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Contents

Monthly Volume 14 Number 6 June 18, 2023

MINIREVIEWS

ORIGINAL ARTICLE

Basic Study

Retrospective Cohort Study

Retrospective Study

Observational Study

SYSTEMATIC REVIEWS

World Journal of Orthopedics

Monthly Volume 14 Number 6 June 18, 2023

Contents

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MINIREVIEWS

Minimally invasive surgeries for insertional Achilles tendinopathy: A commentary review

Kenichiro Nakajima

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Abstract

Studies of minimally invasive surgery for insertional Achilles tendinopathy are limited. To establish this surgery, the following techniques must be minimally invasive: Exostosis resection at the Achilles tendon insertion, debridement of degenerated Achilles tendon, reattachment using anchors or augmentation using flexor hallucis longus (FHL) tendon transfer, and excision of the posterosuperior calcaneal prominence. Studies on these four perspectives were reviewed to establish minimally invasive surgery for insertional Achilles tendinopathy. Techniques for exostosis resection were demonstrated in one case study, where blunt dissection around the exostosis was performed, and the exostosis was resected using an abrasion burr under fluoroscopic guidance. Techniques for debridement of degenerated Achilles tendon were demonstrated in the same case study, where the space left after resection of the exostosis was used as an endoscopic working space, and the degenerated Achilles tendon and intra-tendinous calcification were debrided endoscopically. Achilles tendon reattachment techniques using suture anchors have been demonstrated in several studies. However, there are no studies on FHL tendon transfer techniques for Achilles tendon reattachment. In contrast, endoscopic posterosuperior calcaneal prominence resection is already established. Additionally, studies on ultrasound-guided surgeries and percutaneous dorsal wedge calcaneal osteotomy as minimally invasive surgery were reviewed.

Key Words: Achilles tendon; Endoscopy; Fluoroscopy; Osteotomy; Ultrasonography; Tendinopathy; Surgery

Core Tip: Studies of minimally invasive surgery for insertional Achilles tendinopathy are limited. Therefore, to establish this surgery, the following techniques must be minimally invasive: (1) Exostosis resection at the Achilles tendon insertion; (2) Debridement of degenerated Achilles tendon; (3) Reattachment using anchors or augmentation using flexor hallucis longus tendon transfer; and (4) Excision of the posterosuperior calcaneal prominence. This article reviewed studies from these four perspectives to establish minimally invasive surgery for insertional Achilles tendinopathy. In addition, studies on ultrasound-guided surgeries and dorsal percutaneous dorsal wedge calcaneal osteotomy as minimally invasive surgery were reviewed.

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INTRODUCTION

Insertional Achilles tendinopathy is characterized by exostosis and intra-tendon calcification at the insertion site of the Achilles tendon into the calcaneus[1]. After failing to respond to exhaustive conservative therapy for 3-6 mo, surgery is considered[2,3]. Standard surgical procedures include posterior midline skin incision, calcaneal exostosis resection, partial or total detachment and debridement of the Achilles tendon at its insertion, resection of the posterosuperior calcaneal prominence and retrocalcaneal bursa, and reattachment using anchors or augmentation using flexor hallucis longus (FHL) tendon transfer[4,5]. The surgery's outcomes have been good[6-29]; nonetheless, the recovery was slow due to the invasiveness and the high complication rate due to the large skin incision[6,29-31]. McGarvey *et al*[6] reported a case series of 21 patients where 40% had residual pain for over two years postoperatively[6]. Hörterer *et al*[29] surveyed 118 people who underwent midline incision, partial release and debridement of the Achilles tendon, resection of the posterosuperior calcaneal prominence, and reattachment using anchors. They found that despite the high satisfaction rate, 41% had shoe limitations, and 14% had mild infections[29]. A systematic review by Highlander and Greenhagen[30] reported a 7.0% complication rate for midline incision, and another by Thompson *et al*[31] reported a significantly higher complication rate for midline incision than other incision techniques. Considering these, minimally invasive surgery is preferable. However, studies on minimally invasive surgery for insertional Achilles tendinopathy are scarce[32].

Therefore, to establish minimally invasive surgery for insertional Achilles tendinopathy, all four steps described below must be performed with minimally invasive surgery (Table 1).

This article reviewed studies on the above four techniques, including case reports, cadaver experiments, technical notes, and case series, to establish minimally invasive surgery for insertional Achilles tendinopathy. In addition, reports regarding ultrasound-guided surgeries and percutaneous dorsal wedge calcaneal osteotomy as minimally invasive surgery were also reviewed. In this article, the terms "Haglund disease" and "Haglund syndrome" were avoided because such eponymous terms are unclear[33,34].

ENDOSCOPIC SURGERY FOR INSERTIONAL ACHILLES TENDINOPATHY

Fluoroscopic calcaneal exostosis resection and endoscopic Achilles tendon debridement

In 2022, Nakajima[32] published a case series of 44 patients who underwent minimally invasive surgeries for insertional Achilles tendinopathy involving techniques of exostosis resection at the Achilles tendon insertion and debridement of degenerated Achilles tendon (Table 1)[32]. The outline of this technique included the following: (1) Blunt dissection was performed around the exostosis with fluoroscopic guidance; (2) An abrasion bur was inserted into the space created by the dissection, and the exostosis was resected fluoroscopically; (3) The space left after resecting the exostosis was used as endoscopy working space; and (4) Debridement of the degenerated Achilles tendon was performed endoscopically (Figure 1). The outcome improved based on the median visual analog scale (VAS) and the Japanese society for surgery of the foot scores from 64.5 mm to 6.5 mm and from 67.0 points to 100 points, respectively. The median time to return to sports was 4.5 mo. Furthermore, postoperative magnetic resonance imaging (MRI) revealed that the space left after resecting the exostosis was filled with soft tissue similar to the Achilles tendon, suggesting natural repair of the attachment site (Figure 2)[32]. The novelty of this study is that it allowed exostosis resection at the Achilles tendon insertion and debridement of the degenerative Achilles tendon to be performed with minimal invasiveness. Besides,

Table 1 Techniques required in minimally invasive surgery for insertional achilles tendinopathy

No.	Techniques
1	Exostosis resection at the Achilles tendon insertion
2	Debridement of degenerated Achilles tendon
3	Reattachment using anchors or augmentation using FHL tendon transfer
4	Excision of the posterosuperior calcaneal prominence

FHL: Flexor hallucis longus.

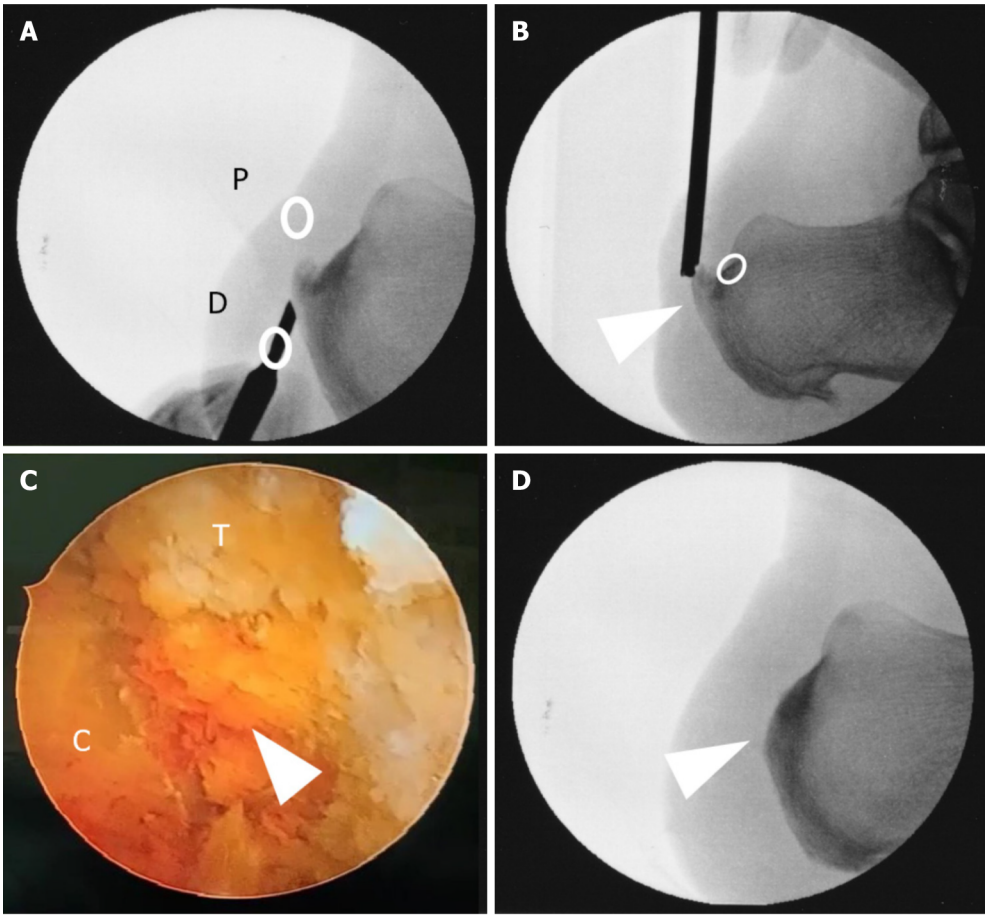

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Figure 1 Fluoroscopic and endoscopic calcaneal exostosis resection and Achilles tendon debridement for insertional achilles tendinopathy[32]. A: Blunt dissection around the exostosis. Two portals were created 1 cm proximal and distal from the exostosis (circles), and blunt dissection around the exostosis was performed using a raspatorium; B: Exostosis resection using an abrasion burr under fluoroscopic guidance (arrowhead). Care was taken not to damage the normal insertion of the achilles tendon (circle). The space left after resection of the exostosis was a working space for endoscopy; C: Endoscopic view from the distal portal. The portion of the achilles tendon that had attached to the exostosis was visible as a free end (T). The unresected exostosis was attached to the tendon (arrowhead). The degenerated Achilles tendon was debrided endoscopically; D: Postoperative fluoroscopic view. The exostosis was totally resected (arrowhead). P: Proximal portal; D: Distal portal; C: The calcaneus; T: Free end.

this case series did not require reattachment or augmentation of the Achilles tendon, as natural repair of the Achilles tendon insertion site was observed. In addition, since there was no preoperative retrocalcaneal bursitis in the cases, resection of the posterior superior eminence was not performed.

Endoscopic Achilles tendon reattachment

Several studies have reported techniques for endoscopic reattachment of the Achilles tendon insertion.

Xu *et al*[35] published a case series that described a technique for endoscopically repairing partial Achilles tendon tear at the Achilles tendon insertion caused by endoscopic posterosuperior calcaneal prominence resection[35]. A suture anchor was placed at the center of the bone-resected surface after the posterosuperior prominence resection, and two stab wounds were made on the medial and lateral

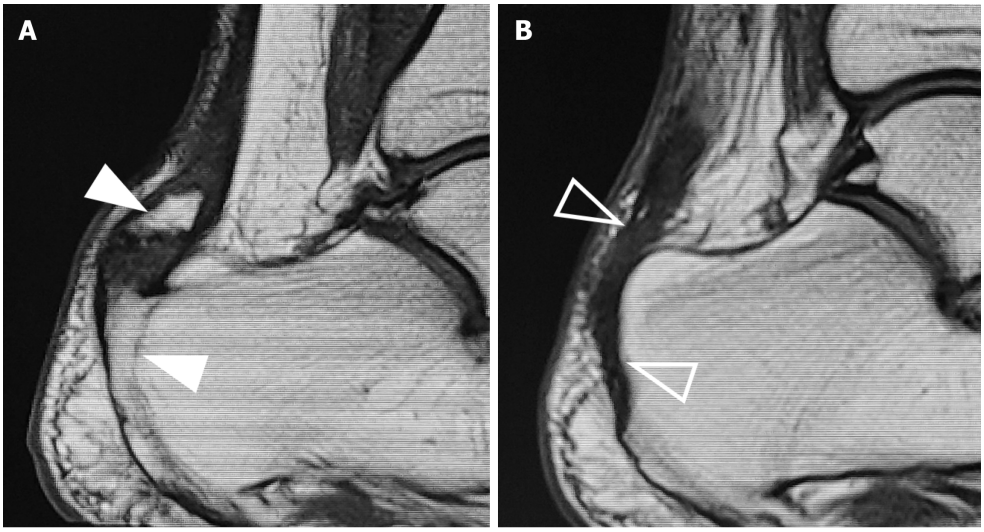

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Figure 2 Pre- and postoperative magnetic resonance imaging of the left calcaneus of a patient with insertional achilles tendinopathy who underwent Fluoroscopic and endoscopic calcaneal exostosis resection and achilles tendon debridement[32]. A: Preoperative magnetic resonance imaging (MRI). Exostosis and intra-tendon ossification were visible (white arrows); B: Postoperative MRI at 9 mo postoperatively. The void space left after resection of the exostosis and intra-tendon ossification was filled with soft tissue providing the same signal as the Achilles tendon, suggesting a natural repair.

margins of the Achilles tendon, respectively. Afterward, the Achilles tendon was sutured using the modified Bunnel technique through these four stab wounds. They performed this procedure in seven patients with insertional Achilles tendinopathy; five reported excellent results [American orthopedic foot and ankle society (AOFAS) score, 90-100], and two reported good results (AOFAS score, 80-89).

Vega *et al*[36] also reported a technique similar to that of Xu *et al*[35] in their case series[36]. An anchor with two sutures (four limbs) was placed at the center of the bone-resected surface after the endoscopic resection of the posterosuperior calcaneal prominence. Two limbs were passed through the medial portion of the Achilles tendon and sutured subcutaneously at the medial portal. The remaining two limbs were similarly sutured at the lateral portal. Twelve patients underwent this surgery, improving their AOFAS score from 70 to 92 and their Victorian institute of sports assessment-Achilles (VISA-A) score from 34 to 92.

Michel *et al*[37] published a case report of a patient undergoing endoscopic posterosuperior prominence resection and endoscopic Achilles tendon repair for retrocalcaneal bursitis with partial Achilles tendon rupture[37]. First, the posterosuperior prominence was resected endoscopically, then a suture anchor with 2 limbs was placed on the bone-resected site. Next, sutures were passed through the Achilles tendon using the shuttle relay technique and sutured subcutaneously at the stab wound.

Maquirriain[38] reported in a technical note that after the posterosuperior prominence resection, the partially detached Achilles tendon insertion was reattached to the surface of bone-resected calcaneus using a percutaneous absorbable screw[38].

Hegewald *et al*[39] reported in a technical note that they made three stab wounds on the medial margin of the Achilles tendon and three stab wounds on the lateral margin, sutured the Achilles tendon using a modified Bunnell technique, and finally fixed the sutures to the calcaneus with interference screws[39].

The following three technical notes demonstrated the sequence of exostosis resection at the Achilles tendon insertion, excision of the posterosuperior calcaneal prominence, and reattachment using anchors [40-42]. Debridement of the degenerated Achilles tendon was not performed. Boniface and Vervoort[40] presented the following procedure. First, two proximal portals (medial and lateral) for posterosuperior prominence resection and three distal portals (medial, lateral, and median) for exostosis resection were created. Next, a working space was created between the skin and the Achilles tendon, and exostosis resection, detachment of the middle portion of the Achilles tendon insertion, and posterosuperior prominence resection were performed endoscopically. Finally, the detached middle portion of the Achilles tendon was then reattached to the bone-resected surface with two rows of speed bridges. When this technique was performed with 10 cadavers, it required 120 min the first time and 70 min the last time. The method presented by Miller *et al*[41] is almost identical to that of Boniface and Vervoort, except that the Achilles insertion was totally detached in the former method[41]. Lopes *et al*'s method differs from that of the two previous studies in that the sutures were placed in the tendon[42]. Six portals were created on the medial and lateral margins of the Achilles tendon. After the posterosuperior prominence was resected endoscopically, the Achilles tendon was fixed with two rows of suture anchors that placed the two sutures in the tendon in S-shapes using the six portals.

Endoscopic augmentation using FHL tendon transfer

Hunt *et al*[17] reported a prospective comparative study that revealed no difference in clinical outcomes between procedures with and without FHL tendon transfer[18]; however, FHL tendon transfer was traditionally performed in cases where more than 50% of Achilles tendon insertion was released[7,10,11,15,17,18,27,43]. The advantage of the FHL transfer for Achilles tendon augmentation is that both tendons act in the same walking cycle phase[44]. In addition, studies have reported no loss of function of the hallux due to FHL transfer. Coull *et al*[45] reported that the patients' hallux after FHL tendon transfer achieved the highest AOFAS score and that functional weakness of the hallux was not observed in daily living[45]. Hahn *et al*[46] observed that the FHL tendon was well integrated with the Achilles tendon on postoperative MRI, with ≥ 15% hypertrophy of the FHL muscle in 8 of 13 patients[46]. Other reported donors for augmentation include plantar tendon[6], sural triceps aponeurosis[47], and bone-patellar tendon[48].

A method for endoscopic FHL tendon harvest was published by Lui *et al*[49]. In this method, the FHL tendon was cut below the hallux's interphalangeal joint, the interconnection tendon between the FHL and the flexor digitorum longus was dissociated using a tendon stripper, and the tendon was pulled out through a small skin incision at the Achilles tendon.

To the best of the current author's knowledge, there are no reports of endoscopic Achilles tendon augmentation using the FHL transfer. However, if a technique to integrate the Achilles and harvested FHL tendons is developed, endoscopic FHL transfer will become possible.

Endoscopic posterosuperior calcaneal prominence resection

Several studies reported that posterosuperior prominence resection only for treating insertional Achilles tendinopathy had poor results[50-54]. Watson *et al*[50] reported that endoscopic posterosuperior prominence resection had a poor outcome in patients with calcaneal exostosis and recognized insertional Achilles tendinopathy and retrocalcaneal bursitis as different etiologies of posterior heel pain [50]. Leitze *et al*[51], Ortmann and McBryde[52], Jerosch[53], and Cusumano *et al*[54] excluded cases with severe insertional calcific Achilles tendinopathy for this endoscopic surgery[51-54]. Natarajan and Narayanan[55] reported that 8 out of 40 people with calcaneal exostosis who underwent endoscopic posterosuperior prominence resection would not recommend this procedure[55]. Kondreddi *et al*[56] reported that patients with Achilles tendon degeneration who underwent this surgery had lower subjective satisfaction[56]. However, Sundararajan and Wilde[57] reported that 5 of 20 patients with insertional Achilles tendinopathy presented with retrocalcaneal bursitis based on clinical and MRI findings[57]. Furthermore, a study by Rufai *et al*[58] observed that the periosteum of the posterosuperior prominence was replaced with fibrocartilage in cadavers with calcaneal exostosis[58], suggesting that insertional Achilles tendinopathy and posterior superior prominence pathology are not totally independent. Therefore, posterosuperior prominence resection should not be used alone for insertional Achilles tendinopathy but can be considered an option when needed.

Endoscopic posterosuperior prominence resection has been performed using two portals (medial and lateral)[59-62]. Wu *et al*[63] reported a case series of 27 patients whose three portals were effective. Van Sterkenburg *et al*[64] reported that the optimal endoscopic portal location varied with the shape of the posterosuperior prominence; thus, no index could be established. Lohrer *et al*[65] compared endoscopic and open osteotomy procedures using cadavers and reported similar rates of peroneal nerve injury and more bone fragments in the open osteotomy[65]. Roth *et al*[66] reported that endoscopic surgery resulted in less bone resection than open surgery, which they speculated may contribute to faster recovery[66]. Lui[67] reported that endoscopy in the supine position allowed for easier identification of anatomical structures than in the prone position[67]. Ferranti *et al*[68] reported that in 27 patients who underwent percutaneous posterosuperior prominence resection, the mean VISA-A score improved from 20 preoperatively to 75 postoperatively, and 84% experienced complete satisfaction[68].

Endoscopic gastrocnemius recession

To the best of the author's knowledge, there is only one report on endoscopic gastrocnemius recession for treating insertional Achilles tendinopathy. Tallerico *et al*[69] followed up on 11 patients who underwent endoscopic gastrocnemius recession for an average of 13.8 mo. Ten of the 11 patients were highly satisfied, and the mean postoperative AOFAS score improved from 52.0 preoperatively to 94.8 postoperatively. Six of the 11 patients had calcaneal exostosis, and their AOFAS scores improved from 51.1 preoperatively to 91.9 postoperatively[69]. Gastrocnemius recession can also be a technique for reattaching the Achilles tendon. Gould reported 49 patients with insertional Achilles tendinopathy who underwent J-shaped skin incision, complete Achilles tendon detachment and debridement, posterosuperior prominence resection, and V-Y lengthening and reattachment[70]. Staggers *et al*[71] compared 25 patients who underwent V-Y lengthening of gastrocnemius and 21 who underwent FHL transplantation during open surgery for insertional Achilles tendinopathy and reported no significant difference in subjective satisfaction, VISA-A scores, and VAS scores between both groups[71].

ULTRASOUND-GUIDED SURGERY FOR INSERTIONAL ACHILLES TENDINOPATHY

Ultrasound-guided surgery also has the potential for minimally invasive surgery. However, Khan *et al* [72] reported that although MRI is effective in diagnosing insertional Achilles tendinopathy, ultrasound does not improve diagnostic accuracy[72]; thus, this surgery may be technically demanding for insertional Achilles tendinopathy.

Chimenti *et al*[73] reviewed 34 patients who underwent ultrasound-guided posterosuperior prominence resection, debridement of the Achilles tendon insertion and intra-tendinous calcifications, and retrocalcaneal bursectomy[73]. At 6-12 wk of follow-up, baseline pain decreased from 68% preoperatively to 5% postoperatively, with a satisfaction rate of 70%. In addition, four patients who were followed up for more than 11 mo were free of pain.

Wang *et al*[74] compared outcomes in 10 patients who underwent ultrasound-guided posterosuperior prominence resection and retrocalcaneal bursectomy and 12 who underwent open surgery[74]. The AOFAS scores at two years postoperatively were 95 in the open group and 94 in the minimally invasive group, with no significant difference.

Freed *et al*[75] performed ultrasound-guided Achilles fasciotomy and tenotomy in 26 people with insertional Achilles tendinopathy, with a mean operating time of 4 min and 32 s, a mean follow-up of 16 mo, and a success rate of 85%[75].

PERCUTANEOUS DORSAL WEDGE CALCANEAL OSTEOTOMY FOR INSERTIONAL ACHILLES TENDINOPATHY

Dorsal wedge calcaneal osteotomy for insertional Achilles tendinopathy has been frequently reported since 2010[76-85]. A closing wedge osteotomy of the calcaneus moves the Achilles tendon insertion upward and forward, loosening the Achilles tendon and widening the gap between the Achilles tendon and the posterosuperior prominence. In 1939, Zadek[86] first published a case series of three patients who underwent this osteotomy. Keck and Kelly[87] also published a 3-patient case series of similar osteotomy in 1965. Therefore, this osteotomy is sometimes called the Zadek osteotomy or the Keck and Kelly[87] osteotomy.

