mobilization was increased and at 6 d after emergency fasciotomy patient was discharged with low dose LMWH (Nadroparine 2850 IE, subcutaneously) as VTE prophylaxis. 11 d after emergency fasciotomy OAC therapy was resumed without any further complications.

At 8 and 12 wk follow-up, the patient did not have signs of any residual neurological deficit.

DISCUSSION

ACS is defined by increased pressure in a closed fascial space compromising the circulation to the nerves and muscles within the involved compartment[5]. ACS in the thigh is a rare complication following primary THA. This can be due to several reasons.

From an anatomical perspective, it could be explained by the large volume of soft tissue of the thigh, therefore requiring extravasation of a large volume of fluid to cause compression of local structures[3]. Aside from the large volume of the three compartments in the thigh, the fascia of the thigh seems to be more dilative compared to the fascia of the lower leg[6]. Furthermore, the compartments of the upper leg are partly open to the pelvis explaining the higher compensation space for increasing an intra-compartmental hematoma[7].

Literature shows cases with ACS both shortly after operation as well as several days following THA, the common denominator often being VTE prophylaxis[3,4,8]. It is our belief that in our patient, the increased intra-compartmental pressure was most likely caused by iatrogenic laceration to the branches of the circumflex femoral arteries aggravated by his regular use of anticoagulation medication and current bridging therapy. We noticed that the ACS progressively developed during the postoperative mobilization, which possibly severed the vessels during exercise. The classical sign of ACS, *i.e.* disproportionate pain, is difficult to judge in a patient after THA in which opiates are regularly required. However due to the alertness of the nurse staff and ward physician the diagnosis was confirmed shortly after the paresthesia developed, which prevented permanent neurological and vascular damage.

ARTICLE HIGHLIGHTS

Case characteristics

A 69-year-old male presented with severe pain, swelling, hematoma and paresthesia of the right leg following elective total hip replacement by anterior approach.

Clinical diagnosis

Severe pain, swelling and hematoma of the upper leg, as well as paresthesia of the lower leg.

Differential diagnosis

Postoperative pain, postoperative dislocation of the hip, periprosthetic fracture, iatrogenic neurological damage.

Laboratory diagnosis

Preoperative international normalized ratio was 1.3 and Hemoglobin level 9.4 g/dL, postoperative Hemoglobin levels were 7.0 g/dL and 3.9 g/dL.

Imaging diagnosis

Ultrasound of the thigh showed an intramuscular hematoma of the anterior compartment of 8.3 cm by 3.5 cm and computed tomography revealed two hematomas of the anterior compartment.

Pathological diagnosis

Cultures of the surgical site showed no infection.

Treatment

Venous thromboembolism (VTE) prophylaxis was discontinued and an emergency fasciotomy through the anterior compartment of the thigh was performed during which a large hematoma was evacuated, the surgical site was extensively irrigated with normal saline solution and tranexamic acid was administered topically in the wound.

Related reports

Acute compartment syndrome is a known complication often following trauma such as fractures or crush injuries. However, a highly uncommon presentation and localization of acute compartment syndrome is that of the thigh following total hip replacement by the anterior approach. The first symptoms of acute compartment syndrome of the thigh can easily be confused with other causes for postoperative pain, swelling, hematoma and paresthesia.

Term explanation

Acute compartment syndrome is defined by increased pressure in a closed

fascial space compromising the circulation to the nerves and muscles within the involved compartment. VTE prophylaxis is a mechanical or pharmacologic method for prevention of venous thromboembolism.

Experiences and lessons

Acute compartment syndrome of the thigh is a highly uncommon complication following total hip replacement by anterior approach and as such should and must be considered in case of postoperative onset of severe pain of the upper leg.

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