Good surgical results have been reported. Georgiannos *et al*[78] reviewed the outcomes of 52 athletes who underwent this osteotomy, with AOFAS scores improving from 59 to 95 and VISA-A scores improving from 65 to 90 at a minimum of three years of follow-up[78]. Maffulli *et al*[82] reported that in 25 patients who underwent this osteotomy, the median VISA-A score improved from 25 to 86, and 3 of 4 patients reported a return to the pre-injury state[82]. Cengiz and Karaoglu[85] followed up on 14 patients who underwent this surgery for more than three years. They reported that the AOFAS score improved from 56 preoperatively to 89 postoperatively, and the VAS score improved from 86 preoperatively to 41 postoperatively[85]. Ge *et al*[80] followed up on 12 patients who underwent this osteotomy for an average of 86 mo, with AOFAS scores improving from 52 to 98 and VISA-A scores improving from 37 to 98. They also reported that these postoperative scores were significantly higher than those of 32 patients who underwent posterosuperior prominence resection[80]. A description of this osteotomy technique was detailed in a review by Syed and Perera[77].

Recently, minimally invasive surgery for this osteotomy has been reported. Vernois *et al*[88] detailed this minimally invasive osteotomy technique using a 3-mm wide and 20-mm long Shannon bur[88]. Nordio *et al*[89] reported that in 26 patients who underwent percutaneous surgery, the Foot function index score improved from 65 to 8. The VAS score improved from 9 to 1, with a mean follow-up of 12 mo, and pain relief was achieved at a mean of 12 wk[89]. Choi and Suh[90] compared the outcomes of 11 patients who underwent minimally invasive osteotomy using a 2.2 mm Shannon bar and 14 patients who underwent open posterosuperior prominence resection. The VISA-A score of this osteotomy improved from 36 to 88, and the VAS score improved from 89 to 36. They also reported that minimally invasive surgery was significantly better than posterosuperior prominence resection at 6 mo postoperatively; however, the outcomes were similar at the final follow-up[90].

CONCLUSION

To establish minimally invasive surgery for insertional Achilles tendinopathy, the following four techniques must be minimally invasive: (1) Exostosis resection at the Achilles tendon insertion; (2) Debridement of degenerated Achilles tendon; (3) Reattachment using anchors or augmentation using FHL tendon transfer; and (4) Excision of the posterosuperior calcaneal prominence. This article reviewed studies from these four perspectives.

Exostosis resection at the Achilles tendon insertion was demonstrated in one case study, where blunt dissection around the exostosis was performed under fluoroscopy, an abrasion bur was introduced into the space created, and the exostosis was resected under fluoroscopic guidance.

Debridement of degenerated Achilles tendon was demonstrated in the same case study, where the space left after resection of the exostosis was an endoscopic working space, and the degenerated Achilles tendon and intra-tendinous calcification were debrided endoscopically.

Achilles tendon reattachment techniques have been demonstrated in several studies, where anchors were placed on the calcaneal surface after the posterosuperior prominence resection, and sutures were passed through the Achilles tendon using several stab wounds and fixated to the anchors.

In contrast, FHL tendon transfer techniques have not yet been published. The minimally invasive FHL harvest was reported in a technical note. Therefore, if a technique to integrate the Achilles tendon and the harvested FHL tendon is developed, endoscopic FHL transfer will become possible.

Endoscopic posterior superior prominence resection has already been established.

As with other minimally invasive surgeries for insertional Achilles tendinopathy, several studies on ultrasound-guided surgery and percutaneous dorsal wedge calcaneal osteotomy have been published.

FOOTNOTES

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MINIREVIEWS

Subtalar dislocations: Mechanisms, clinical presentation and methods of reduction

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Abstract

Subtalar joint is a complex joint in hindfoot formed by the talus superiorly and the calcaneus and navicular inferiorly. Subtalar dislocations are high-mechanism injuries, which are caused by simultaneous dislocation of both talonavicular and talocalcaneal joints, without major fracture of the talus. They are usually classified as medial (most common), lateral, anterior and posterior dislocations, based on the position of foot in relation to talus and the indirect forces that have been applied to cause this significant injury. They are usually diagnosed by X rays, but computed tomography and magnetic resonance imaging can be used to identify associated intra-articular fractures and peri-talar soft tissue injuries respectively. Majority being closed injuries, can be managed in ED by closed reduction and cast immobilisation, but if they are open, have poor outcomes. Complications that ensue open dislocations are post-traumatic arthritis, instability and avascular necrosis.

Key Words: Joint; Subtalar; Joint dislocations; Flatfoot; Clubfoot; Talus

Core Tip: Subtalar dislocations are rare, high mechanism injuries. Comprehensive trauma assessment, along with limb specific assessment is the key approach to deal with these injuries. Lateral dislocations constitute for open injuries commonly, and must be managed according to the BOAST-Open fracture guidelines. Avascular necrosis of the talus due to injury to the canalis tarsi artery, are troublesome complication. Thus, one needs to have high index of suspicion when the dislocation is open or associated with talus fracture.

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INTRODUCTION

Subtalar dislocation is defined as the simultaneous dislocation of both talonavicular and talocalcaneal joints without major fracture of the talus[1]. The first cases of subtalar dislocations were described by Dufaurest[2] and Judey[3] in 1811, yet there followed a considerable period of senescence in exploring this injury. It was not till 1853 that Broca[4] delivered the first classification of subtalar dislocation, which Malgaigne and Buerguer[5] subsequently amended in 1856.

The classifications are founded on the four anatomical positions into which the foot dislocates in relation to talus[5]. The dislocations of the articulations of the talus include talocalcaneal, talonavicular or talo-crural joint. Subtalar dislocations account for approximately 1% of all dislocations[6]. This is a rare injury due to the anatomical and biomechanical stability afforded by the talo-calcaneal and talo-navicular joints, such that it is predominantly as a result of trauma and high-energy mechanisms[7,8]. One must be cognisant to deliver care as per suitable trauma protocols, and there must be a high degree of suspicion for attendant injuries to the talus, ankle, foot, soft tissue compromise, open fracture or dislocation and trauma to alternate body systems[9-11].

The aim of this review is to provide a concise overview of subtalar dislocations including anatomy, classification of injury, clinical presentation, diagnosis, treatment options, outcomes and complications. As a result of this article, we aim to improve the reader's understanding of this topic.

ANATOMY OF SUBTALAR JOINT

The subtalar joint is a complex joint in the hindfoot with many normal anatomic variations[12]. Considered a synovial joint structurally and a plane joint functionally, it is formed by the talus superiorly and the calcaneus and navicular inferiorly[13], it is comprised of three articulating surfaces, the anterior facet is a small articulation between the talus head and the anterior calcaneus facet, the middle facet between medial facet of talus and the middle facet of the calcaneus and a large posterior facet between the posterior facet of talus and the posterior facet of the calcaneus[14].

Anatomically it is considered as two separate chambers; an anterior chamber also known as the talocalcaneal navicular joint is formed by the often congruent anterior and middle facets[14], the floor is formed by the plantar calcaneo-navicular ligament (spring ligament) which has a cartilaginous articular surface[13]. This ligament complex plays a key role in stabilising the talus head, insufficiency can lead to acquired flat foot deformity[12]. The posterior chamber also referred to as the talocalcaneal joint or the anatomical subtalar joint formed by the posterior facet.

The differentiation of the subtalar joint into two distinct joints is only really preferred by anatomists [13]. From a functional point of view the two joints have a common single axis of motion and neither joint has movement independent of the other, therefore many orthopaedic surgeons consider the talocalcaneonavicular joint and the talocalcaneal joint to be one functional unit[15].

EPIDEMIOLOGY

Subtalar dislocations account for 1%-2% of all dislocations and 15% of all peri-talar injuries. Most frequent age of presentation is in the third decade. It occurs 6-10 times more frequently in men than in women and also dislocations were found to be more common on the right foot than the left[16]. Open injuries are present in 20%-25% of cases, where lateral dislocations are open in 41.8% of cases, while medial dislocations are open in 21.9% of cases[17]. These are typically as a result of high-energy injuries, 50% motor vehicle accidents, 20%-30% fall from heights and 14% from sport injuries[16].

CLASSIFICATION OF INJURY

In 1853, Broca[4] then classified the injury according to the direction of dislocation: Medial, lateral and posterior. Subsequently in 1855 and 1856 that Henke *et al*[17], and Malgaigne and Buerguer[5] modified the Broca classification to include anterior subtalar dislocations. The foundation of classification is the anatomy of the foot in relation to the talus (Table 1)[18-21]. It is intriguing that the same system has continued for over a century and this may reflect the uncommon nature of the injury as well as the limited number of studies undertaken.

MECHANISM OF INJURY

This is often associated with high energy trauma, usually, motor vehicle accidents, or falls from a height [6]. However, patients may get these injuries from lower energy mechanisms such as sports injuries, twisting injuries of the foot or fall from standing, especially if the patient is elderly or obese[6]. Subtalar dislocation involves disruption of the surrounding ligaments: Interosseous talocalcaneal ligament (most important), anterior, posterior, lateral and medial talocalcaneal ligament[22]. Typically to cause this dislocation, an axial load is applied, when the patient has plantar flexed foot. The position of the foot in relation to the talus and the indirect forces that have been applied to cause significant and progressive ligamentous and capsular injury determine the type of dislocation, which can be either medial, lateral, anterior, posterior or total[22].

Medial dislocation (acquired clubfoot)

There is a forced inversion of a plantarflexed foot followed by external rotation of the talus with the lateral malleolus acting as a buttress which result in initial rupture of the talonavicular ligament followed by tearing of the interosseous ligament from anterior to posterior. The sustentaculum tali also act as fulcrum for the neck of the talus to pivot around. The reduction might be difficult and blocked by peroneal tendons, EDB (Extensor Digitorum Brevis) or talonavicular joint capsule, with the foot locked into supination[23].

Lateral dislocation (acquired flatfoot)

There is a forced eversion of a dorsiflexed foot followed by external rotation of the talus which leads to initial rupture of the deltoid ligament followed by the interosseous ligament and the talocalcaneal joint, then dorsal talonavicular ligament rupture. Here, the anterior process of the calcaneus acts as fulcrum for the anterolateral corner of the talus to pivot around. The reduction might be difficult and blocked by peroneus tertius (PT) tendon, flexor hallucis longus (FHL), or flexor digitorum longus (FDL), with the foot locked into pronation[6].

Posterior dislocation (shortened foot)

There is a heavy forced plantarflexion of the foot followed by a talocalcaneal joint slip[6]. This is an exceedingly rare entity. It is important to recognize that not all posterior subtalar dislocations are true posterior dislocations. Inokuchi *et al*[1] suggest that the position of the foot is important to define the type of subtalar dislocation: Supination or pronation of the foot at the time of injury leads to medial or lateral displacement. Usually, subtalar dislocation occurs with an associated rotational component. Few reports of posterior subtalar dislocation have been described to date, and all of these describe medial or lateral displacement[24].

Anterior dislocation (elongated foot)

There is an anterior traction of the foot on a fixed lower leg followed by a talocalcaneal joint slip[6]. Pure anterior subtalar dislocation is very rare, with few cases being reported in the past[8]. The first reported case of anterior subtalar dislocation was described by Malgaigne and Burger[5]. Zimmer *et al*[25] summarised eight series of 115 cases of subtalar dislocation-only about 1% of them were anterior dislocations.

Various mechanisms of injury have been proposed. Kanda *et al*[20] believe that anterior subtalar dislocation can be caused by forceful foot supination and ankle dorsiflexion when a patient falls from a height. Tabib *et al*[21] reported that the dislocation followed a direct rear impact over the posterior aspect of heel after a fall injury. Chuo *et al*[26] reported that anterior subtalar dislocation occurred when the patient withdrew the trapped foot.

CLINICAL PRESENTATION WITH ASSOCIATED TALAR INJURIES

One of the commonest presenting complaints in patients with subtalar dislocations is of pain and swelling of the ankle and/or midfoot. On examination, there may be bruising, an obvious gross swelling

Table 1 Classification of subtalar dislocation and associated mechanism of injury

Direction of dislocation	Percentage of all subtalar dislocations (%)	Position of foot at time of injury	Mechanism of injury
Medial (Calcaneus is medial to talus)	65-85[10]	Plantarflexion	"Acquired club foot", forceful inversion of forefoot[10], foot locked in supination
Lateral (Calcaneus is lateral to talus)	15-35[18]	Plantarflexion	"Acquired flat foot", forceful eversion of forefoot[10], foot locked in pronation
Posterior	0.8-2.5[7]	Hyper-plantarflexion	"Shortened foot", force applied to dorsum of foot leading to hyperplantarflexion[10]
Anterior	1[19]	Hyper-dorsiflexion	"Elongated foot", forceful foot supination and ankle dorsiflexion [20] or direct rear impact to posterior heel[21]

which might mask the bony deformity. Surrounding soft tissue involvement depends on the amount of energy involved and on the elapsed time from the injury[27]. There will be reduced range of motion as well as the foot may be locked in a position depending on the type of subtalar dislocation. Often subtalar dislocations as a result of the particular pattern and mechanism of injury will have adjacent bone fractures and injuries including the talus, cuboid, navicular and fibula (Table 2).

Medial subtalar dislocations are characterized by medial displacement of the foot and calcaneus[27]. The talar head is often palpable on the dorsum of the foot between the extensor digitorum longus and extensor hallucis longus tendons, usually locked in supination with inversion of the foot. It is sometimes called "basketball foot" as this is a common mechanism and another term for this injury is "acquired clubfoot"[28]. This type of dislocation is usually associated with fractures of the posterior process of talus, dorsomedial talar head, and navicular bone[29].

Lateral subtalar dislocations are most likely to result in an open dislocation (in upto 25% of the cases [30]) due to the high-energy mechanism leading to injury. Clinically lateral subtalar dislocations can be locked in pronation with eversion of the foot[28]. This type of dislocation is often associated with fractures of the lateral process of talus, anterior calcaneus, cuboid, and fibula[29]. The reduction might be blocked by PT tendon, FHL or FDL, and so the foot becomes locked in pronation.

Posterior subtalar dislocations are commonly accompanied by fractures of the malleoli, talus, or fifth metatarsal[31] and anterior subtalar dislocations are extremely rare and highly unstable injuries involving talus, calcaneal and navicular injuries[26].

DIAGNOSIS

Subtalar dislocations are almost always associated with bony injuries including fractures of the ankle, talar (lateral process and sustentaculum tali), calcaneal and navicular bones carrying the highest risk. The cuneiforms, cuboid and metatarsals might be injured as well[6]. Therefore, all parts of the foot which are at risk of being injured as a result of a subtalar dislocation have to be examined radiographically[9]. Radiographs and computed tomography (CT) are the mainstay of investigations and here we explore the appropriate techniques and findings.

Plain radiographs

The diagnosis of subtalar dislocation is usually made on AP, lateral, and oblique radiographs of the foot or ankle. Some special views might be also useful in diagnosis, *e.g.*, Canale view for evaluating talar neck fractures, which are often oblique to the transverse or sagittal plane of the foot, and are commonly associated with subtalar dislocation, and Harris view of the calcaneus, which allows visualization of the posterior and middle talocalcaneal joints[32]. The nature of the deformity often limits radiographic positioning. Remembering that the talar head and navicular should be congruent on all views can help overcome this limitation. Medial subtalar dislocation results in medial and plantar displacement of the navicular relative to the talar head and medial displacement of the calcaneus relative to the talus. Lateral subtalar dislocation results in lateral and dorsal displacement of the navicular relative to the talar head and lateral displacement of the calcaneus relative to the talus. Talonavicular impaction may prevent successful closed reduction and should therefore be recognized[32]. After reduction, AP and lateral radiographs of the foot as well as AP and mortise views of the ankle are obtained to confirm optimal results. In the absence of deformity, post-reduction radiographs are usually of better quality than those obtained at the time of injury and associated fractures become more apparent[6].

CT scan

Associated intra-articular fractures are difficult to identify at plain radiography and their presence can hinder anatomic reduction and worsen the overall prognosis. Therefore, routine post-reduction CT has

Table 2 Associated bony injuries with each type of dislocation

Bony involvement	Medial dislocation[28]	Lateral dislocation[28]	Posterior dislocation[29]	Anterior dislocation[30]
Talus	+	+	+	+
Navicular	+	-	-	+
Cuboid	-	+	-	-
Fibula	-	+	+	-
Calcaneum	-	+	-	+

been recommended to detect these fractures more accurately[32] and to look for subtalar debris[9].

Magnetic resonance imaging scan

Given the sensitivity of CT in diagnosis, further imaging is not typically indicated; however, magnetic resonance imaging has proven useful for persistent pain after trauma to aid in diagnosis of peri-talar soft tissue injuries and osteochondral injuries such as those in the talar head or dome[33].

TREATMENT

Taking into account that the majority of subtalar dislocations result from high energy mechanisms, there is the potential for adjacent attendant injuries. Following Advanced Trauma Life Support protocols[34], to start with Airway including cervical spine protection, Breathing, Circulation, Disability and Exposure (ABCDE) assessment of the patient, and then limb specific management, necessitating assessment of the neurovascular status and soft tissue.

Majority of these dislocations could be treated by closed reduction and cast immobilisation or by operative stabilisation with an external fixator or if necessary percutaneous K-wire arthrodesis of subtalar and talonavicular joint as a temporizing measure[35].

Early treatment with closed reduction under sedation or more commonly general anaesthetic is required to avoid progressive soft tissue and neurovascular damage[9]. Closed reduction is best achieved through relaxation of the gastrocnemius and soleus which may act as a significant deforming force at the calcaneus, by knee flexion and subsequent traction-countertraction manoeuvre. Once reduction achieved, it is important to reassess the limb neurovascular status, and a plaster backslab offers a simple yet effective method of immobilisation and splintage. Circumferential casting and constrictive bandages should be avoided as this may exacerbate residual swelling and lead to increased compartment pressures, whereas limb elevation will help counteract this process[23]. The table below shows treatment modalities for different dislocations (Table 3).

Open dislocations depict the more severe spectrum of injuries with poor outcomes. Common challenges including infection, post-traumatic arthrosis, and higher chance of talus avascular necrosis [36,37]. These injuries must be treated urgently, with initial broad-spectrum antibiotics in line with local antimicrobial stewardship and tetanus prophylaxis and managed with the same respect as open fractures. Although not directly related, we can utilise the principles through comparative guidance on the management of open fractures, one example is the British Orthopaedic Standards for Trauma-open fractures[38]. Coordinated care with plastic surgical specialists may help with timely preparations for reconstructive care if required. Acute treatment requires wound debridement and extensive irrigation of the injury zone, as well as reduction to an anatomical position. Immobilisation with plaster slab may be sufficient in some cases, yet where there is greater instability and loss of soft tissue coverage, Kirschner wires or even an external fixator may be required as alternative methods of stabilisation[39,40].

COMPLICATIONS + OUTCOMES

The sequelae of subtalar dislocations are grossly described through three key areas: Avascular necrosis of the talus (following injury to canalis tarsi artery), posttraumatic osteoarthritis and instability[41].

Avascular necrosis (AVN) also known as osteonecrosis, is defined as bone death due to ischemia, characterised by stereotypical pattern of cell death and complex repair process of bone resorption and formation[42]. The unique extra and intraosseous vascular anatomy of the talus predisposes for compromised healing potential and AVN as severe sequelae[43]. Avascular necrosis of the talus is a troublesome complication, which is more common in open subtalar dislocations or with talus fractures with rates of up to 50%[40].

Table 3 Reduction methods as per dislocation anatomy

Direction of Dislocation	Reduction manoeuvre (in addition to traction)	Structures that commonly obstruct reduction	Open reduction approach
Medial	Dorsiflexion and eversion of foot	Talar head, extensor digitorum brevis	Ollier's approach or antero-lateral approach
Lateral	Plantarflexion and inversion of foot	Flexor digitorum longus and tibialis posterior	Direct incision atop of talar head
Posterior	Plantarflexion of foot and once talar head disengages from navicular, the foot is dorsiflexed and tractioned distally		
Anterior	Posterior translation of foot whilst under traction		

Post-traumatic arthritis is of variable incidence, however high energy mechanism of injury, evidence of intra-articular talar and calcaneus fractures with osteochondral defects and open fractures are associated with a worse prognosis[36,19]. This can be a cause of significant pain and disability in the longterm[23]. Management is dependent on the pain and functional impact to the patient. For those with more advanced disease and poorly managed pain, physiotherapy and analgesia are unlikely to be adequate. In the presence of adjacent talonavicular and calcaneocuboid arthritis a triple fusion may be considered. Yet subtalar fusion may be reserved for those patients without adjacent arthrosis[39].

Instability is present as a result of ligamentous disruption following dislocation.

CONCLUSION

Subtalar dislocations are rare, high mechanism injuries. Comprehensive trauma assessment, along with limb specific assessment is the key approach to deal with these injuries. Lateral dislocations constitute for open injuries commonly, and must be managed according to the BOAST-Open fracture guidelines. Avascular necrosis of the talus due to injury to the canalis tarsi artery, are troublesome complication. Thus, one needs to have high index of suspicion when the dislocation is open or associated with talus fracture.

FOOTNOTES

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ORIGINAL ARTICLE

Basic Study

Automated patellar height assessment on high-resolution radiographs with a novel deep learning-based approach

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Abstract

BACKGROUND

Artificial intelligence and deep learning have shown promising results in medical imaging and interpreting radiographs. Moreover, medical community shows a gaining interest in automating routine diagnostics issues and orthopedic measurements.

AIM

To verify the accuracy of automated patellar height assessment using deep learning-based bone segmentation and detection approach on high resolution radiographs.

METHODS

218 Lateral knee radiographs were included in the analysis. 82 radiographs were utilized for training and 10 other radiographs for validation of a U-Net neural network to achieve required Dice score. 92 other radiographs were used for automatic (U-Net) and manual measurements of the patellar height, quantified by Caton-Deschamps (CD) and Blackburne-Peel (BP) indexes. The detection of required bones regions on high-resolution images was done using a You Only Look Once (YOLO) neural network. The agreement between manual and automatic measurements was calculated using the interclass correlation coefficient (ICC) and the standard error for single measurement (SEM). To check U-Net's

generalization the segmentation accuracy on the test set was also calculated.

RESULTS

Proximal tibia and patella was segmented with accuracy 95.9% (Dice score) by U-Net neural network on lateral knee subimages automatically detected by the YOLO network (mean Average Precision mAP greater than 0.96). The mean values of CD and BP indexes calculated by orthopedic surgeons (R#1 and R#2) was 0.93 (± 0.19) and 0.89 (± 0.19) for CD and 0.80 (± 0.17) and 0.78 (± 0.17) for BP. Automatic measurements performed by our algorithm for CD and BP indexes were 0.92 (± 0.21) and 0.75 (± 0.19), respectively. Excellent agreement between the orthopedic surgeons' measurements and results of the algorithm has been achieved (ICC > 0.75, SEM < 0.014).

CONCLUSION

Automatic patellar height assessment can be achieved on high-resolution radiographs with the required accuracy. Determining patellar end-points and the joint line-fitting to the proximal tibia joint surface allows for accurate CD and BP index calculations. The obtained results indicate that this approach can be valuable tool in a medical practice.

Key Words: Medical imaging; Artificial intelligence in orthopedics; Patellar index; Deep learning; Bone segmentation; Region of interest detection

Core Tip: This study presents an accurate method for automatic assessment of patellar height on high-resolution lateral knee radiographs. First, You Only Look Once neural network is used to detect patellar and proximal tibial region. Next, U-Net neural network is utilized to segment bones of the detected region. Then, the Caton-Deschamps and Blackburne-Peel indexes are calculated upon patellar end-points and joint line fitted to proximal tibia joint surface. Experimental results show that our approach has the potential to be used as a pre- and postoperative assessment tool.

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INTRODUCTION

Patellofemoral joint (PFJ) disorders are common structural and functional problems that may cause pain and instability leading to joint degeneration. The knee osteoarthritis (OA) is one of the most common diseases and its incidence is increasing due to the aging and obesity[1]. Overall, the treatment costs related to knee OA are substantial. Recent developments in medical informatics and artificial intelligence have led to an increasing number of studies on medical imaging of knee OA, but most of the research is focused on the tibiofemoral joint[2]. However PFJ, a third articulation has received insufficient attention. The assessment of patellar height (PH) is a fundamental parameter in diagnosing PFJ pathologies, selection of appropriate treatment and postoperative evaluation[3]. The standard approach for PH assessment is achieved by measuring ratios on X-ray images in the lateral view[4]. PH abnormalities can be recognized using Insall-Salvati, Blackburne-Peel (BP), and Caton-Deschamps (CD) indexes measured on lateral knee radiographs[5]. Patella Baja (PB) and pseudo-Patella Baja are common complications after total knee replacement (TKR) and related to poor outcomes[6]. From a therapeutic point of view, pseudo-Patella Baja with the elevated femorotibial joint line without shortening the patellar tendon can be recognized with the lower BP and CD indexes. The CD and BP ratios are also more important in the diagnosis of PB after TKR[6].

Recently, a substantial attention to reliability of these parameters have been devoted, among others, due to increasing importance of PH in knee replacement surgery, tibial osteotomy, and anterior cruciate ligament reconstruction[3,7,8]. However, such routine tasks are tedious, time-consuming, and prone to considerable inter-observer and intraobserver variability[9]. In recent years, deep-learning (DL) algorithms have gained popularity in medicine, particularly in different aspects of orthopedics[10-12]. They have been used for image classification[13], fracture detection[14] or osteoarthritis diagnosis[15]. Moreover, DL algorithms have also been developed for automatic segmentation of bones on X-ray images to estimate hallux-valgus angles, axial alignment[16,17] and skeletal metastases[18]. Bone

segmentation on X-ray images enables calculation of critical radiological parameters. It is a very difficult task[19], but some work has been done in this area[20,21].

To the best of our knowledge, there are no papers describing the application of neural networks for segmentation of lateral knee radiographs and measurements of patellar indexes on high-resolution radiographs. The method is automatic as it detects the region of interest (ROI) with the patella and proximal tibia region on a high-resolution radiograph, performs bone segmentation on the cropped ROI and then calculates the patellar indexes. The rest of the article is organized as follows. In the next Section we present our dataset for training You Only Look Once (YOLO) neural network, our dataset for training U-Net neural network, training procedure to achieve assumed Dice score and our algorithm for automated calculation of patellar indexes using segmented bones. In the following Section we present experimental results. The last part is devoted to discussion and conclusions.

MATERIALS AND METHODS

The overall pipeline of our method is shown in Figure 1. In order to detect ROI on radiographs we trained a YOLO neural network[22]. We have trained a U-Net model for automatic segmentation of bones of interest. The U-Net segmented the patella and tibia bones. On the segmented patella we extracted two landmark points and then fitted a patellar articular joint line to them. A second line has been fitted to the segmented proximal tibial articular surface. These lines have been used to calculate the CD and the BP indexes. The CD and BP indexes estimated in such a way have been compared with indexes calculated by medical doctors. The YOLO and U-Net networks have been trained on data collected and labelled by us. Radiological images were acquired using Shimadzu BR120 X-Ray Stand (Shimadzu Medical Systems, United States) and CDXI Software (Canon, United States).

Data

In this research, retrospective analysis of prospectively collected images was conducted on radiographs from an electronic database acquired in our institution. Patients whose radiographs were included in this study were examined in the authors' institution from January 2019 to April 2021. We collected a dataset for ROI detection and a dataset for bone segmentation. A dataset used for training the YOLO neural network is described below. The flowchart of data collection and methodology of training a U-Net neural network for bone segmentation is depicted in Figure 2 and described in more detail in subsequent paragraphs.

Dataset for training YOLO

The images in our database are high-resolution images, and only a portion of the radiographs contains pixels belonging to the knee and patella, which are required for calculation of BP and CD indexes. Thus, a YOLO neural network has been used to automatically detect the area of interest[23], *i.e.*, the patella and the proximal tibial artricular surface. One thousand radiographs from our database were selected, anonymized and then manually labeled. On each image we manually determined a rectangle surrounding the patella and a second rectangle surrounding the proximal tibial artricular surface. The YOLO neural network has been trained on 900 images and evaluated on 20 images.

Dataset for U-Net training

For training a U-Net neural network we randomly selected semiflexed lateral knee radiographs from the electronic database of our institution (stage A in Figure 1 and in Figure 2). The exclusion criteria were: Radiographs performed with improper rotational positioning, grade III or more osteoarthritis in Kellgren-Lawrence scale[24] and/or severe axial knee deformations, visible growth plate, artificial elements distorting the image of the bone outline (*e.g.*, osteosynthesis material or knee prosthesis implant), and heterotopic ossifications around the knee joint. The exported input X-ray images have been anonymized and stored in the lossless .png image format (stage B in Figure 2). Afterward, the bones on radiographs were manually labelled by an orthopedic surgeon (tibia and patella) in Adobe Photoshop ver. 22.0 (Adobe Systems, United States). The labelled images were included in the training and validation set (stage C in Figure 2).

Training and validation of U-Net

Bone segmentation has been performed using a U-Net[25]. The U-Net has been trained on the training set with verification of the accuracy of automatic segmentation (on validation set). The input images with knee area were automatically cropped on the basis of YOLO detections and then scaled to size 512 × 512 (stage B and C in Figure 1). During training, the resized radiographs were fed to the input of the U-Net, whereas corresponding labeled images were fed to the output of the U-Net. Initially, we manually labelled 50 X-rays of which 10 X-rays were included in the validation set to verify the accuracy of bone segmentation, (stage C in Figure 2). The accuracy was assessed using the Dice score[26] (Figure 3).

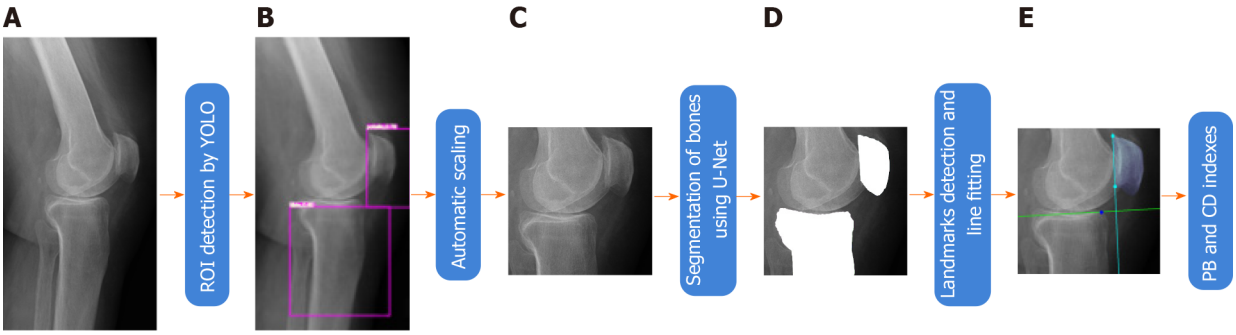

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Figure 1 Flowchart of the proposed method. A: Input radiograph; B: Bones detected by the You Only Look Once; C: Detected region of interest, resized to size 512 × 512; D: Segmented bones by the U-Net; E: Landmarks detected on the patella and line fitted to them (cyan), and line fitted to tibial surface (green). YOLO: You Only Look Once; CD: Caton-Deschamps; ROI: Region of interest.

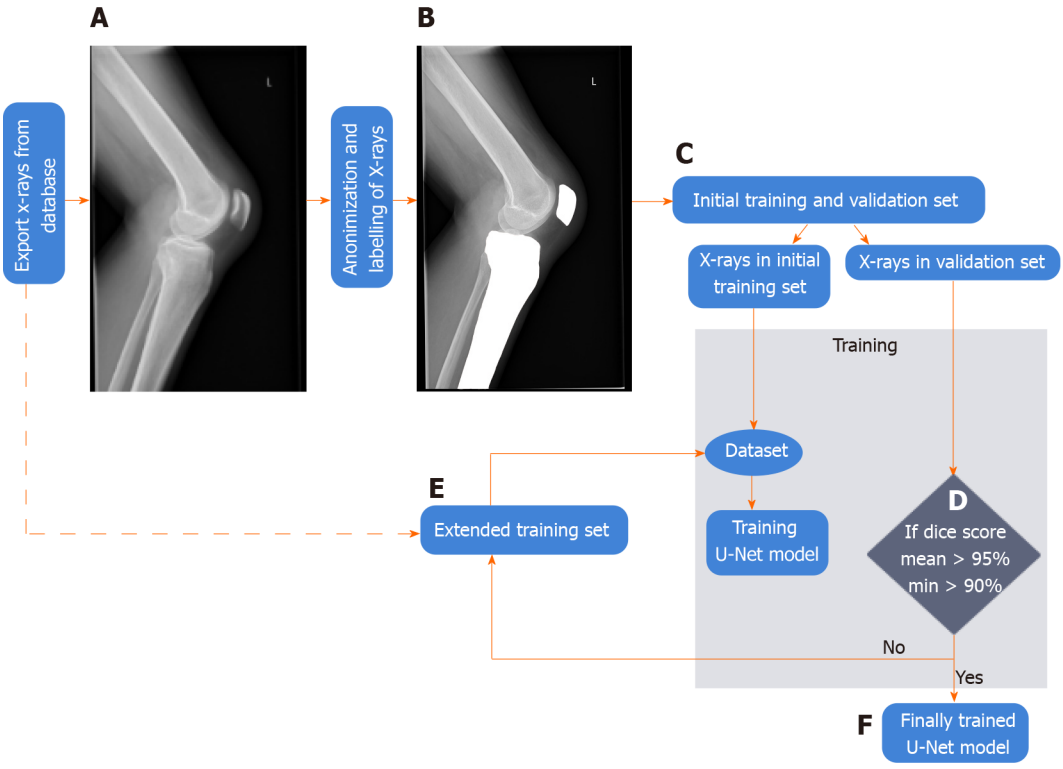

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Figure 2 Flow diagram of the methodology of data collection and training of the U-Net for bone segmentation. A: Radiograms from database; B: Labeled radiograms for training and validation; C: Split of radiograms into training and validation subsets; D: Conditional block for stop the training; E: Extended training set; F: Trained U-Net model.

Training procedure to achieve assumed Dice score

The validation set did not change during the training[27]. The U-Net was initially trained on a dataset consisting of 40 X-rays, which was then extended by 10 subjects to achieve the assumed segmentation quality (stage D in Figure 2). After every extension (by 10 radiographs), the U-Net was trained on the extended data from scratch, and the Dice score was calculated (on the validation set). If it was lower than 90%, the extension of the dataset and training of the network were repeated. If Dice score ≥ 90% was achieved, single radiographs were added to the training subset to gain a Dice score ≥ 95% (with minimal Dice score ≥ 90% for each subject (stage E in Figure 2). After the training, we obtained the final U-Net model and final training set (stage F in Figure 2, stage B in Figure 4). The final U-Net model was utilized to segment bones on the test subset. On the segmented bones we determined the characteristic points as well as necessary lines in order to calculate the patellar height and the indexes (stage D and E in Figure 1, stage C in Figure 4). The person responsible for training and evaluating the neural network has not participated in the manual calculation of the patellar indexes and has not seen the results before the final analysis.

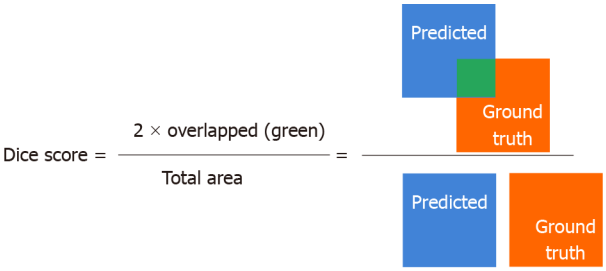

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Figure 3 Dice score calculation used to asses bone segmentation performance.

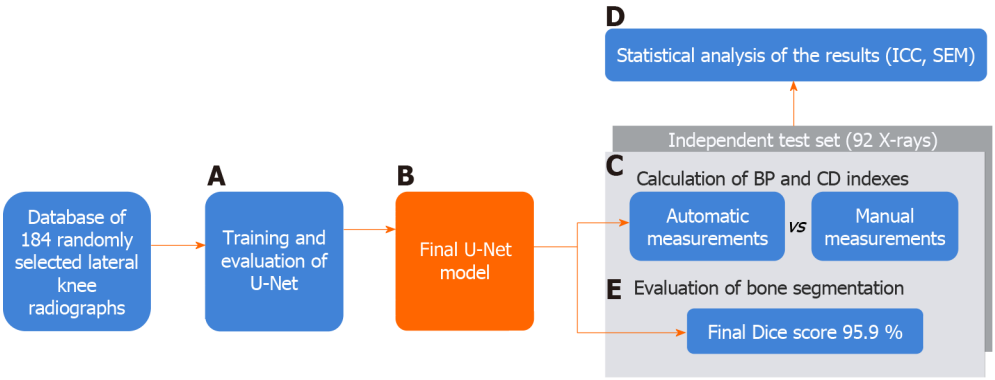

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Figure 4 Flow diagram of patient selection and attaining the required segmentation score. A: Training and evaluation of U-Net; B: Final U-Net model; C: Calculation of blackburne-peel and Caton-Deschamps indexes; D: Statistical analysis; E: Final Dice score. CD: Caton-Deschamps; BP: Blackburne-peel; ICC: Interclass correlation coefficient; SEM: Single measurement.

Algorithm for automated calculation of patellar indexes using segmented bones

The outcomes of the U-Net model (output images with segmented bones - tibia and patella) were used to determine characteristic points and lines (stage E in Figure 1). Articular surface of proximal tibia was automatically determined. Firstly, the anterior corner of the tibial plateau and posterior end-point were determined. Given such boundaries, a line to the points of the proximal tibia joint surface has been fitted. This way the joint line was determined on the basis of many boundary points. An alternative approach would be to determine some landmark points representing articular surface of proximal tibia and then using them to determine the joint line. In contrast to the approach mentioned above, in our approach the joint line is determined more robustly, *i.e.*, on the basis of large number of boundary points segmented by the U-Net. Afterwards, the superior and inferior patellar articular surface endpoints have been determined through simple image analysis, and then used to determine the second line. Finally, these characteristic points and joint lines were automatically used to calculate the CD and the BP[28]. The calculation of the characteristic points and joint lines was done on images with height/ with ratio equal to ROI ratio. The novelty of this research is an innovative approach to estimating joint lines based on the line fitting using automatic bone segmentation (more accurate than method based on the characteristic points, c.f. Discussion Section).

Automatic and manual measurements

We used 92 randomly selected another lateral knee radiographs, collected from the authors' institutional electronic database for the automatic and manual calculations of patellar indexes (stage F in Figure 1; stage C in Figure 4). We carefully examined if there is no overlap of patients (or images) in train/valid and test datasets. Like Lee *et al*[27], we did not create a test set until we had developed the final U-Net model (stage F in Figure 2; stage from B to C in Figure 4). According to Zou *et al*[29], we assumed a minimal number of subjects to estimate the agreement of the measurements between the two methods as 46.

Comparison of measurements

Automatic and manual measurements were performed on 92 X-rays. The computer-generated results were compared with manual measurements performed independently by two orthopedic surgeons (6 and 38 years of experience, stage C in Figure 4). According to the guidelines[30,31], two orthopedic surgeons performed manual measurements of the CD and BP patellar height indexes. They used

Carestream Software ver.12.0 (Carestream Health, United States).

Statistical analysis

Statistical analysis was performed using Statistica 13.1 Software (Tibco Software, United States) and Microsoft Excel 2019 (Microsoft, United States). The intraclass correlation coefficient (ICC) and the standard error for a single measurement (SEM) were calculated for statistical assessment of reliability and compliance of the measurements stage (D in Figure 4). The ICC of 0.4 demonstrates poor, between 0.4 and 0.75 good, and more than 0.75 indicates excellent reliability of the measurements[32].

Accuracy of the bone segmentation of the final U-Net model

The accuracy of bone segmentation (of the final U-Net model) was assessed on the test set to check if the neural network had sufficient generalization capability (whether U-Net could achieve satisfactory results on unknown radiographs). For this evaluation, the X-rays in the test set were manually labelled by the orthopedic surgeon. We compared the Dice scores between the automatically and manually segmented bones (stage E in Figure 4).

Details of image pre-processing, architecture of neural network, and training

Image pre-processing: The labelled images were used for training a U-Net neural network. We designed a U-Net neural network that operates on input images of size 512 × 512 and output images of 512 × 512 with segmented bones. Small holes in automatically segmented bones that can arise from imperfect segmentation were automatically filed.

The architecture and training of neural network

Each U-Net encoder and decoder contained four layers. It has been trained by optimizing Dice loss in 60 epochs using Adam optimizer, learning rate equal to 0.0001, batch size set to 2. During the training a data augmentation consisting of vertical mirroring of images and scaling of images have been executed. The neural network has been trained on the notebook's GPU (RTX3070 GPU, 6GB RAM). Phyton language was utilized to implement the whole algorithm, the U-Net as well as the YOLO (using Keras API).

RESULTS

At the beginning we evaluated the performance of the trained YOLO in detecting the ROI. We determined mean Average Precision (mAP) on 20 test images. The mAP was equal to 0.962. Figure 5 depicts the detected areas on high-resolution radiographs using YOLO. The rectangles representing the bones of interest were then used to calculate the ROIs.

Finally, 184 randomly selected lateral knee radiographs of the 218 (initially prepared database) were included for the analysis. The mean age of patients was 61.9 (± 17.8) years. There were 65 males (35%) and 119 females (65%). The demographic data of the subgroups of patients are presented in Table 1.

Training and validation of the U-Net

The final training set consisted of 82 X-ray images, as well as 10 X-rays in the validation set (which did not change during the training). To compare the reliability of automatic and manual measurements, 92 randomly selected lateral radiographs of the knee in the test set were used.

Comparison of automated and manual measurements

The mean value of CD indexes calculated by orthopedic surgeon (R#1 and R#2) was 0.93 (± 0.19) and 0.89 (± 0.19). For BP indexes it was 0.80 (± 0.17) and 0.78 (± 0.17). Automatic measurements performed by the artificial intelligence (AI) for CD index was 0.92 (± 0.21) and for BP index was 0.75 (± 0.19) (Table 2).

The accuracy of image segmentation performed on the test set was 95.9% (± 1.26). The range of Dice score for individual X-ray images varied from 90% to 97.8% (Figure 6). This result demonstrates that even on a small amount of training data, it is possible to achieve a satisfactory segmentation quality with good generalization on unknown test radiographs that can be used in everyday clinical practice. Our research findings align with Ronneberger *et al*'s conclusions, which pointed out that it is possible to train the U-Net model on very few annotated images[25]. On Google Colab (using CPU) the time needed for the measurement of the patella height on 20 radiographs was equal to about 240 s.

DISCUSSION

This proposed method uses a U-Net to segment bones making the patellofemoral joint and subsequently measures the Caton-Deshamps and Blackburne-Peel patellar height indexes. Our study revealed that

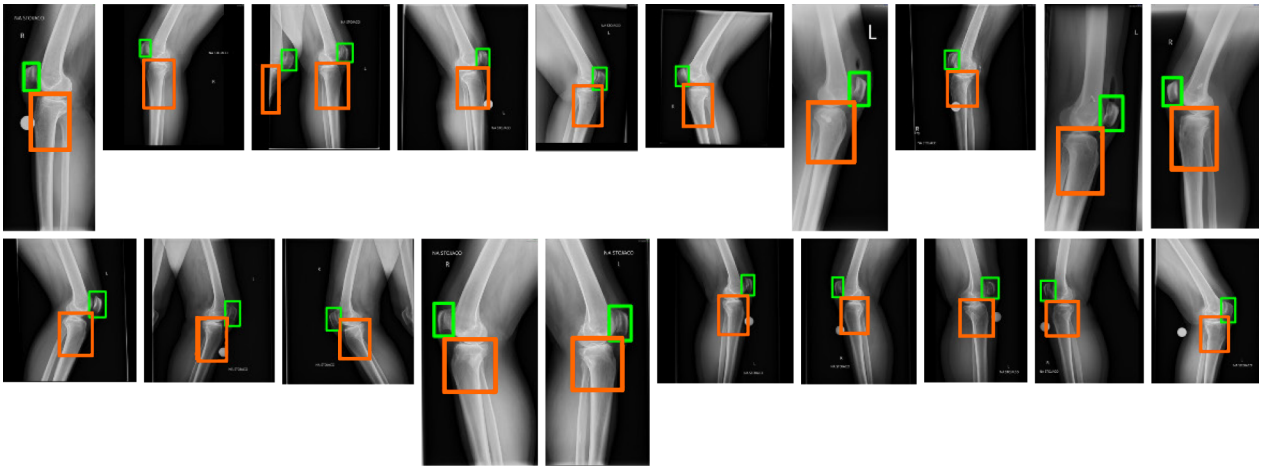
Table 1 Demographic information among the training and testing groups

	Total (*n* = 184)	Training group (*n* = 82)	Validation group (*n* = 10)	Testing group (*n* = 92)
Males/Females	65/119	26/56	4/6	35/57
Left/Right knee	99/85	47/35	3/7	49/43
Age (yr)	61.9 ± 17.83	64.0 ± 17.62	53.7 ± 11.21	61.1 ± 18.37

Table 2 The results of patellar height indexes calculated by two orthopedic surgeons and those achieved by artificial intelligence (based on a deep learning algorithm and neural network)

	CD index	BP index
Orthopedic surgeon (R#1)	0.93 ± 0.19	0.80 ± 0.17
Orthopedic surgeon (R#2)	0.89 ± 0.19	0.78 ± 0.17
Artificial intelligence	0.92 ± 0.21	0.75 ± 0.19

R#1: Senior specialist; R#2: Younger specialist; CD: Caton-deschamps; BP: Blackburne-Peel. Results of indexes are presented as means ± SD.



DOI: 10.5312/wjo.v14.i6.387

Figure 5 Detected bones (patella and proximal tibia) on high-resolution radiographs using You Only Look Once.

automatic bone segmentation of lateral knee radiographs can be performed with the Dice score of 95.9% (± 1.26). Additionally, a novel approach to automatic estimation of patellar indexes has been proposed. The key points and lines needed for measuring the patellar height indexes were automatically determined based on automatically segmented patella and tibia. Excellent reliability between AI calculations and those performed by orthopedic surgeons for CD [R#1 *vs* AI: ICC = 0.86 (± 0.38), SEM = 0.015; R#2 *vs* AI: ICC = 0.80 (± 0.33), SEM = 0.013] and BP [R#1 *vs* AI: ICC = 0.88 (± 0.38), SEM = 0.015; R#2 *vs* AI: ICC = 0.79 (± 0.32), SEM = 0.014] were obtained (Table 3, Figure 7).

For comparison, a method for patella segmentation[20] uses the principal component analysis to construct a patella shape model and a dual-optimization approach with genetic algorithm and Active Shape Model to fit the model to the patella boundary. The method has been tested on 20 images. However, this method segments only the patella and requires manually cropped images in which the patella occupies considerable part of the images. In a recently proposed method[21], a convolutional neural network was used to detect landmark points to measure patellar indexes. The detection was performed by a pretrained VGG-16 neural network. It has been trained and evaluated on 916 and 102 images, respectively, with manually annotated landmarks. The method has been evaluated on 400 radiographs. The ICC, Pearson correlation coefficient, mean absolute difference, Root Mean Square and Bland-Altman plots have been calculated to compare this method with manual measurements. However, the method operates on images with the patella and the proximal tibial articular occupying considerable part of the images, *i.e.* it is not fully automatic as the ROI was manually cropped from the high-resolution x-ray images. Moreover, only radiographs with clear patellar height landmarks have been utilized in experiments.

Table 3 Reliability assessed with the use of interclass correlation coefficient (± SD) and single measurement among the interobserver measurements

	ICC	SEM
CD index		
R#1 *vs* AI	0.86 ± 0.38	0.015
R#2 *vs* AI	0.88 ± 0.38	0.015
BP index		
R#1 *vs* AI	0.80 ± 0.33	0.013
R#2 *vs* AI	0.79 ± 0.32	0.014

R#1: Senior specialist; R#2: Younger specialist; AI: Artificial intelligence; SEM: Single measurement; CD: Caton-deschamps.

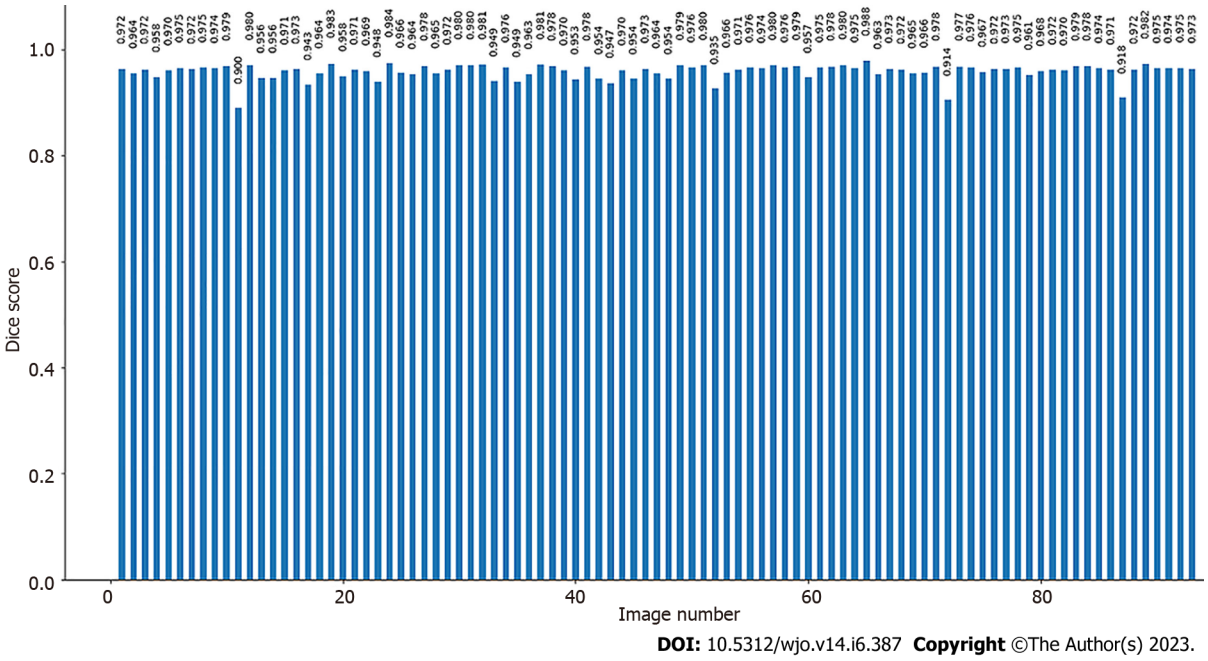


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Figure 6 Distribution of dice score results for test images (92 subjects).

The method of Ye *et al*[21] relies on keypoints, which needs far bigger number of annotated radiographs for training the network. In contrast, our work is in line with recent research direction which focuses on training deep models on small datasets. It is worth noting that this is an important aspect as acquiring and labeling medical data is expensive, among others due to privacy concerns. In contrast to keypoint-based methods, our method relies on a large number of boundary points, making it more resistant to outliers and errors (through boundary-aware analysis). Our initial experimental results show that even in the case of training a neural network for keypoints regression on several times larger number of labeled images, the errors are much larger in comparison to the errors of our method. The method is fully automatic as the YOLO detects bones making the patellofemoral joint on high-resolution images, U-Net segments the bones, a line is fitted to the segmented proximal tibial articular surface, and a second line passing through two landmarks detected on the segmented patella are determined. Then they are used to calculate the patellar height indexes. However, good technical execution and sufficient quality of the input images are mandatory to obtain reliable results for automatic measurements. In some specific cases, additional hardware (screws, plates), heterotopic ossifications, large osteophytes that distort the bone outline and oblique view (instead of proper lateral), may slightly reduce quality of bone segmentation, which is the main limitation of this method. We agree with Zheng *et al*[33], who emphasized that absolute errors may be reduced by increasing the number of subjects in the training group.

Strengths, limitations and future work

Our algorithm for automatic measurements of patellar indexes permits the evaluation of indexes on

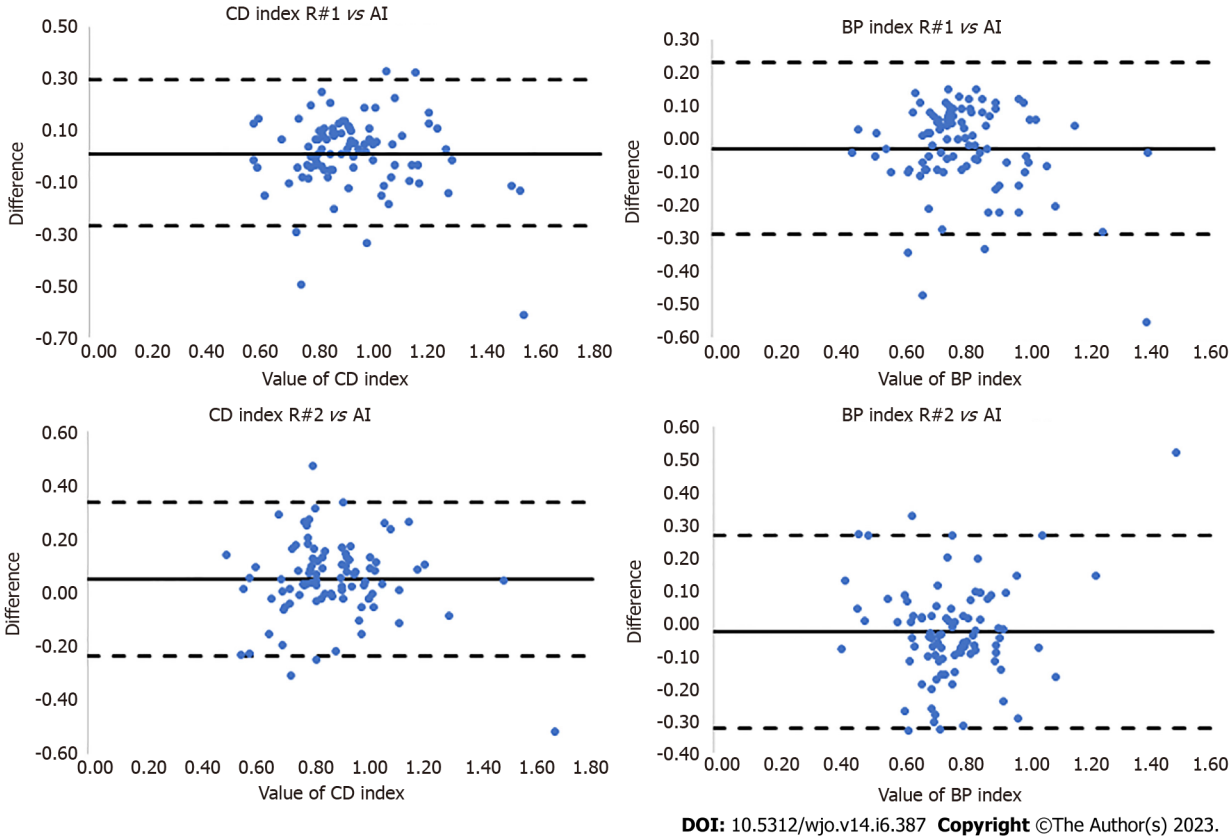

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Figure 7 Bland-Altman plots illustrating the differences between R#1 *vs* artificial intelligence (AI) and R#2 *vs* AI for Caton-Deschamps and Blackburne-Peel indexes. Continuous lines represent a mean (bias), dashed lines represent +2 and -2 SD values. BP: Blackburne-peel; CD: Caton-deschamps; AI: Artificial intelligence.

high data volume. Taking into account that the proposed algorithm allows measurements on high-resolution radiographs, low effort is needed to get patellar indexes, *i.e.* no manual cropping of knee region is required in contrast to the previous methods. One of the advantage of the proposed method is that relatively small amount of manually labelled bones on images is needed to achieve reliable bone segmentation. Although, higher number of manual annotations for training YOLO responsible for knee detection is needed, the labelling of knee regions can be done in relatively short time. This study has some limitations. Firstly, in the current study, the ROIs that were determined on the basis of YOLO detections were resized to size required by the U-Net, *i.e.*, 512 × 512. This means that the keypoints and lines were determined on images with somewhat smaller resolution than the original radiographs. Secondly, the accuracy of the results depends on: The manual segmentation performed by the researcher during the training phase; the amount and quality of training data, and the architecture of the applied neural network. In current work, the training of neural networks and evaluation of the algorithm was performed on images acquired in a single institution, *i.e.* our hospital. Thus, further work is needed to collect radiographs from various hospitals to train networks and asses accuracy of the algorithm on radiograms acquired by different devices. Moreover, the input images may have different levels of intensity and quality. These technical aspects should be emphasized and resolved in medical centers that will implement the algorithm for automatic measurement of patellar indexes. In future work we are planning to combine boundary-aware analysis with landmark-based DL measurements. We also plan to extend the U-Net and compare it with recent networks for image segmentation. Additionally images from different hospitals will be used in the research.

CONCLUSION

The aim of this study was to investigate the reliability of automated patellar height estimation using DL-based bone segmentation and detection on high-resolution images. It showed that reliable automatic patellar height measurements can be achieved on lateral knee radiographs with the accuracy required for the clinical practice. We demonstrated that proximal tibia and patella bones can be segmented precisely (Dice score greater than 95%) by U-Net neural network on knee regions automatically detected by the YOLO network (mean Average Precision mAP greater than 0.96). Determining patellar end-points and the joint line by fitting to points of the proximal tibia joint surface enables calculating the

Caton-Deschamps and Blackburne-Peel indexes with very good reliability. Automated measurements are comparable to measurements performed by orthopedic surgeons (SEM greater than 0.75). Experimental results indicate that our approach can be valuable as a pre-operative and potentially as a postoperative assessment tool for big volume data analysis in medical practice.

ARTICLE HIGHLIGHTS

Research background

Recent advancements in artificial intelligence and deep learning have contributed to the development of medical imaging techniques, leading to better interpretation of radiographs. Moreover, there is an increasing interest in automating routine diagnostic activities and orthopedic measurements.

Research motivation

The automation of patellar height assessment using deep learning-based bone segmentation and detection on high-resolution radiographs could provide a valuable tool in medical practice.

Research objectives

The aim of this study was to verify the accuracy of automated patellar height assessment using a U-Net neural network and to determine the agreement between manual and automatic measurements.

Research methods

Proximal tibia and patella was segmented by U-Net neural network on lateral knee subimages automatically detected by the You Only Look Once (YOLO) network. The patellar height was quantified by Caton-Deschamps and Blackburne-Peel indexes. The interclass correlation coefficient and standard error for single measurement were used to calculate agreement between manual and automatic measurements.

Research results

Proximal tibia and patella were segmented with 95.9% accuracy by the U-Net neural network on lateral knee subimages automatically detected by the YOLO network (mean Average Precision mAP greater than 0.96). Excellent agreement achieved between manual and automatic measurements for both indexes (interclass correlation coefficient > 0.75, SEM < 0.014).

Research conclusions

Automatic patellar height assessment can be achieved with high accuracy on high-resolution radiographs. Proximal tibia and patella can be segmented precisely by U-Net neural network on lateral knee subimages automatically detected by the YOLO network. Determining patellar endpoints and fitting the line to the proximal tibia joint surface enables accurate Caton-Deschamps and BP index calculations, making it a valuable tool in medical practice.

Research perspectives

Future research can focus on the clinical implementation of this automated method, which has the potential to enhance diagnostic accuracy, reduce human error, and improve patient outcomes.

FOOTNOTES

Author contributions: Kwolek Ka, Grzelecki D, Tyrakowski M designed research; Kwolek Ka, Kwolek Ko performed research; Kwolek Ka, Kwolek Ko elaborated analytic tools, Kwolek Ka, Tyrakowski M, Kowalczewski J, Marczak D analyzed data; Kwolek Ka, Dariusz G, Kwolek Ko, Tyrakowski M wrote the paper.

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Institutional animal care and use committee statement: No animals were used in the study.

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ORIGINAL ARTICLE

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Two surgical pathways for isolated hip fractures: A comparative study

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Abstract

BACKGROUND

Hip fractures (HF) are common among the aging population, and surgery within 48 h is recommended. Patients can be hospitalized for surgery through different pathways, either trauma or medicine admitting services.

AIM

To compare management and outcomes among patients admitted through the trauma pathway (TP) *vs* medical pathway (MP).

METHODS

This Institutional Review Board-approved retrospective study included 2094 patients with proximal femur fractures (AO/Orthopedic Trauma Association Type 31) who underwent surgery at a level 1 trauma center between 2016-2021. There were 69 patients admitted through the TP and 2025 admitted through the MP. To ensure comparability between groups, 66 of the 2025 MP patients were

propensity matched to 66 TP patients by age, sex, HF type, HF surgery, and American Society of Anesthesiology score. The statistical analyses included multivariable analysis, group characteristics, and bivariate correlation comparisons with the χ^2 test and *t*-test.

RESULTS

After propensity matching, the mean age in both groups was 75-years-old, 62% of both groups were females, the main HF type was intertrochanteric (TP 52% *vs* MP 62%), open reduction internal fixation was the most common surgery (TP 68% *vs* MP 71%), and the mean American Society of Anesthesiology score was 2.8 for TP and 2.7 for MP. The majority of patients in TP and MP (71% *vs* 74%) were geriatric (≥ 65-years-old). Falls were the main mechanism of injury in both groups (77% *vs* 97%, $P = 0.001$). There were no significant differences in pre-surgery anticoagulation use (49% *vs* 41%), admission day of the week, or insurance status. The incidence of comorbidities was equal (94% for both) with cardiac comorbidities being dominant in both groups (71% *vs* 73%). The number of preoperative consultations was similar for TP and MP, with the most common consultation being cardiology in both (44% and 36%). HF displacement occurred more among TP patients (76% *vs* 39%, $P = 0.000$). Time to surgery was not statistically different (23 h in both), but length of surgery was significantly longer for TP (59 min *vs* 41 min, $P = 0.000$). Intensive care unit and hospital length of stay were not statistically different (5 d *vs* 8 d and 6 d for both). There were no statistical differences in discharge disposition and mortality (3% *vs* 0%).

CONCLUSION

There were no differences in outcomes of surgeries between admission through TP *vs* MP. The focus should be on the patient's health condition and on prompt surgical intervention.

Key Words: Isolated hip fractures; Admitting service; Trauma center; Time to surgery; American Society of Anesthesiologists score; Preoperative consultations

Core Tip: We evaluated 2094 hip fracture patients admitted for surgery to a level 1 trauma center over a 5-year period. Patients were stratified based on the admitting service, either trauma or medical. After a propensity score matching comparison of 66 patients in each group it was revealed that there was no difference in outcomes. Predictors of a prolonged hospital length of stay were increased American Society of Anesthesiology score and delayed time to surgery. Predictors of mortality were increased American Society of Anesthesiology score and increased age. The health condition of the patient, but not the admitting service, was the defining factor for management and outcomes.

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INTRODUCTION

As life expectancy rises around the world along with the number of elderly individuals, the incidence of hip fractures (HF) is estimated to reach 6.3 million in 2050[1]. Each year in the United States alone over 300000 people aged 65 and older are hospitalized for HF[2-4].

Patients can be hospitalized for operative fixation of HF through different pathways, including trauma, orthopedic, and medicine admitting services[5-8]. In the studies comparing surgical *vs* nonsurgical pathways it has been reported that the admitting service can affect the management patterns and outcomes of patients with HF[5,6,9].

For example, in one study by Greenberg *et al*[5], the authors determined that patients with HF admitted to the medicine service had longer hospital stays than patients admitted to the orthopedic service, even after controlling for demographics and preoperative comorbidities. A 2018 study by Lott *et al*[6] also concluded that patients with HF admitted to the medicine service had longer lengths of stay (LOS) and more complications compared to patients admitted to the trauma/orthopedic service. In contradiction to these conclusions, other studies determined that there were no differences in complication rates or LOS between the admitting services[8,10].

The impact of preoperative pathways on the outcomes was previously addressed in diverse cohorts of patients, which differed in inclusion/exclusion criteria such as age, hospital settings, mechanism of injury, preoperative medication, or surgical management[7,8,10-12]. The rationale for our study was the existing controversy over which hospital service is best suited for the optimal admission process for patients with HF and associated with the best outcomes.

At our institution patients with HF can be admitted through the Emergency Department or through the Trauma Department depending on how they are transported to the hospital by the first responders. If the patient is admitted through the Emergency Department, the hospitalist or internal medicine physician will admit the patient to the Medical Service. If the patient is admitted through the Trauma Department, the trauma surgeon will admit the patient to the Trauma Service. After a radiographic confirmation of a HF, a consultation of the orthopedic surgeon is requested by the admitting service. After admission to either service, the internal medicine physician or the trauma surgeon may request additional consultations if necessary for preoperative clearance.

We analyzed the clinical characteristics and outcomes of patients admitted for HF surgery through trauma services and compared to those admitted through medical services.

MATERIALS AND METHODS

This Institutional Review Board-approved retrospective cohort study was granted a waiver of informed consent and included 2094 adult patients (≥ 18-years-old) with HF who underwent operative fixation at an urban level 1 trauma center between January 1, 2016 and May 31, 2021. All patients presented with AO/Orthopedic Trauma Association fracture Type 31A-C[13]. Patients with other traumatic, non-orthopedic injuries requiring surgical intervention, including head, thoracic, or abdominal injuries were excluded. Additional exclusion criteria were: In-hospital HF; patients with pathologic fractures; periprosthetic fractures; open fractures; previous fracture; or surgery at the current fracture site.

Patients were stratified in two groups based on the admitting service: Those who were admitted through the trauma pathway (TP) of the level 1 trauma center (n = 69); and those who were admitted through the medical pathway (MP) (n = 2025).

To ensure comparability between groups, propensity matching by age, sex, type of HF, type of HF surgery, and American Society of Anesthesiology (ASA) score was performed, which resulted in 66 patients in each group for comparison (Figure 1). In the propensity matching process there were 3 TP patients who did not match and therefore were excluded from the comparison.

Analyzed variables included age, sex, body mass index, mechanism of injury, Glasgow Coma Score, comorbidities, pre-injury anticoagulation use, ASA score, insurance status, admission day of the week, number of preoperative consultations, type of HF, presence of fracture displacement, time to surgery, time of surgery, type of HF surgery, intensive care unit and hospital lengths of stay (ICULOS, HLOS), discharge disposition, and mortality. We also analyzed the weekend effect of admissions in the propensity matched groups.

Variables were identified *via* the International Classification of Diseases 9th and 10th edition and extracted from patient's electronic medical records. Geriatric age was defined as 65 years or older[14]. Weekend effect was defined as any of the following due to admission from Friday to Sunday: A longer time to surgery; longer HLOS; or higher mortality[12,15-17]. Extended HLOS was defined as more than 6 d. This number was based on our data and the commonly reported HLOS for patients with HF[3,18-20].

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics software version 23.0 (IBM, Armonk, NY, Untied States). Propensity score matching was completed without replacement, with a 0.2 caliper and with a randomized order of patients while drawing matches, which resulted in a one-to-one paired selection. The analyses included group characteristics and bivariate correlation comparisons. Categorical variables were analyzed with the χ^2 test. Variable means were analyzed using independent samples t-test and Mann Whitney U test. Multivariable analysis for the predictors of extended LOS and mortality was performed in the total population. Receiver operating characteristic (ROC) area under the curve analysis was used to determine threshold values for extended length of stay and mortality prediction variables. One way analysis of variance was used for the analysis of age and HLOS by ASA score. Statistical significance was assumed when the calculated P value was below 0.05.

RESULTS

Over the duration of 65 mo, 2094 patients with HF were admitted for surgical repair: 69 (3.3%) patients through TP; and 2025 (96.7%) through MP.

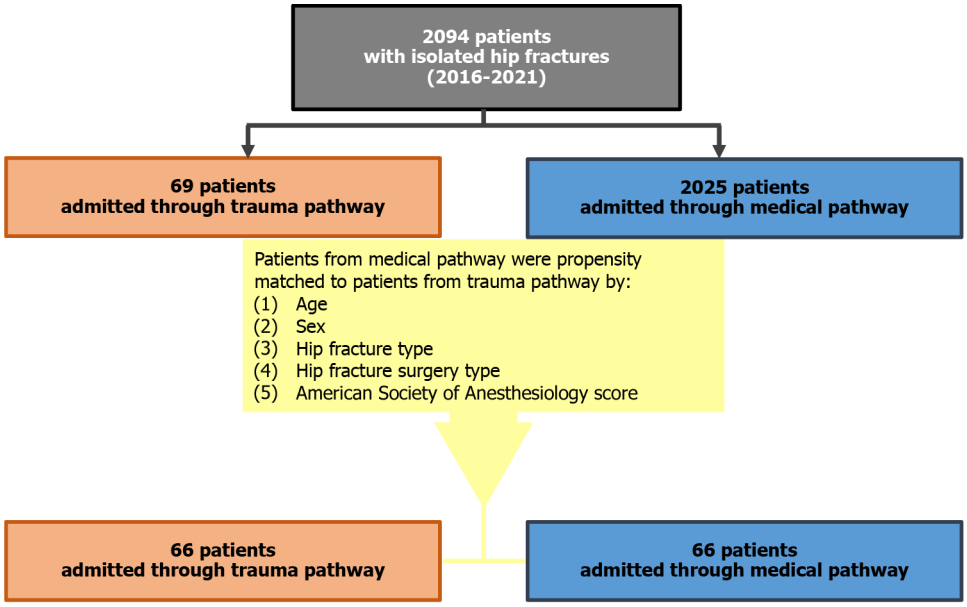

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Figure 1 Study design and flow chart of all patients with hip fractures.

General comparison

The general comparison between all TP and MP patients is presented in Table 1. MP patients were older and included more geriatric patients; however, geriatric patients comprised more than two-thirds of each group. Falls were the prevailing mechanism of injury in both groups, comprising at least 74% in each group. The analyzed cohorts had slightly different types of HF. There were no differences in sex, admission day, ASA score distribution, time to surgery, type of HF surgery, HLOS, discharge disposition, and mortality.

Multivariable analysis and ROC analysis showed that increased ASA score and extended time from admission to surgery were two statistically significant predictors for the extended HLOS. The significant predictors for mortality were age > 83 (P = 0.000, odds ratio: 6.0) and ASA score ≥ 4 (P = 0.000, odds ratio: 5.1). The threshold values were based on the ROC curve with area under the curve or concordance index of 0.697 (95% confidence interval: 0.640-0.755) and 0.698 (95% confidence interval: 0.630-0.765).

Propensity matched comparison

The comparison of propensity matched patients, 66 TP and 66 MP, is presented in Table 2. Propensity matched TP patients had statistically higher motor vehicle collisions as a mechanism of injury (falls were still the prevailing mechanism of injury in more than three-quarters of patients in both groups), a higher presence of HF displacement, more requests for neurological consultation, and a longer duration of surgery.

There were no differences between the groups in body mass index, comorbidities, anticoagulation use, admission day, number of consultations before surgery, insurance status, and mean time from admission to HF surgery. An additional analysis of the time from admission to surgery through TP and MP divided in 12-h increments is presented in Figure 2. At any 12 h interval, the number of patients in the TP and MP groups was similar, with two-thirds (63.6% in TP and 66.7% in MP) having surgery within 24 h and over 90% (95.5% in TP and 93.9% in MP) having surgery within 48 h of admission.

The two groups had comparable ICULOS and HLOS. The similar distribution of HLOS in propensity matched TP and MP is shown in Figure 3. The discharge disposition and mortality were also comparable. The 2 expired patients in the TP group were 87-years-old and 96-years-old. One patient had renal failure and was discharged to hospice. The other patient had a cardiac arrest during surgery.

Within the propensity matched TP group there were 41 patients admitted on a weekday and 25 patients admitted on a weekend. The two sub-groups had comparable time to surgery (22.8 h *vs* 22.5 h, P = 0.926), HLOS (5.6 d *vs* 7.6 d, P = 0.130), and mortality (2.4% *vs* 4.0%, P = 0.720). Within the propensity matched MP group there were 37 patients admitted on a weekday and 29 patients admitted on a weekend. The two sub-groups had comparable time to surgery (21.7 h *vs* 24.7 h, P = 0.490) and HLOS (5.3 d *vs* 6.9 d, P = 0.239). There was no mortality in the MP sub-groups.

Mean age and HLOS stratified by ASA score in the different patient groups is presented in Table 3. One way analysis of variance demonstrated that in the total population, age and HLOS both increased significantly (both P = 0.000) as ASA increased. In the propensity matched TP population, age increased significantly (P = 0.001) as ASA increased from 2 to 4. Higher ASA was associated with older age and longer HLOS.

Table 1 General comparison between all trauma pathway and medical pathway patients, *n* (%)

Variable	Trauma, *n* = 69	Medicine, *n* = 2025	*P* value
Age in yr	72.9 (17.5)	83.2 (9.2)	0.000[a]
Geriatric	47 (68.1)	1928 (95.2)	0.000[a]
Sex, female/male	44 (63.8)/25 (36.2)	1367 (67.5)/658 (32.5)	0.515
Mechanism of injury	-	-	0.000[a]
Fall	51 (73.9)	2005 (99.0)	-
MVC	18 (26.1)	11 (0.5)	-
Stress fracture	0 (0.0)	9 (0.4)	-
Admission day	-	-	0.171
Monday	10 (14.5)	317 (15.7)	-
Tuesday	12 (17.4)	281 (13.9)	-
Wednesday	16 (23.2)	268 (13.2)	-
Thursday	5 (7.2)	311 (15.4)	-
Friday	10 (14.5)	297 (14.7)	-
Saturday	7 (10.1)	276 (13.6)	-
Sunday	9 (13.0)	275 (13.6)	
Hip fracture type	-	-	0.000[a]
Femoral neck/head	28 (40.6)	972 (48.0)	-
Intertrochanteric	35 (50.7)	1020 (50.4)	-
Intertrochanteric with subtrochanteric	6 (8.7)	33 (1.6)	-
Hip surgery type	-	-	0.205
Total arthroplasty	4 (5.8)	177 (8.7)	-
Hemi arthroplasty	15 (21.7)	613 (30.3)	-
Open reduction and internal fixation	47 (68.1)	1116 (55.1)	-
Pinning	3 (4.3)	119 (5.9)	-
ASA score before hip surgery	2.8 (0.6)	2.9 (0.6)	0.044[a]
ASA score before hip surgery	-	-	0.079
I	1 (1.4)	9 (0.4)	-
II	21 (30.4)	393 (19.4)	-
III	41 (59.4)	1393 (68.8)	-
IV	6 (8.7)	230 (11.4)	-
No. of consultations before hip surgery	0.9 (0.9)	0.9 (0.8)	0.620
Time: Admission to hip surgery in h	23.0 (13.4)	27.0 (28.5)	0.255
Hospital length of stay in d	6.3 (4.4)	5.7 (4.9)	0.347
Mortality	2 (2.9)	62 (3.1)	0.938
Hospital disposition	-	-	0.068
Skilled nursing facility	28 (40.6)	1147 (56.6)	-
Rehabilitation	25 (36.2)	589 (29.1)	-
Home	13 (18.8)	212 (10.5)	-
Hospice	1 (1.4)	51 (2.5)	-
Expired in hospital	1 (1.4)	11 (0.5)	-
Long-term acute care facility	1 (1.4)	15 (0.7)	-

[a]*P* < 0.005 denotes significant difference.
ASA: American Society of Anesthesiologists; MVC: Motor vehicle collision; SD: Standard deviation.

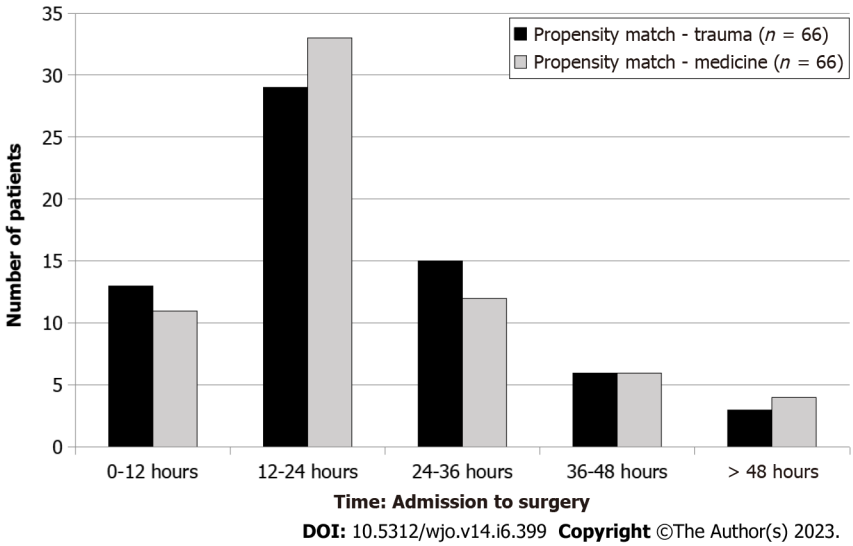

Figure 2 Time from admission to surgery in propensity matched trauma and medical pathway groups in 12 h increments.

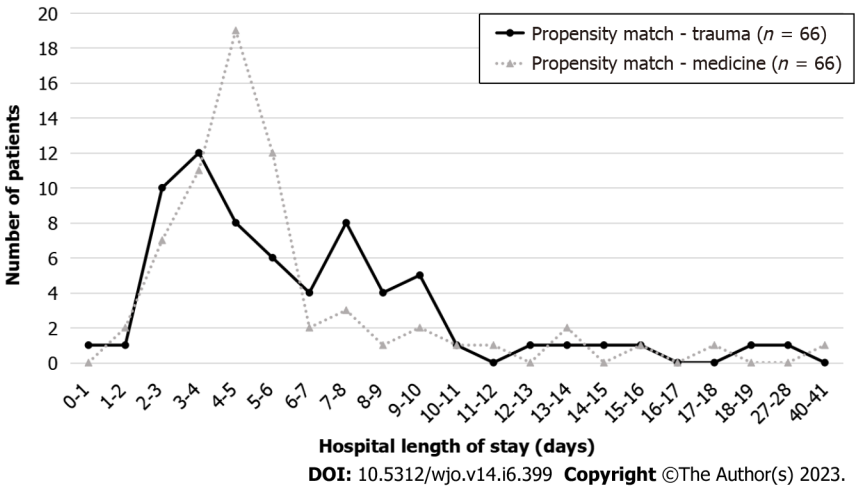

Figure 3 Number of patients in propensity matched trauma and medical pathway groups stratified by hospital length of stay.

DISCUSSION

In studies that relate to different admission pathways and how the admission pathway affects the outcomes in patients with HF, there is a noticeable difference in the age of included patients, ranging from 50-years-old to 75-years-old[7,9-11]. Other inclusion/exclusion criteria also differ significantly, as some HF studies exclude patients undergoing total hip replacement, patients who expired before hospital discharge, patients who were not admitted to a surgical ICU, or include only patients with mechanism of injury as fall or only patients with presurgical transthoracic echocardiography[7,12,17,19,21]. There is also a broad array of different settings ranging from level 1 trauma centers to safety-net and tertiary hospitals[8,19,22,23].

In our study, we utilized propensity score matching to address the imbalance in the characteristics of TP and MP patients, as was recommended by Chuang *et al*[10] in their comparison of medicine *vs* orthopedic service for management of HF. There are only two published studies on patients with HF that utilized the propensity score matching methodology. However, they were conducted to evaluate the impact of preoperative echocardiography[24,25].

Our results indicated that ASA score as a measure of patient's condition is a predictor of a longer HLOS and mortality. Our findings support the conclusions reported by Garcia *et al*[26] that an increase

Table 2 Characteristics of propensity matched patients admitted through the trauma pathway and medical pathways, *n* (%)

Variable	Trauma, *n* = 66	Medicine, *n* = 66	*P* value
Age	75.0 (14.5)	75.0 (13.3)	0.990
Sex, female/male	41 (62.1)/25 (37.9)	41 (62.1)/25 (37.9)	1.000
ASA Score before hip surgery	-	-	0.498
II	19 (28.8)	23 (34.8)	-
III	41 (62.1)	40 (60.6)	-
IV	6 (9.1)	3 (4.5)	-
Hip fracture type	-	-	0.057
Femoral neck/head	27 (40.9)	25 (37.9)	-
Intertrochanteric	34 (51.5)	41 (62.1)	-
Intertrochanteric with subtrochanteric	5 (7.6)	0 (0.0)	-
Hip surgery type	-	-	0.650
Total arthroplasty	4 (6.1)	6 (9.1)	-
Hemi arthroplasty	15 (22.7)	10 (15.2)	-
Open reduction and internal fixation	45 (68.2)	47 (71.2)	-
Pinning	2 (3.0)	3 (4.5)	-
Geriatric	47 (71.2)	49 (74.2)	0.696
BMI	24.9 (6.6)	24.9 (5.0)	0.988
Comorbidities	62 (93.9)	62 (93.9)	1.000
Cardiac comorbidities	47 (71.2)	48 (72.7)	0.846
Anticoagulation	32 (48.5)	27 (40.9)	0.381
Mechanism of injury, Fall/MVC	51 (77.3)/15 (22.7)	64 (97.0)/2 (3.0)	0.001[a]
Admission day	-	-	0.401
Monday	9 (13.6)	7 (10.6)	-
Tuesday	11 (16.7)	8 (12.1)	-
Wednesday	16 (24.2)	10 (15.2)	-
Thursday	5 (7.6)	12 (18.2)	-
Friday	10 (15.2)	13 (19.7)	-
Saturday	7 (10.6)	10 (15.2)	-
Sunday	8 (12.1)	6 (9.1)	-
Glasgow coma score	14.6 (0.8)	15.0 (0.2)	0.000[a]
Hip fracture displacement	50 (75.8)	26 (39.4)	0.000[a]
No. of consultations before hip surgery	1.8 (0.9)	1.7 (0.9)	0.198
Consultations before surgery	-	-	-
Cardiology	29 (43.9)	24 (36.4)	0.375
Neurology/neurosurgery	12 (18.2)	1 (1.5)	0.001[a]
Pulmonology	2 (3.0)	5 (7.6)	0.244
Time: Admission to hip surgery in h	22.7 (12.7)	23.0 (16.9)	0.892
Orthopedic surgery length in h	1.0 (0.6)	0.7 (0.3)	0.000[a]
ICULOS in d	4.5 (4.3)	8.0 (4.6)	0.066
HLOS in d	6.3 (4.5)	6.0 (5.4)	0.709
Mortality	2 (3.0)	0 (0.0)	0.154

Hospital disposition	-	-	0.507
Skilled nursing facility	29 (43.9)	31 (47.0)	-
Rehabilitation	29 (43.9)	26 (39.4)	-
Home	6 (9.1)	9 (13.6)	-
Expired in hospital/hospice	2 (3.0)	0 (0.0)	-
Insurance status	-	-	0.060
Public	48 (72.7)	47 (71.2)	-
Private	10 (15.2)	17 (25.8)	-
Uninsured	8 (12.1)	2 (3.0)	-

[a]$P < 0.005$ denotes significant difference.

ASA: American Society of Anesthesiologists; BMI: Body mass index; HLOS: Hospital length of stay; ICULOS: Intensive care unit length of stay; MVC: Motor vehicle collision; SD: Standard deviation.

Table 3 Mean age and hospital length of stay stratified by American Society of Anesthesiologists score, *n* (%)

ASA, score	All patients, *n* = 2094			Propensity matched trauma group, *n* = 66			Propensity matched medicine group, *n* = 66		
	n %	Age, mean	HLOS, mean	*n*	Age, mean	HLOS, mean	*n*	Age, mean	HLOS, mean
1	10 (0.5)	65.0	5.3	-	-	-	-	-	-
2	414 (19.8)	77.1	4.7	19	65.6	5.8	23	74.0	5.7
3	1434 (68.5)	84.1	5.7	41	77.5	6.5	40	76.4	6.3
4	236 (11.3)	85.8	7.5	6	87.7	6.9	3	64.0	4.4

ASA: American Society of Anesthesiologists; HLOS: Hospital length of stay.

in ASA score has a strong association with an increased LOS in elderly patients with HF. Our observations are also in compliance with reports that the ASA score is associated with mortality, LOS, and time to surgery[17,27,28]. Mok *et al*[28] correspondingly recommended that ASA score be added as a criterion for allocation of high-risk patients with HF and for indicating the appropriate admitting service.

In our study, the average number of consultations per patient was similar in all groups. Cardiology was the most common consultation in the TP and MP cohorts. While cardiac comorbidities were registered in approximately 70% of patients, cardiology consultations were implemented in only around 40% of patients. Our data are remarkably similar to that recently reported by Hoehmann *et al*[19], with a 44.4% rate of cardiology consultations in patients with HF in a geriatric population of 65 years and older. Neurology was the second most common consultation in TP patients, while pulmonology was the second most common in MP patients. Having a similar Glasgow Coma Score in both groups and having excluded traumatic brain injury patients, the higher rate of neurological consultations in TP patients may be a result of precaution, attributed to the higher number of motor vehicle collisions as a mechanism of injury.

Surgical intervention for HF is recommended within 48 h[29,30]. Recent studies indicate that surgery within 24 h of admission is associated with shorter HLOS or mortality[31-33]. Delaveau *et al*[11] also recommended "early" surgery within 24 h of admission in orthogeriatrics. Two-thirds of our patients underwent hip surgery within 24 h of admission, and the majority of patients were geriatric. In our study, less than 5% of patients had surgery later than the recommended 48 h benchmark, compared to 9.5% in the report from level I and II trauma centers by deMeireles *et al*[7] and compared to 16.3% in the review of the National Trauma Data Bank by Bhatti *et al*[2] that included level I-IV trauma centers and other hospitals. Our findings support the notion that a longer time to surgery is correlated with extended HLOS. The longer time of orthopedic surgery in our TP patients can be attributed to displaced HF occurring more often.

Elkbuli *et al*[9] in his comparison conducted in a similar setting to ours found that patients with isolated HF admitted to a surgical service had shorter ICULOS and that mortality did not differ from the nonsurgical admission pathway. However, nonsurgical admission patients were younger. In our propensity matched comparison study, mortality was also not statistically different. ICULOS tended to be shorter in TP patients, but the difference did not reach statistical significance. However, our patients

were propensity matched by age.

Our data did not show the weekend effect reported by others, as there was no delay of surgery, longer HLOS, or higher mortality[15,16,34,35]. Our observations were in line with reports by Nijland *et al*[12] and Yeo *et al*[22] who also did not find the weekend effect.

The distribution of insurance types between TP and MP patients did not show statistical significance. However, it seems that there was a trend towards less insured patients in TP. In the study by Bhatti *et al* [2] there was no difference in repair times for patients with public insurance or no insurance when compared to patients with private insurance.

The main conclusion of our study was that the health condition of the patient, but not the admitting service, was the defining factor in the management and outcomes of patients with HF. Our conclusion was similar to a recent report by Bauman *et al*[8] concluding that the severity of illness impacts the outcomes more than the admitting service.

In an analysis of geriatric patients with isolated HF as a result of a fall surgically treated at 35 level 1 or level 2 trauma centers, deMeireles *et al*[7] did not find an association between the admitting service and mortality or hospice discharge. However, they found that it was the comorbidity burden that correlated with an increased risk of mortality.

Limitations

This study had limitations that must be considered when interpreting the results. The retrospective nature of this study brings up deficiencies in prerecorded data and the assessments available for extraction and analysis. Although collection of data was completed for a considerable amount of time, the records of only one hospital were analyzed.

CONCLUSION

There were no notable differences in the management and outcomes between patients who underwent HF surgery but were admitted through two different pathways (trauma *vs* medicine). Prolonged LOS was associated with an increased ASA score and longer time to surgery, while mortality was associated with an increased ASA score and age. The admission pathway was not the defining factor in the management of patients with HF. The focus should be on the patient's health condition upon admission and a prompt surgical intervention.

ARTICLE HIGHLIGHTS

Research background

Isolated hip fractures (HF) are common, especially among the elderly population, and falls are the main mechanism of injury. Depending on the hospital settings and institutional policies, patients can be admitted for surgery through different pathways (medicine or trauma). There is a scarcity of studies utilizing the propensity score matching methodology in the analysis of the data on this subject.

Research motivation

It has been reported that the admitting service may influence the outcomes of patients with HF. The motivation behind this study were the conflicting conclusions and ongoing debates over which admitting service is associated with better results. We hypothesized that it is necessary to contribute new data and a new outlook to help achieve improvements in the treatment of patients with HF.

Research objectives

To analyze the characteristics and compare the outcomes of similarly injured patients with HF admitted through trauma *vs* medicine service at an urban level 1 trauma center.

Research methods

This was a retrospective cohort study. Patients with HF were divided into two groups based on the admitting service: Trauma *vs* medicine. Propensity score matching was utilized to ensure comparability between the groups. Patients were propensity matched by age, sex, HF type and surgery, and the American Society of Anesthesiology score. The statistical analyses included group characteristics, bivariate correlation comparisons, multivariable analysis, and one way analysis of variance.

Research results

Time to surgery, time in the intensive care unit, hospital length of stay, discharge disposition, and mortality were not statistically different between the two groups. The average number of preoperative consultations was similar in both groups with cardiology consultation being the most common. Higher

American Society of Anesthesiology score was associated with a longer hospital stay and mortality.

Research conclusions

The health condition of the patient, but not the admission pathway, is the defining factor in the management and outcomes of patients with HF.

Research perspectives

Research should be conducted across multiple medical centers to include larger cohorts with more focus on predictors of adverse outcomes as well as the potential cost differences between the admission pathways.

FOOTNOTES

Author contributions: Fokin AA and Weisz RD conceptualized the research study; Fokin AA, Wycech Knight J, Puente I, and Weisz RD designed the methodology; Fokin AA, Puente I, and Weisz RD were the project administrators and supervisors; Wycech Knight J, Darya M, and Stalder R performed the research; Wycech Knight J performed the software analysis; Fokin AA, Wycech Knight J, Darya M, Stalder R, Puente I, and Weisz RD performed formal data analysis and validation; Fokin AA, Wycech Knight J, Darya M, and Stalder R wrote the original draft of the manuscript; Fokin AA, Wycech Knight J, Darya M, Stalder R, Puente I, and Weisz RD performed manuscript review and editing; and all authors read and approved the final manuscript.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Surgical and long-term functional outcomes of patients with Duchenne muscular dystrophy following spinal deformity correction

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Abstract

BACKGROUND

Life expectancy in patients with Duchenne muscular dystrophy (DMD) has improved due to advances in medical care. DMD patients develop progressive spinal deformity after loss of ambulatory function and onset of wheelchair dependence for mobility. There is limited published data on the effect of spinal deformity correction on long-term functional outcomes, quality of life (QoL), and satisfaction in DMD patients.

AIM

To investigate the long-term functional outcomes following spinal deformity correction in DMD patients.

METHODS

This was a retrospective cohort study from 2000-2022. Data was collected from hospital records and radiographs. At follow-up, patients completed the muscular dystrophy spine questionnaire (MDSQ). Statistical analysis was performed by linear regression analysis and ANOVA to analyse clinical and radiographic factors significantly associated with MDSQ scores.

RESULTS

Forty-three patients were included with mean age 14.4 years at surgery. Spino-pelvic fusion was performed in 41.9% of patients. Mean surgical time was 352.1 min and mean blood loss was 36% of estimated total blood volume. Mean hospital stay was 14.1 d. Postoperative complications occurred in 25.6% of patients. Mean preoperative scoliosis was 58°, pelvic obliquity 16.4°, thoracic kyphosis 55.8°, lumbar lordosis 11.1°, coronal balance 3.8 cm, and sagittal balance + 6.1 cm. Mean

surgical correction of scoliosis was 79.2% and of pelvic obliquity was 80.8%. Mean follow-up was 10.9 years (range: 2-22.5). Twenty-four patients had died at follow-up. Sixteen patients completed the MDSQ at mean age 25.4 years (range 15.2-37.3). Two patients were bed-ridden and 7 were on ventilatory support. Mean MDSQ total score was 38.1. All 16 patients were satisfied with the results of spinal surgery and would choose surgery again if offered. Most patients (87.5%) reported no severe back pain at follow-up. Factors significantly associated with functional outcomes (MDSQ total score) included greater duration of post-operative follow-up, age, scoliosis postoperatively, correction of scoliosis, increased lumbar lordosis postoperatively, and greater age at loss of independent ambulation.

CONCLUSION

Spinal deformity correction in DMD patients leads to positive long-term effects on QoL and high patient satisfaction. These results support spinal deformity correction to improve long-term QoL in DMD patients.

Key Words: Duchenne muscular dystrophy; Scoliosis; Surgical; Functional; Outcomes

Core Tip: Duchenne muscular dystrophy (DMD) patients develop progressive spinal deformity after loss of independent ambulation. There is limited data on the effect of spinal deformity correction on long-term functional outcomes or satisfaction in DMD patients. This retrospective cohort study investigated long-term functional outcomes following spinal deformity correction in DMD patients, reporting clinical, surgical, radiographic and functional outcomes. All patients were satisfied with surgical outcomes at long-term follow-up. Surgical correction of spinal deformity can have favourable long-term effects on quality of life (QoL) in DMD patients. These results support surgical correction of spinal deformity to improve long-term QoL in DMD patients with spinal deformity.

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INTRODUCTION

Duchenne muscular dystrophy (DMD) is an inherited X-linked disease. Mutations in the Xp21 region of the X chromosome leads to absence of dystrophin resulting in skeletal, respiratory, and cardiac muscle weakness[1,2]. The natural history of untreated DMD is progressive muscle weakness with loss of independent ambulation by 9-10 years of age, as well as progressive cardiomyopathy and respiratory failure[3]. The mean survival in the absence of ventilatory support is 19.5 years[4]. Advances in medical therapy have improved the life expectancy for patients with DMD into their third and fourth decades of life[5]. Patients with DMD develop scoliosis after loss of ambulatory capacity and onset of wheelchair dependence for mobility[6]. The scoliosis is typically a long thoracolumbar C-shaped curve, with at least 85% of DMD patients experiencing a progression of deformity at a mean rate of 2.1° per month[7,8]. Respiratory function, measured by forced vital capacity (FVC), declines after loss of ambulation, and the rate of decline increases with progression of scoliosis[9]. Progressive spinal deformity also results in pelvic obliquity which impairs wheelchair sitting ability[10].

Bracing is ineffective in controlling progression of scoliosis in patients with DMD[10]. Surgical correction of scoliosis is indicated when scoliosis develops; surgical correction of scoliosis aims to correct spinal deformity, pelvic obliquity, and to prevent further curve progression with the aim to improve sitting balance, wheelchair mobility, and quality of life (QoL)[6,10-12]. DMD patients undergoing surgical correction of spinal deformity are at high risk of perioperative morbidity and mortality due to cardiomyopathy, respiratory dysfunction, reactions to anaesthetic agents, soft tissue compromise, osteoporosis, risk of instrumentation failure and prolonged intensive care unit (ICU) admission[6].

There is limited published data on the effect of surgical correction of spinal deformity on long-term functional outcomes, QoL and satisfaction in patients with DMD[13-15]. The aim of this study was to investigate the clinical, surgical and long-term functional results following surgical correction of scoliosis in patients with DMD, and to investigate clinical and radiological factors that predict long-term

functional outcomes following surgery.

MATERIALS AND METHODS

Study population and data collection

We retrospectively reviewed prospectively-collected data of 113 consecutive patients with DMD who were seen in a National Spinal Deformity Service (NSDS) between January 2000 and August 2022; forty-three of these patients (38%) who were wheelchair-dependent underwent correction of spinal deformity by posterior instrumented spinal fusion. All patients had an established diagnosis of DMD prior to referral to the NSDS and were receiving treatment. Indications for surgical correction of spinal deformity included progressive spinal deformity associated with deteriorating pain, sitting ability, function, and ability to provide nursing care. All patients had minimum data available including pre-operative clinical and demographic details, comorbidities, operative details including complications, pre- and post-operative radiographic parameters, and minimum post-surgical follow-up of two years. Exclusion criteria were patients diagnosed with a non-DMD myopathy, patients managed non-operatively, and patients without clinical, demographic, or operative details available for minimum follow-up of two years. Functional outcomes were assessed by the Muscular Dystrophy Spine Questionnaire (MDSQ)[16]. Cause of death was recorded for patients deceased at follow-up. This study was approved by the institutional review board and the requirement for a signed informed consent was waived.

Preoperative assessments

All patients were regularly reviewed in multidisciplinary medical clinics at our institution before and after surgery and assessed in dedicated multidisciplinary pre-assessment anaesthetic-led clinics to optimise their co-morbidities and provide preparation for spinal surgery. Preoperative assessments included overnight sleep studies, as well as anaesthetic, cardiology, dietician, gastroenterology, neurology, physiotherapy, and respiratory team reviews. All patients were wheelchair dependent at the time of referral to the NSDS.

Operative technique

All patients underwent correction of spinal deformity with posterior instrumented spinal fusion with use of hybrid (pedicle hooks/screws, sublaminar wires) or all pedicle screw instrumentation with local autograft and supplemental allograft bone. Pelvic fixation was performed with use of bilateral iliac screws. Intraoperative spinal cord monitoring was performed recording cortical/cervical somatosensory evoked potentials, which remained stable in all patients; transcranial motor evoked potentials were not recorded as none of the patients in the cohort were able to ambulate. Surgical technique also included use of arterial and central venous lines, prophylactic IV antibiotics, cell salvage, urinary catheter, and placement of a nasogastric tube.

Postoperative care

Patients were transferred to the ICU for postoperative care, including haemodynamic support, non-invasive ventilation (NIV), chest physiotherapy, early mobilisation into their wheelchair, and administration of nasogastric feeds. Patients were transferred to a normal ward when medically stable, and discharged to home when oral nutrition, pain control, pulmonary function and wound healing were stable and well-established.

Radiographic measurements

The radiological parameters of scoliosis were measured on spinal radiographs by two authors using digital software (Vue PACS, Carestream Health, United Kingdom) based on consensus agreement on the anatomical landmarks; the mean of the two values was used in the data set for analyses. The same landmarks were used for measurement of the curves on consecutive radiographs. Spinal radiographs were performed including posteroanterior and lateral sitting scoliosis views, and preoperative supine traction views. The following parameters were measured preoperatively and at follow-up: Scoliosis (Cobb angle), scoliosis flexibility index (%): [(Preoperative Cobb angle – supine traction Cobb angle)/(preoperative Cobb angle) × 100], pelvic obliquity (°), pelvic obliquity flexibility index (%): [(Preoperative pelvic obliquity angle – supine traction pelvic obliquity angle)/(preoperative pelvic obliquity angle) × 100], pre- and post-operative lumbar lordosis (T12-S1, °), pre- and post-operative thoracic kyphosis (T1-T12, °), pre- and postoperative sagittal balance (C7 plumb line, cm), pre- and post-operative coronal balance (C7 plumb line, cm), correction of scoliosis (%): [(Preoperative Cobb angle – postoperative Cobb angle)/(preoperative Cobb angle) × 100)], and correction of pelvic obliquity (%): [(Preoperative pelvic obliquity angle – postoperative pelvic obliquity angle)/(preoperative pelvic obliquity angle) × 100)].

Statistical analysis

All data were entered into Microsoft Excel and analysed using XLSTAT (Microsoft Corporation, Washington, United States). Clinical, operative, and both preoperative and postoperative radiographic variables for the patient cohort were analysed for their correlation with MDSQ total scores. Stepwise multiple linear regression analysis was performed to determine which individual quantitative variables correlated with MDSQ total scores. Quantitative variables included postoperative follow-up (years), age at final follow-up (years), age at loss of independent ambulation (years), age at surgery (years), duration of surgery (minutes), intraoperative blood loss (mLs), length of ICU stay postoperatively, total length of hospital stay (days) and radiographic measurements. Qualitative variables were analysed for their association with MDSQ total scores using ANOVA; qualitative variables included preoperative gastrostomy for nutrition, preoperative NIV, instrumented fusion to the pelvis, and occurrence of postoperative complications.

RESULTS

Characteristics of patients and surgical outcomes

A total of 43 patients with DMD underwent posterior correction of scoliosis with use of instrumentation and bone graft. The mean age at surgery was 14.4 years (SD: ± 1.6; range: 10.8-18.2). The clinical, operative, and pre- and post-operative radiographic details of the patient cohort are shown in Table 1. Four patients (9.3%) required gastrostomy placement for nutrition preoperatively, five patients (11.6%) required NIV preoperatively, and five patients had moderate left ventricular systolic dysfunction. The distal extent of spinal fusion was L4 in four patients (9.3%, Figure 1), L5 in 21 patients (48.8%), and the pelvis in 18 patients (41.9%, Figure 2).

The mean length of stay in ICU and in hospital are shown in Table 1. Patients requiring hospital stay greater than two weeks after surgery had ongoing nutritional or respiratory difficulties, including the establishment of NIV which required patient familiarisation and carer training before discharge. Postoperative complications included early deep wound infection treated by debridement, antibiotics and retention of instrumentation (four patients; 9.3%), removal of prominent pelvic screws and lateral connectors with trimming of the distal end of the rods while the spine was fused (one patient; 2.3%), pneumonia (two patients, 4.6%), and hepatotoxicity related to paracetamol administration (four patients; 9.3%). During the postoperative follow-up period, 24 patients (55.8%) died; the cause of death for these patients is shown in Table 2. The mean time between surgical correction of spinal deformity and death for these patients was 8.9 years (SD: ± 3.8 years; range 3.9-16.1 years). The incidence of surgical correction of scoliosis in patients with DMD has reduced over the two decades of the study period (32 patients underwent surgical correction of scoliosis from 2000-2010; 11 patients underwent surgical correction from 2011-2022).

Radiographic outcomes

Preoperative and postoperative radiographic parameters of spinal deformity for the cohort are shown in Table 1. The mean preoperative scoliosis was 57.5° (SD: ± 31.4°; range: 10°-120°), which was corrected to mean 15.9° postoperatively (SD: ± 16.6°; range: 0°-60°); resulting in mean scoliosis correction of 79.2% (SD: ± 18.7%; range: 40%-100%). The mean preoperative pelvic obliquity was 16.3° (SD: ± 13.2°; range: 0°-46°), which was corrected to mean 4.6° postoperatively (SD: ± 6.4°; range: 0°-23°), resulting in mean pelvic obliquity correction of 80.8% (SD: ± 25.2%; range: 19%-100%).

Thoracic kyphosis improved from mean 55.8° (SD: ± 28.7°; range: 0°-98°) preoperatively to mean 33.3° (SD: ± 7.7°; range: 20°-55°) postoperatively. Lumbar lordosis improved from mean 11.1° (SD: ± 20.7°; range: 0°-79°) preoperatively to mean 35.6° (SD: ± 8.9°; range: 20°-55°) postoperatively. Coronal balance was 3.8 cm (SD: ± 2.7 cm; range: 0-12 cm) preoperatively, improving to mean 0.68 cm (SD: ± 1.1 cm; range: 0-4.5 cm) postoperatively. Sagittal balance was 6.1 cm (SD: ± 6.4 cm; range: -11.4 to 1 cm) preoperatively, improving to mean -0.18 cm (SD: ± 1.6 cm; range -4 to 5.4 cm) postoperatively (Table 1).

Long-term functional status

Nineteen patients were alive and invited to complete the MDSQ to assess their functional outcome at long-term follow-up; two patients refused, and one patient was unable to report their outcomes. Sixteen patients completed the MDSQ at a mean postoperative follow-up of 10.9 years (SD: ± 4.7; range: 2-22.5 years); their mean age at completion of the MDSQ was 25.4 years (SD: ± 5.4; range: 15.2-37.3 years). Two (12.5%) of these patients were bed-ridden and 7 (43.75%) were on home ventilatory support. The mean MDSQ total score for these 16 patients was 38.1 (SD: ± 25.9; range: 1-100). All 16 patients were satisfied with the results of scoliosis surgery and reported that they would choose surgical correction of scoliosis again if offered. Fourteen patients (87.5%) reported no significant back or hip pain at long-term follow-up (Table 3).

Table 1 Summary demographics, and radiographic and operative details for patients with Duchenne muscular dystrophy and spinal deformity treated by posterior instrumented spinal fusion (mean ± SD)

Parameter (units)	Patient cohort
Number of patients (*n*)	43
Clinical/operative	
Age at surgery (yr)	14.4 (± 1.6; 10.8-18.2)
Spinal deformity, *n* (%)	
Scoliosis	33 (76.7)
Kyphoscoliosis	10 (23.3)
Single thoracolumbar curve	40 (93)
Double thoracic and lumbar curve	3 (7)
Gastrostomy for nutrition pre-operatively, *n* (%)	4 (9.3)
NIV pre-operatively, *n* (%)	5 (11.6)
Moderate left ventricular systolic dysfunction, *n* (%)	2 (4.6)
Operative time (minutes)	352.1 (± 72.7; 150-490)
Intraoperative blood loss (%; TBV)	36 (± 23.5; 12-150)
Distal fusion extent, *n* (%)	
L4	4 (9.3)
L5	21 (48.8)
Pelvis	18 (41.9)
Length of stay in ICU (days)	6.5 (± 3.1; 3-17)
Length of stay in hospital (days)	14.1 (± 7.2; 7-30)
Postoperative complications, *n* (%)	11 (25.6)
Early wound infections	4 (9.3)
Removal of instrumentation (pelvic fixation)	1 (2.3)
Hepatotoxicity	4 (9.3)
Pneumonia	2 (4.6)
Preoperative radiographs	
Scoliosis (Cobb angle; °)	57.5 (± 31; 10-120)
Scoliosis on traction radiographs (°)	32 (± 24; 0-92)
Scoliosis flexibility index (%)	52 (± 27.5; 7-100)
Pelvic obliquity (°)	16.3 (± 13.2; 0-46)
Pelvic obliquity on traction radiographs (°)	9.2 (± 9.3; 0-35)
Pelvic obliquity flexibility index (%)	58 (± 31; 0-100)
Thoracic kyphosis (T5-T12; °)	55.8 (± 28.1; 0-98)
Lumbar lordosis (T12-S1; °)	11.1 (± 20.3; 0-79)
Coronal balance (C7PL, cm)	3.8 (± 2.7; 0-12)
Sagittal balance (C7PL, cm)	6.1 (± 6.4; -11.4-1)
Postoperative radiographs	
Scoliosis (Cobb angle; °)	15.6 (± 16.4; 0-60)
Scoliosis correction (%)	79.2 (± 18.6; 40-100)
Pelvic obliquity (°)	4.6 (± 6.4; 0-23)
Pelvic obliquity correction (%)	80.8 (± 25; 19-100)

Thoracic kyphosis (T5-T12; °)	33.7 (± 7.3; 20-55)
Lumbar lordosis (T12-S1; °)	35.8 (± 8.7; 20-55)
Coronal balance (C7PL, cm)	0.68 (± 1.1; 0-4.5)
Sagittal balance (C7PL, cm)	-0.18 (± 1.6; -4 to 5.4)

C7PL: C7 plumb line; NIV: Non-invasive ventilation; TBV: Total blood volume; ICU: Intensive care unit; L: Luque sublaminar wires.

Table 2 Aetiology of death during follow-up in patients with Duchenne muscular dystrophy after surgical correction of spinal deformity, *n* (%)

Cause of death	Number of patients
Respiratory failure	10 (41.6)
Pneumonia	7 (29.2)
Severe left ventricular systolic dysfunction	6 (25)
Tracheostomy bleeding	1 (4.2)

In our cohort of 43 patients with Duchenne muscular dystrophy who underwent surgical correction of spinal deformity, 24 patients died during follow-up due to respiratory failure, pneumonia, severe left ventricular systolic dysfunction, or tracheostomy bleeding.

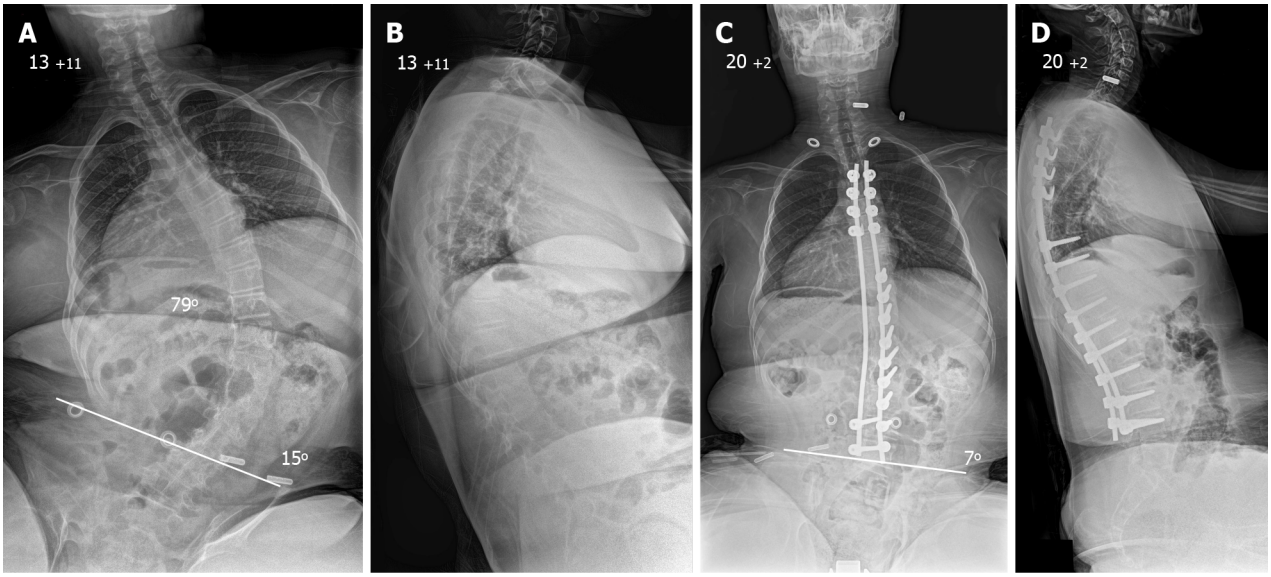

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Figure 1 A patient aged 13 years and 11 months. A and B: With a thoracolumbar collapsing kyphoscoliosis and associated pelvic obliquity; C and D: He underwent a posterior spinal fusion extending from T3-L4 which achieved a balanced spine in the coronal and sagittal planes with good correction of the spinal and pelvic misalignment.

Effect of clinical and radiographic factors with long-term functional status

The relationship between clinical and radiographic parameters and the functional outcomes (MDSQ total score) was assessed (Table 4). Greater duration of postoperative follow-up, increased patient age, higher degree of scoliosis postoperatively, lesser correction of scoliosis, and increased lumbar lordosis postoperatively were significantly associated with lower MDSQ total scores. Greater age at loss of independent ambulation was significantly associated with higher MDSQ total scores.

The demographic details, surgical techniques, radiographic and functional outcomes in our cohort of DMD patients managed by surgical correction of scoliosis are compared with previously published series in Table 5. Our cohort is one of a few published studies reporting both surgical and functional outcomes at long-term follow-up using a validated disease-specific patient-reported outcome measure, the MDSQ. The mean MDSQ total score reported by our cohort at long-term follow-up (completed at mean age 25.4 years) following surgical correction of scoliosis compared favourably with previous published studies, despite greater duration of follow-up (Table 5). The follow-up (mean 10.9 years) for

Table 3 Muscular Dystrophy Spine Questionnaire results

Item	Question	Item mean score	SD	Range
	"Last week how difficult was it to…"			
1	Get dressed	0	0	0
2	Go to the toilet	0	0	0
3	Lean forward and reach out in front of me	1.06	1.34	0-4
4	Move myself around in bed	0.5	0.8	0-2
5	Write (*e.g.*, a short note and sign it)	1.06	1.69	0-4
6	Do up my zipper	0	0	0
7	Sit up in bed	1.93	1.52	0-4
8	Lift my arms to reach	0.8	1.25	0-4
9	Lift my head when lying down	0.9	1.18	0-4
10	Transfer or move from one position to other	0.4	0.89	0-3
11	Use both hands (*e.g.*, put toothpaste on my toothbrush)	0.8	1.16	0-4
12	Use 1 arm and hand for balance while reaching in front with the other hand	0.75	1.12	0-4
13	Hold a spoon or fork by myself as part of a meal	0.8	1.47	0-4
14	Lift a cup/glass to my mouth by myself to drink	0.68	1.25	0-4
15	Sit comfortably in a good position, in my wheelchair all day	2.06	1.61	0-4
16	Shift weight or change my hip position in my wheelchair	0.68	1.01	0-3
17	Use the computer	2	1.46	0-4
18	Finish brushing my teeth	0.56	1.15	0-4
19	Change my arm position in my arm rests	1.18	1.51	0-4
20	Turn to reach for something	0.5	1.09	0-4
21	Bend forwards to eat	1	1.36	0-4
22	Sit in my chair all day without breaks	2	1.86	0-4
23	Sleep comfortably in bed	2.375	1.6	0-4
24	Sit at the table for meals	3	1.3	0-4
25	Bend forward to drink from a straw	1.43	1.67	1-4
26	Keep balance while sitting in my wheelchair	3	1.31	0-4
27	Look good while sitting in my wheelchair	3	1.46	0-4
	"Last week, how bad was…"			
28	Pain in my hips or back last week	3.125	1.2	0-4
29	Me being out of breath last week	2.43	1.8	0-4
	Total score	38.1	25.9	1-100

Items 1-27 are rated 0-4 (0: I can't do it at all; 1: Very difficult; 2: Moderately difficult; 3: A little difficult; 4: Not difficult); items 28 and 29 are rated 0-4 (0: Extremely bad; 1: Very bad; 2: Bad; 3: A little bit bad; 4: Not a problem). Results of the Muscular Dystrophy Spine Questionnaire (16) completed by patients (n = 16) with Duchenne Muscular Dystrophy at long-term follow-up after surgical correction of scoliosis (mean follow-up: 11 years).

the assessment of functional outcomes in our cohort was the longest among published studies. The complications and hospital stay outcomes in our cohort of patients are compared with previously published series in Table 6. In our cohort of DMD patients, there was a low overall incidence of postoperative complications (25.6%), and no perioperative deaths (Table 6).

Table 4 Correlation between clinical, operative, and both preoperative and postoperative radiographic variables with patient-reported Muscular Dystrophy Spine Questionnaire total scores: Quantitative clinical, operative and radiographic variables were assessed for correlation with Muscular Dystrophy Spine Questionnaire total scores by linear regression analysis; standardised coefficients are displayed

Clinical/radiological variable	Value/coefficient estimate (95%CI)	*P* value
Clinical/Operative parameters		
Postoperative follow-up (yr)	-0.766 (-1.138, -0.394)	0.001[a]
Age (yr)	-0.651 (-1.086, -0.216)	0.006[a]
Age at loss of independent ambulation (yr)	0.496 (0.127, 0.865)	0.013[a]
Age at surgery (yr)	-0.146 (-0.519, 0.227)	0.410
Preoperative gastrostomy (Y/N)[1]	-0.036 (-1.072, 1.001)	0.941
Preoperative NIV use (Y/N)[1]	0.110 (-0.731, 0.951)	0.777
Duration of surgery (minutes)	-0.030 (-0.603, 0.543)	0.911
Intraoperative blood loss (%, TBV)	-0.297 (-0.841, 0.247)	0.257
Instrumented fused to pelvis (Y/N)[1]	0.542 (-0.221, 1.306)	0.145
Length of ICU stay (days)	0.123 (-1.010, 1.255)	0.817
Length of stay in hospital (days)	-0.535 (-1.663, 0.593)	0.322
Postoperative complications (Y/N)[1]	0.010 (-0.703, 0.723)	0.975
Preoperative radiographic parameters		
Scoliosis (Cobb angle) (°)	0.268 (-5.330, 5.867)	0.907
Scoliosis on traction radiographs (Cobb angle)	-2.771 (-9.706, 4.164)	0.351
Scoliosis flexibility index (%)	-2.797 (-6.952, 1.359)	0.144
Pelvic obliquity (°)	-0.531 (-4.784, 3.723)	0.761
Pelvic obliquity on traction radiographs (°)	1.036 (-4.511, 6.582)	0.651
Pelvic obliquity flexibility index (%)	1.368 (-2.465, 5.200)	0.401
Lumbar lordosis (T12-S1; °)	0.346 (-1.880, 2.571)	0.706
Thoracic kyphosis (T5-T12; °)	0.153 (-2.283, 2.589)	0.878
Sagittal balance (C7PL, cm)	0.533 (-1.041, 2.106)	0.424
Coronal balance (C7PL, cm)	0.213 (-1.401, 1.828)	0.748
Postoperative radiographic parameters		
Scoliosis (Cobb angle) (°)	-3.005 (-4.718, -1.292)	0.004[a]
Correction of scoliosis (%)	2.167 (1.053, 3.282)	0.002[a]
Pelvic obliquity (°)	0.367 (-0.765, 1.499)	0.468
Correction of pelvic obliquity (%)	0.433 (-0.263, 1.129)	0.185
Lumbar lordosis (T12-S1; °)	-0.642 (-1.184, -0.100)	0.027[a]
Thoracic kyphosis (T5-T12; °)	0.043 (-0.345, 0.430)	0.802
Sagittal balance (C7PL, cm)	-0.190 (-0.768, 0.389)	0.464
Coronal balance (C7PL, cm)	0.886 (-0.215, 1.987)	0.099

[1]Indicates qualitative variable.
[a]Indicates statistically significant result ($P < 0.05$).
L: Luque sublaminar wires; C7PL: C7 plumb line; NIV: Non-invasive ventilation; TBV: Total blood volume; ICU: Intensive care unit.

DISCUSSION

Surgical correction of spinal deformity in patients with DMD aims to prevent curve deterioration, correct spinal balance and pelvic obliquity in order to permit more comfortable positioning, sitting in

Table 5 Clinical and radiographic outcomes of surgical correction of scoliosis in patients with Duchenne muscular dystrophy, the current and previous studies reporting clinical and radiographic outcomes are summarized

Study	Current	Heller	Sengupta		Marsh	Cervellati	Hahn	Mehta	Modi	Takaso	Debnath		Alexander	Duckworth	Suk	Nedelcu	Scannell		Takaso	Yang
Year	2022	2001	2002		2003	2004	2008	2009	2010	2010	2011		2013	2014	2014	2016	2017		2018	2020
Patients (*n*)	43	31	50		30	20	20	36	18	28	22	18	28	26	40	13	47	13	27[1]	99
Instrumentation (*n*)	PH/PS/SL or PS	I	L/G or L-rod	L/G or L-rod	C/HL/USS/S	L/CD	PS/G	PS	PS	PS	SL	PS	L/G and/or PS	SL or PS	CD	UR	L	PS	PS	CD
Distal instrumented level [*n* = (if subset)]	L4 (21), L5 (4), P (18)	SP	P (31)	L5 (19)	P	SP	P	L5 (26); P (10)	L5 (7); SP (11)	L5	P	L5	NA	L4/5 (14); SP (12)	LL (5); P (40)	SP	P	P	L5	LL (5); P (94)
Age at surgery (yr)	14.4	14.1	14	11.7	14.7	13	14	13.5	14.4	13	12.5	11.8	14.2	14.2	14.9	12.7	13	14	13.5	15.1
Pre-op FVC%	NA	54.3	44	58	33	NA	55	NA	NA	NA	57	53	NA	NA	NA	NA	59	48	NA	NA
Post-op FVC%	NA	NA	NA	NA	NA	NA	54	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
FVC% at final F/U	NA	52.7	NA	NA	NA	NA	47	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Pre-op scoliosis (°)	57.5	48.6	48.4	19.8	61	48	44	71	76.4	74	45.3	42.8	56.4	59	65.5	30	31	43	70	65.8
Scoliosis (initial post-op) (°)	NA	12.5	16.7	3.2	24.2	22	10	25.5	30.1	14	NA	NA	21.6	13	NA	2	16	12	15	NA
Correction of scoliosis (%)	79.2	74.3	66	80	60.3	54.2	77	65	63.3	81	NA	NA	61.7	78	NA	93.3	NA	NA	78.6	50.6
Scoliosis at final F/U (°)	15.6	12.5	22	5.2	NA	28	9	28.5	31.3	17	17.7	7.3	NA	NA	36.2	4.2	21	12	17	32.5
Scoliosis loss of correction (°)	NA	0	5.2	2	NA	6	1	3	1.2	3	NA	NA	NA	NA	NA	2.2	5	0	2	NA
Pre-op pelvic obliquity (°)	16.3	18.2	19.8	8.9	18.1	19.8	14	14.8	18.1	9	14.5	11.2	NA	21	20.7	7.7	7	6	15	21
Pelvic obliquity (initial post-op) (°)	NA	3.8	7.2	2.2	NA	10	3	6.7	8.6	3	NA	NA	NA	3	NA	0.6	5	3	5	NA
Correction of pelvic obliquity (%)	80.8	79.1	63.6	76	NA	49.5	65	54.7	52	66.7	NA	NA	NA	85.7	NA	92.2			66.7	53.8
Pelvic obliquity at final F/U (°)	4.6	5.1	11.6	2.9	NA	NA	3	9.3	8.8	6	5.6	2	NA	NA	11.4	1.5	5	2	6	9.7
Fusion to sacropelvis (%)	41.9	100	100	0	100	100	100	27.8	66.7	0	100	0	NA	46.2	89.9	100	100	100	0	94.9

Duration of surgery (min)	352.1	363	310	240	212	180	307	332	348	282	260	216	NA	260	NA	170	227	332	270	NA
Blood loss (mL or % TBV)	36%	3373	4100	3300	4900	1200	2642	2955	2561	950	3400	2000	NA	1882	NA	2553	1327	1596	910	NA
F/U (yr)	10.9	1.8	4.6	3.5	Until discharge	5	5.2	1.6	1.4	3.3	4.5	2.3	1	2	3.86	6.9	4	4	3	6.6
MDSQ score at F/U	38.1	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	35.1	NA	NA	NA	NA	NA

[1]This cohort included 20 Duchenne muscular dystrophy patients and 7 patients with spinal muscular atrophy.

C: Colorado; CD: Cotrel-Dubousset; FVC: Forced vital capacity; F/U: Follow-up; G: Galveston technique; H: Harrington; HL: Harrington-Luque; L: Luque sublaminar wires; LL: Lower lumbar; MDSQ: Muscular Dystrophy Spinal Questionnaire; P: Pelvis; PH: Pedicle hooks; PS: Pedicle screws; S: Synergies; SL: Sublaminar instrumentation; SP: Sacropelvis; USS: AO universal spine system; NA: Not available; TBV: Total blood volume; NA: Not available.

wheelchair, day-to-day activities and QoL[10]. There is limited published literature reporting surgical and functional results at long-term follow-up after surgical correction of spinal deformity in patients with DMD. This retrospective cohort study describes validated patient-reported functional outcomes at the longest available follow-up and surgical outcomes following correction of scoliosis in DMD patients.

Posterior instrumented spinal fusion is indicated for treatment of progressive scoliosis in patients with DMD[12,17,18]. Surgical correction of spinal deformity is recommended before respiratory and cardiac function deteriorate to the extent that general anaesthesia and complex major surgery are unsafe and whilst spinal deformity remains flexible[19-21]. Early surgery may lead to potential sitting height loss, but this is not perceived as a problem[22]. Luque instrumentation and sublaminar wiring for spinal stabilisation in patients with DMD resulted in high patient satisfaction[23]. Results of surgical correction with hybrid constructs utilising pedicle-based anchors and/or instrumentation to the pelvis indicated improved radiographic correction of spinal deformity[24]. Subsequent comparison of sublaminar instrumentation, hybrid instrumentation, and pedicle screw constructs demonstrated that pedicle screw constructs provided a marginally better correction and maintained coronal deformity correction better at follow-up[25]. Pedicle screw instrumentation in patients with DMD achieves better correction of both spinal deformity and pelvic obliquity[10,26]. The patients in our cohort were treated by hybrid or all pedicle screw instrumentation. This resulted in a satisfactory correction of scoliosis from 57.5° to 15.6° at final follow-up (mean 79.2% correction), compared to other reported cohorts of DMD patients managed by hybrid and all pedicle screw constructs (Table 5).

The distal extent of spinal instrumentation to correct spinal deformity and pelvic obliquity remains controversial in the published literature. Traditional management principles include fixation to the sacrum or pelvis to correct pelvic obliquity and improve sitting balance[27]. Distal fixation to the lower lumbar spine with Luque instrumentation has been associated with progression of pelvic obliquity postoperatively, whereas no progression occurred after fixation to the pelvis[28]. Distal instrumentation to the lower lumbar spine using pedicle screws may produce satisfactory results when surgery is performed at a younger age and with milder curves without significant pelvic obliquity (< 15°)[27]. Pedicle screw fixation in multiple levels of the thoracic and lumbar spine provides sufficient stability for spinal correction and mild pelvic obliquity correction. In the presence of significant pelvic obliquity, a combination of L5 pedicle screws and iliac screws provides a stable foundation to correct spinal and

Table 6 Complications and hospital stay outcomes following surgical correction of scoliosis in patients with Duchenne muscular dystrophy; the current and previous studies reporting complications and hospital stay outcomes are summarised

Study	Current	Heller	Sengupta		Marsh	Cervellati	Hahn	Mehta	Modi	Takaso	Debnath		Alexander	Duckworth	Suk	Nedelcu	Scannell	
Year	2022	2001	2002		2003	2004	2008	2009	2010	2010	2011		2013	2014	2014	2016	2017	
Patients (*n*)	43	31	50		30	20	20	36	18	28	22	18	28	26	40	13	47	13
Instrumentation (*n*)	PH/PS/SL or PS	I	L/G or L-rod	L/G or L-rod	C/HL/USS/S	L/CD	PS/G	PS	PS	PS	SL	PS	L/G and/or PS	SL or PS	CD	UR	L	PS
Distal instrumented level (*n*)	L4 (21), L5 (4), P (18)	SP (31)	P (31)	L5 (19)	P (30)	SP (*n* = 20)	P (*n* = 20)	L5 (26), P (10)	L5 (7), SP (11)	L5 (28)	P (22)	L5 (18)	NA	L4/5 (14), SP (12)	LL (5), P (40)	SP (13)	P (47)	P (13)
ICU stay (days) (patient, *n*)	6.5	3	NA	NA	NA	2	3.2	0.4 (*n* = 10)	0.45 (*n* = 4)	NA	2.3	1.8	NA	4.5	NA	NA	2	4
Hospital stay (days)	14.1	21	16.7	7.7	22	NA	19	17.9	19	NA	8.5	7	NA	13	NA	NA	7	7
Complications (%; *n*)	25.6%; WIRI (4), ROPI (1), pn (2), hep (4)	D (5%), pu (24%), instr 10%, WHP (28%), GI (23%), Thr (5%), Bl (5%)	16%; DIAR (1), RI (4)	10.5%; DIARI (1); RI (1)	30%; PE (1), REI (4), CA (1), TR (2), LFT (1), Pn (2), WI (2)	30%; CA (1), NB (1), SPS (1), Instr (3)	20%; D (1), PO (1), WHP (1), DIARI (1)	47%; D (1), Instr (3), Co (7), PI (6)	48.1%; D (CA; 1), UTI (2), Co (6), HT (3), TIL (1), AT (2), CBP (2), Instr (1)	17.9%; I (5)	54.5%; Bl (2), WI (5), PRS (3), Instr (2)	16.7%; WI (2), Instr (1)	17.8%; WI (3), An (2)	38.5%; WI (6), Hep (4), GI (2), Pn (2)	52.5%; Pu (20), WI (1)	53.8%; WHP (3), WI (2), Instr (2),	68%; Instr (12), Inf (2)	54%; PJK (1), WI (3)

C: Colorado; CD: Cotrel-Dubousset; FVC: Forced vital capacity; G: Galveston technique; H: Harrington; HL: Harrington-Luque; L: Luque sublaminar wires; LL: Lower lumbar; P: Pelvis; PS: Pedicle screws; S: Synergies; SL: Sublaminar instrumentation; SP: Sacropelvis; USS: AO universal spine system; NA: Not available. Complications abbreviations: An: Aneamia; AT: Atelectasis; Bl: Bleeding; CA: Cardiac arrest; CBP: Convex back pain; Co: Coccygodynia; D: Death; DIAR: Deep infection and reinstrumentation; DIARI: Deep infection and removal of instrumentation; GI: Gastrointestinal; Hep: Hepatotoxicity; HT: Haemothorax; I: Ileus; Inf: Infections (not categorised); Instr: Instrumentation complication/failure; LFT: Abnormal liver function tests; NB: Neurogenic bladder; PE: Pleural effusion; PI: Prominent instrumentation; PJK: Proximal junction kyphosis; Pn: Pneumonia; PO: Pulmonary oedema; PRS: Prolonged respiratory support; Pu: Pulmonary; REI: Reintubation; RI: Revision of instrumentation; ROPI: Removal of prominent instrumentation; SPS: Sacral pressure sore; Thr: Thrombosis; TIL: Tingling in legs; TR: Tracheostomy; UTI: Urinary tract infection; WHP: Wound healing problems; WI: Wound infection; WIRI: Wound infection and retention of instrumentation; NA: Not available.

pelvic deformity[10]. Segmental pedicle screw instrumentation and fusion to lower lumbar spine may be sufficient if the curve apex is at L2 or higher and if the L5 tilt is less than 15°[29]. It is important to balance this, with avoidance of progression of pelvic obliquity and the potential for further surgery in patients with DMD whose cardiopulmonary health will predictably deteriorate[24]. In our cohort of DMD patients treated with hybrid and all pedicle screw constructs, satisfactory correction of pelvic obliquity was achieved from mean 16.4° preoperatively to 4.6° postoperatively (mean correction of 80.8%) (Table 5).

Hybrid constructs have been associated with a high incidence of instrumentation-related complications (21%), pseudarthrosis (10%), junctional and thoracic kyphosis[30-32]. All pedicle screw constructs provide better maintenance of coronal correction, with loss of correction only 1°-3° over follow-up

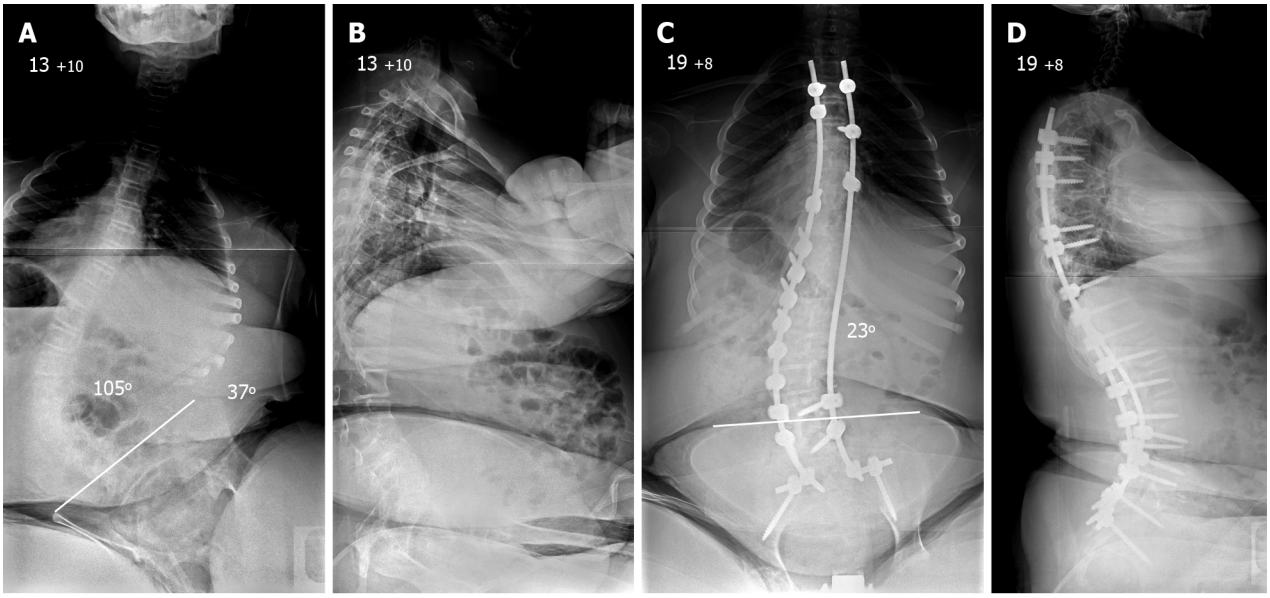

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Figure 2 A patient aged 13 years and 10 months. A and B: With a thoracolumbar collapsing kyphoscoliosis and severe associated pelvic obliquity which was rigid on supine traction; C and D: A posterior spinal fusion extending from T3 to the sacrum with pelvic fixation of the rods achieved good correction of the spino-pelvic imbalance in the coronal and sagittal planes.

(Table 5). Rigid pedicle screw instrumentation also allows immediate postoperative mobilisation which is critical for patients with DMD to avoid respiratory complications[10]. Pelvic fixation has been associated with a higher complication rate compared to distal fixation to the lower lumbar spine, including increased blood loss and length of hospital stay[27]. A higher incidence of deep wound infections postoperatively has been reported in patients with DMD, but no increased risk of blood loss, compared to other neuromuscular conditions[33].

Risk factors for prolonged postoperative ICU stay for DMD patients after spinal surgery have been reported, including greater preoperative scoliosis angle, greater estimated blood loss during surgery, and cardiopulmonary complications[34]. Preoperative forced expiratory volume < 40% has been associated with development of respiratory complications postoperatively[34]. DMD patients in our cohort had a low incidence of complications (25.6%), similar total hospital stay (mean 14.1 d) but greater ICU stay (mean 6.5 d) after spinal surgery compared to other cohorts in the published literature (Table 6); this may be due to availability and selection of patients for postoperative care in ICU. All patients in our cohort were routinely transferred to ICU for postoperative care, whereas this was reserved for selected patients in previous cohorts.

Respiratory function declines most rapidly in patients with DMD during the accelerated growth spurt in adolescence[35]. FVC in patients with DMD reduces at a rate of 4% per year after loss of ambulation, and an additional 4% decline is associated with each 10° progression of scoliosis[9]. Spinal surgery improves postoperative respiratory muscle strength; respiratory muscle training can reduce perioperative complications and effectively maintain pulmonary function perioperatively[36]. Following surgical correction of spinal deformity, FVC decline improved from 4% per year preoperatively to 1.75% per year postoperatively[37]. Spinal deformity correction is associated with a lesser rate of decrease in FVC, reduced need for NIV, and patients reporting that they can breathe more easily postoperatively [15]. DMD patients with high-risk pulmonary dysfunction (FVC < 30%) and severe scoliosis can undergo spinal surgery with all pedicle screw instrumentation and general anaesthesia after respiratory muscle training. Surgical correction was maintained at follow-up, while patients and parents were highly satisfied and believed scoliosis surgery improved their function, sitting balance and QoL despite high rates for significant complications[38].

Surgical treatment for DMD patients with scoliosis delays the decline in pulmonary function and is correlated with improved survival[13]. The combination of surgical correction of spinal deformity and provision of home nocturnal ventilation has an additive effect on survival for patients with DMD; the presence of severe cardiomyopathy is also a determining factor in life expectancy in patients with DMD [3]. Surgical management of scoliosis in DMD patients has been associated with a significantly lower mortality rate at 6.4 years follow-up, compared to those managed without surgery (8.1% *vs* 22%)[13].

There is limited evidence in the literature reporting validated patient-reported outcome measures following surgical correction of spinal deformity in patients with DMD. Previous studies have described patients and their carers reporting improved sitting balance, wheelchair mobility, appearance, functional freedom of their arms, nursing care, satisfaction and respiratory function following surgery compared to their preoperative status[39]. The MDSQ is a validated patient-reported questionnaire

assessing symptoms and functional abilities important to children with scoliosis and muscular dystrophy[16]. A single study previously reported MDSQ scores in DMD patients with scoliosis treated surgically or nonoperatively at mean 3.8 years follow-up; significantly higher scores were reported by patients after spinal surgery compared to those managed nonoperatively. Better scores were reported by patients managed surgically regarding sitting in wheelchair or chairs, mobility and positioning in wheelchair, appearance, pain, and respiratory symptoms when sitting, compared to patients treated conservatively[15].

This study is the first to describe functional outcomes for DMD patients following surgical correction of scoliosis at long-term follow-up (mean 10.9 years). The MDSQ total score was 38.1, similar to previously reported postoperative scores at follow-up (Table 5), with higher scores for sitting comfortably in wheelchair, sleeping comfortably in bed, pain in my hips and back, and being out of breath (Table 3). Factors significantly associated with lower MDSQ total score, and therefore predictive of worse long-term function, included greater duration of post-operative follow-up, increased patient age, greater residual scoliosis postoperatively, lesser degree of scoliosis correction, and increased lumbar lordosis postoperatively (Table 5). Greater age at loss of independent ambulation was significantly associated with higher MDSQ total scores. Due to the natural history of progressive muscular weakness causing gradual functional decline in patients with DMD, it follows that greater duration of postoperative follow-up and higher age at last assessment are associated with worse function as indicated by the MDSQ. Greater residual scoliosis and lesser scoliosis correction at follow-up suggest a more severe preoperative spinal deformity probably due to a more severe underlying disease and therefore were also associated with worse function assessed by the MDSQ. Conversely, greater age at loss of independent ambulation may indicate a less severe disease course and be related to higher MDSQ total scores (Table 5).

The relationship between increased lumbar lordosis postoperatively and worse functional scores is unclear. Five patterns of sagittal plane spinal deformity have been described in DMD patients[40]; greater number of patients will need to be assessed with clinical, radiological, and functional outcomes to determine optimal restoration of lumbar lordosis and sagittal profile for non-ambulatory DMD patients. Patients in our cohort reported high satisfaction at long-term follow-up after surgery and all replied that they would choose surgical correction of spinal deformity again if offered. These results indicate that surgical correction of spinal deformity can improve QoL in DMD patients and is, therefore, indicated in the presence of a severe/progressive deformity despite an increased risk of complications compared to patients with no underlying neuro-disability.

This study has strengths and limitations. This is a single-centre retrospective cohort review assessing surgical results and validated patient-reported functional outcomes using the MDSQ following surgical correction of spinal deformity in DMD patients at the longest reported postoperative follow-up (mean 10.9 years). This provided a standardised approach for the treatment and management of these patients. Increased number of patients completing MDSQ at long-term follow-up may help to investigate the relationship between sagittal spinal balance and functional scores. Further tests of function have been reported and may help to provide a comprehensive functional assessment in patients with DMD. The manual muscle test is a quantitative muscle test. The modified Rancho scale and Swinyard scale assess mobility and function in neuromuscular patients. However, these tests of function may not be useful in the evaluation of function in patients with advanced DMD and scoliosis[15].

CONCLUSION

This study reports surgical and validated patient-reported functional outcomes at long-term follow-up after surgical correction of scoliosis in DMD patients. Posterior instrumented spinal fusion is associated with satisfactory correction of spinal deformity and pelvic obliquity which is maintained at follow-up. All patients were satisfied with surgical results at long-term follow-up. Long-term functional outcomes were predicted by patient age, age at loss of ambulation, duration of follow-up, severity of residual scoliosis postoperatively, degree of scoliosis correction and lumbar lordosis. Surgical correction of spinal deformity can have positive long-term effects on QoL and is recommended in DMD patients with spinal deformity.

ARTICLE HIGHLIGHTS

Research background

Life expectancy in patients with Duchenne muscular dystrophy (DMD) has improved due to advances in medical care. DMD patients developed progressive spinal deformity after loss of ambulatory function and onset of wheelchair dependence for mobility. Surgical correction of scoliosis in patients with DMD aims to improve sitting balance, wheelchair mobility and quality of life (QoL). DMD patients undergoing surgical correction of spinal deformity are at high risk of perioperative morbidity and

mortality.

Research motivation

There is limited published data on the effect of spinal deformity correction on long-term functional outcomes, QoL, and satisfaction in DMD patients.

Research objectives

The aim of this study was to investigate the clinical, surgical, and long-term functional results following surgical correction of scoliosis in patients with DMD, and to investigate clinical and radiological factors that predict long-term functional outcomes following surgery.

Research methods

This was a retrospective cohort study, reviewing data from 113 consecutive patients with DMD who were seen in a National Spinal Deformity Service between January 2000 and August 2022. Data were collected from hospital records and radiographs. All patients had minimum data available including pre-operative clinical and demographic details, comorbidities, operative details including complications, pre- and post-operative radiographic parameters, and minimum post-surgical follow-up of two years. Functional outcomes were assessed by the muscular dystrophy spine questionnaire (MDSQ).

Research results

Forty-three patients underwent correction of spinal deformity by posterior instrumented fusion, comprising 38% of the whole cohort (43/113 patients); spinopelvic fusion was performed in 41.9% of patients, the mean surgical time was 351 min, mean blood loss was 36% of estimated total blood volume, mean hospital stay was 14.1 d, and postoperative complications occurred in 25.6% of patients. The mean correction of scoliosis was 79.2%, mean correction of pelvic obliquity was 80.8%, and mean post-surgical follow-up was 10.9 years. Mean MDSQ total score at follow-up was 38.1; all 16 patients completing the MDSQ were satisfied with the results of spinal surgery and would choose surgery again if offered, and most patients (87.5%) reported no severe back pain at follow-up. Factors significantly associated with functional outcomes (MDSQ total score) included greater duration of post-operative follow-up, age, scoliosis postoperatively, correction of scoliosis, increased lumbar lordosis postoperatively, and greater age at loss of independent ambulation.

Research conclusions

Spinal deformity correction in DMD patients leads to positive long-term effects on QoL, and high patient satisfaction. These results support spinal deformity correction to improve long-term QoL in DMD patients.

Research perspectives

Posterior instrumented spinal fusion is indicated for treatment of progressive scoliosis in patients with DMD; surgical correction of spinal deformity is recommended before respiratory and cardiac function deteriorate to the extent that general anaesthesia and complex major surgery are unsafe and whilst spinal deformity remains flexible. DMD patients in our cohort had a low incidence of complications compared to other cohorts in the published literature. Surgical management of scoliosis in DMD patients has been associated with a significantly lower mortality rate at 6.4 years compared to those managed without surgery, and patients and parents were highly satisfied and believed scoliosis surgery improved their function, sitting balance, and QoL. Surgical correction of spinal deformity can improve QoL in DMD patients and is, therefore, indicated in the presence of a severe/progressive deformity despite an increased risk of complications compared to patients with no underlying neurodisability.

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FOOTNOTES

Author contributions: Tsirikos AI was the guarantor, treated the patients, designed the study, participated in acquisition, analysis and interpretation of the data and drafted the manuscript; Arshad A and Roberts S participated in analysis and interpretation of the data and drafted the manuscript.

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ORIGINAL ARTICLE

Retrospective Study

Incidence of sports-related sternoclavicular joint dislocations in the United States over the last two decades

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Abstract

BACKGROUND

Epidemiological understanding of acute sternoclavicular (SC) dislocations secondary to sports across the United States is poorly defined.

AIM

To identify and assess epidemiological trends of SC dislocations occurring secondary to sports-related mechanisms across United States over the past two decades.

METHODS

This cross-sectional, descriptive epidemiological study evaluates epidemiological trends of SC dislocations from sports that present to emergency departments (EDs) across the United States. Data were obtained from the National Electronic Injury Surveillance System database spanning two decades. Data on incidence,

patient demographics, mechanisms of injury, dislocation types, incident locales, and patient dispositions were collected.

RESULTS

1622 SC dislocations occurred nationwide from 2001 to 2020 [incidence = 0.262/1000000 people, confidence interval (CI) = 0.250-0.275], comprising 0.1% of shoulder/upper trunk dislocations. Most patients were male (91%, *n* = 1480) and aged 5-17 (61%, *n* = 982). Football, wrestling, and biking were the most frequently implicated sports, with contact sports responsible for 59% of athletic injuries (*n* = 961). Recreational vehicle-related sports injuries, such as all-terrain vehicles, dirt bikes, and mopeds accounted for 7.8% of all injuries (*n* = 126), with dirt bikes specifically comprising 3.7% (*n* = 61). Ultimately, 82% were discharged from the ED (*n* = 1337), 12% were admitted (*n* = 194), and 6% were transferred (*n* = 90). All recorded posterior dislocations were admitted or transferred from the ED. Patients sustaining SC dislocations from contact sports had a significantly increased risk of hospital admission or transfer rather than discharge from the ED as compared to patients whose injuries were from non-contact sports (incidence rate ratio = 1.46, CI: = 1.32-1.61, $P < 0.001$).

CONCLUSION

SC dislocations from sports continue to be rare with a stably low incidence over the past two decades, likely comprising a smaller proportion of shoulder dislocations than previously thought. Contact sports are a frequent source of injury, especially among school-aged and teenage males. Most patients are discharged directly from the ED; however, a substantial number are hospitalized, many of which had documented posterior dislocations. Ultimately, understanding the epidemiology and mechanism-related trends of acute SC dislocations is important given the potential severity of these injuries, concentration in a specific population, and uncertainty linked to rare presentation.

Key Words: Sternoclavicular dislocation; Sternoclavicular joint; Epidemiology; Football; Contact sports

Core Tip: Sternoclavicular (SC) dislocations from sports continue to be rare with a stably low incidence over the past two decades, likely comprising a smaller proportion of shoulder dislocations than previously thought. Contact sports are a frequent source of injury, especially among school-aged and teenage males. Most patients are discharged directly from the emergency department; however, a substantial number are hospitalized, many of which had documented posterior dislocations. Ultimately, understanding the epidemiology and mechanism-related trends of acute SC dislocations is important given the potential severity of these injuries, concentration in a specific population, and uncertainty linked to rare presentation.

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INTRODUCTION

Dislocations of the sternoclavicular (SC) are rare: In 1958, Cave *et al*[1] reported that this diarthrodial saddle joint accounts for less than 3% of joint dislocations involving the shoulder[1-3]. The rarity of these injuries imputes why many orthopedic surgeons will not treat an SC dislocation during their career[4]. Even among shoulder and elbow surgeons, SC dislocations are uncommon: An international survey of these pertinent subspecialists reveals only half treat at least one anterior SC dislocation annually[4,5]. Subsequently, there is limited consensus regarding the epidemiology of SC dislocations, which is further exacerbated by how published data is often limited to smaller observational studies given the low SC dislocation volume at individual institutions[6,7].

Despite limited epidemiological data, injury biomechanics are well-defined in the existing literature. Due to the presence of a strong, stabilizing posterior capsule as well as intrinsic and extrinsic ligamentous structures, SC dislocations typically occur in the anterior rather than posterior direction[3,4,

6,8-10]. Injury may occur as a result of direct forces applied to the anteromedial clavicle that cause posterior migration behind the sternum or by indirect forces applied to the anterolateral or posterolateral shoulder[10,11]. Sports and athletic activities are frequent sources of SC dislocations, with contact sports notably increasing an athlete's risk of sustaining direct blows to the medial clavicle or, more commonly, indirect rolling and compression forces on the shoulder[8,10,11]. The potential for posterior dislocation increases the risk of mediastinal penetration that may require emergency operative management with a vascular or cardiothoracic surgeon on standby, increasing the general clinical concern surrounding the acute injury[4,5,9,10,12].

The purpose of the present study is to provide an updated epidemiological analysis of primary, acute SC dislocations secondary to athletic activities that presented to emergency departments (EDs) across the United States over the last two decades. We hypothesize that SC dislocations from sports are rare and comprise less than 1% of estimated shoulder dislocations that present to EDs in general. Given existing concern for injury to structures surrounding the SC joint and the risk that reduction of the SC joint may entail, we further hypothesize that a substantial portion of patients presenting to EDs is admitted or transferred to another facility rather than directly discharged and that patients with injuries secondary to contact sports are more likely to be hospitalized than those from non-contact sports, reflective of greater potential for severe injury.

MATERIALS AND METHODS

This epidemiological study is a cross-sectional, descriptive assessment of SC dislocations from athletic activities presented to EDs across the United States over the past 20 years. Data were sourced from the National Electronic Injury Surveillance System (NEISS) database, a creation of the United States Consumer Product Safety Commission to track and estimate product-related injuries occurring nationwide. NEISS data are collected and deidentified by a hospital coordinator assigned to one of approximately 100 facilities across the United States that are purposefully selected to create a probability sample of EDs across the country. Data is sourced from both clinical information and follow-up telephone communication as needed.

Database query

The NEISS database was queried for all primary and secondary "upper trunk" and "shoulder" dislocations occurring over the twenty years from 2001 to 2020, although secondary injuries were only coded beginning in 2019. All narrative summaries were reviewed. Patients were excluded if the qualitative description did not reflect SC dislocation related to sports participation.

Data collection

National incidences were calculated from census numbers based on the injuries reported in the NEISS. Patient demographics included age and sex, with age-stratified into categories of patients less than five, 5-17, 18-44, 45-64, and over 65 years old. Dislocations were classified as anterior or posterior if this information was explicitly available in the narrative summary. Mechanisms of injury as identified by product involvement, incident locale, hospital size, and disposition from the ED were also collected and reviewed.

Statistical analysis

Weighted descriptive statistics were calculated for included patients based on population estimates. Incidence rates per 1000000 persons at risk and corresponding 95% confidence intervals (CIs) were also calculated based on United States census data population and by demographic-based distribution numbers. Mid-p two-sided P values were calculated for all incidence rate ratios and Poisson approximations to construct incidence rate CIs. Trends regarding injury rates over the two-decade period were assessed with linear regression. χ^2 tests were used to compare dislocation rates in comparable patient cohorts. All analyses were conducted in Stata 17 software[13].

RESULTS

Cumulatively, 1622 SC dislocations occurred nationwide over the twenty-year study period from 2001 to 2020, comprising 0.10% of upper trunk and shoulder dislocations (n = 1616268). In total, there were 0.262 dislocations per 1000000 people (95%CI: 0.250-0.275) from 2001 to 2020 (Figure 1). All SC dislocations were primary injuries. There was no appreciable linear trend among injury incidence compared between relevant years (P = 0.338).

Demographics

A majority of patients with SC dislocations were male (91%, n = 1480) (Table 1). The incidence of sports-

Table 1 Patient demographics, incident locale, and emergency department disposition

	% (Estimated *n*)
Sex	
Male	91% (1480)
Female	9% (142)
Age	
< 5	-
5-17	61% (982)
18-44	28% (456)
45-64	11% (184)
> 65	-
Incident locale	
Home	14% (235)
Street	3% (49)
Other public property	2% (32)
School	5% (82)
Place of recreation/sports	57% (917)
Unspecified	19% (307)
Disposition	
Released	82% (13370)
Transferred	6% (90)
Admitted	12% (194)

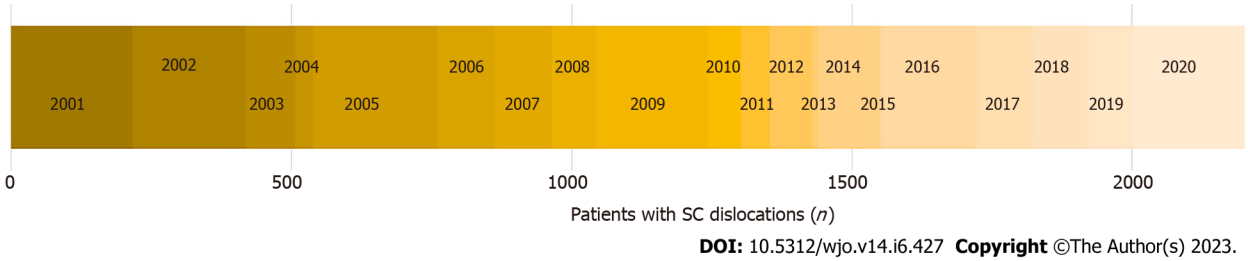

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Figure 1 Annual sternoclavicular dislocations over two decades. SC: Sternoclavicular.

related dislocations in male patients was 0.471 per 1000000 person-years (CI: 0.447-0.496), ultimately tenfold higher than the incidence among female patients (0.046 dislocations per 1000000 person-years, CI: 0.039-0.055) with statistical significance (ratio = 10.1, CI: 8.49-12.1, $P < 0.001$). Trends in age revealed that 61% of dislocations occurred in patients aged 5-17 (n = 982) followed by 28% in patients 18-44 (n = 456). Among patients aged 5-17, the incidence rate was 0.913 dislocations per 1000000 people (95%CI: 0.856-0.971), which represents a substantially higher incidence in this population than both 18-44-year-old patients (0.200 dislocations per 1000000 people, CI: 0.182-0.219) as well as all other age groups combined (0.317 dislocations per 1000000 people).

Mechanism of injury

Football-related injuries were the most common and accounted for 49% of all sport-related SC dislocations (n = 795), followed by wrestling (n = 151) and biking (n = 121) injuries (Figure 2, Table 2). The three contact sports linked to SC dislocations - football, wrestling, and hockey - accounted for two-thirds of all injuries (59%; n = 961). All contact sport-related dislocations occurred in male patients. While SC dislocations from sports were uncommon in women, general exercise-related injuries and horseback riding-related injuries (n = 120; n = 22, respectively) were the most common mechanisms among female patients. Recreational vehicle-related sports injuries, such as all-terrain vehicles, dirt

Table 2 Mechanisms of injury

Sport	% (Estimated *n*)
Football	49% (795)
Wrestling	9% (151)
Bicycle	8% (121)
General exercise	7% (120)
Weightlifting	5% (79)
Trampoline use	4% (71)
Dirt bike	4% (61)
All terrain vehicle	3% (48)
Skateboard	3% (47)
Swimming	2% (39)
Horseback riding	1% (22)
Soccer	1% (21)
Moped	1% (17)
Gymnastics	< 1.0% (15)
Hockey	< 1.0% (15)
Total	1622

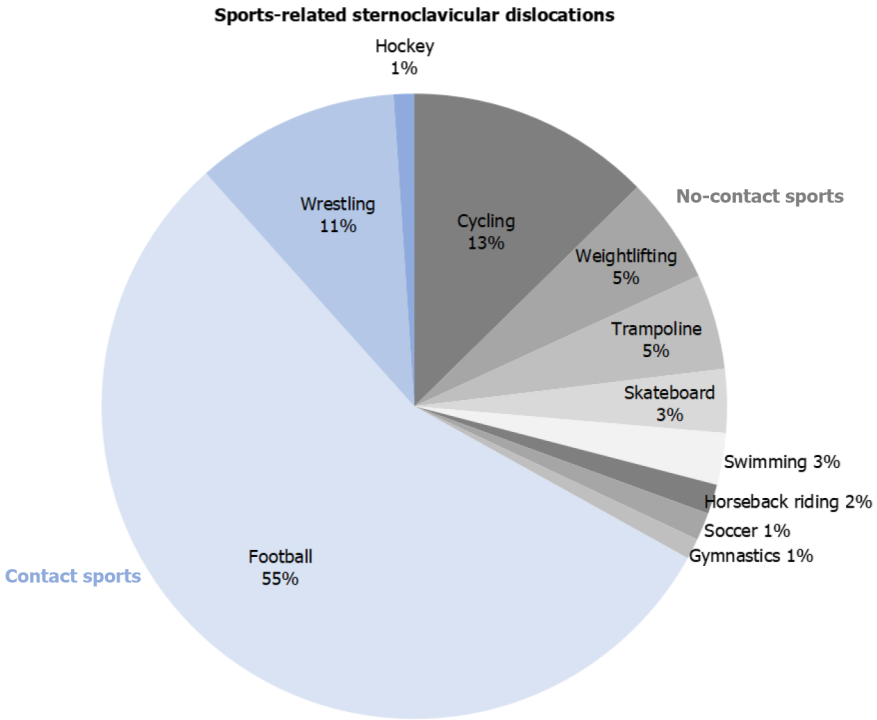

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Figure 2 Sports-related sternoclavicular dislocations.

bikes, and mopeds, accounted for 7.8% of all injuries (n = 126), with dirt bikes specifically comprising 3.7% (n = 61).

Dislocation type

Anterior *vs* posterior dislocations were not specified in NEISS data in most patients (71%; n = 1552). Anterior dislocations were specifically reported in 0.26% of cases (n = 6,), while posterior dislocations were reported in 2.9% of cases (n = 64). All posterior dislocations specified in NEISS occurred in 15- to

17-year-old males during athletic activity, with half of the raw reported dislocations sustained in football (n = 28). Other patients sustained posterior SC dislocations during wrestling (n = 16), hockey (n = 5), and skateboarding (n = 15).

Incident locale

SC dislocations were most commonly sustained at places of recreation or sport (57%; n = 917). Injuries in homes were the second most common (14%; n = 235). Of patients whose dislocations occurred at recreational facilities, 85% were male (n = 782) with an average age of 19 SD = 10. This reflects a similarly aged but less predominantly male population as compared to the patients who sustained sports-related SC dislocations in homes, of which all were male (n = 235) with an average age of 18 (SD = 14).

Patient disposition

Overall, disposition for 82% of patients occurred as discharge directly from the ED (n = 1337). Otherwise, 12% of patients were admitted to the facility (n = 194) and 6% underwent transfer to another facility (n = 90). Although very few dislocations were coded as anterior *vs* posterior, all that were coded as posterior were admitted or transferred and all that were coded as anterior were discharged directly from the ED. Patients sustaining SC dislocations from contact sports had a significantly increased risk of hospital admission or transfer rather than discharge from ED as compared to patients whose injuries were from non-contact sports (incidence rate ratio = 1.46, CI: 1.32-1.61, P < 0.001).

DISCUSSION

SC dislocations from sports are rare, with only 1622 cases presenting to United States ED's over the last two decades. A majority of afflicted patients are male and between 5-17 years old. Dislocations are frequently sustained during contact sports and often occur at places of recreation or sporting activity. For the few patients with specified anterior *vs* posterior dislocations, all posterior dislocations occurred in males aged 15-17 and were admitted or transferred upon presentation to the ED. In total, 82% of patients were discharged directly from the ED with the remainder admitted or transferred to another facility.

Given that SC dislocations are consistently reported as rare injuries, much of the published literature can only report small case series, rendering an injury burden across the United States more difficult[10]. However, there is evidence that most patients with concern for SC pathology present to medical care early after injury, with approximately 80% of patients in a case series by Laffosse *et al*[14] receiving a diagnosis and undergoing a closed reduction within the first 48 hours of injury. Because of the rarity of these injuries and the relative promptness after which patients present to medical attention, the larger and nationally representative NEISS database enables a more targeted assessment of the epidemiology of acute and traumatic SC dislocations.

Our epidemiological assessment of acute sports-related SC dislocations suggests that the incidence may be lower than previous literature suggests[1,10,12,15,16]. Estimates by Cave *et al*[1] from 1958 indicate that SC dislocations account for less than 3% of all shoulder-related dislocations and continue to be quoted throughout current literature[4]. Comparatively, our assessment of weighted NEISS data suggests that SC joint injuries comprise approximately a tenth of a percent of shoulder and upper trunk dislocations. A meta-analysis by Tepolt *et al*[16] found that 71% of SC dislocations injuries in existing literature were linked to athletics while Cave *et al*[1] estimated that SC dislocations comprise 3% of shoulder and elbow dislocations overall; subsequently, our findings indicating that SC dislocations from sports comprise 0.1% of overall shoulder dislocations suggest that SC dislocations from athletics are even rarer than previously estimated. In our assessment of sports-related SC dislocations, there is a notably strong tendency for SC injury from contact sports. The link between SC dislocations in football players, rugby players, and wrestlers is well-documented in literature[11,14,17-19], with a 1996 study published in the British Journal of Sports Medicine going so far to title their paper, "Posterior SC dislocation: an American football injury." Football-related injuries are not limited to high-school-aged or recreational athletes, and there are documented accounts of professional football players treated for SC dislocations[19]. The strong link between SC dislocations and American football offers a potential explanation for why American shoulder and elbow surgeons report seeing proportionally more SC dislocations than Canadian or Flemish surgeons, as a small survey of international shoulder and elbow surgeons revealed that 25% of the 53 American shoulder specialists reported at least three anterior dislocations per year compared to 19% of the 28 Flemish surgeons and 5% of the 128 Canadian surgeons [5]. Due to the rarity of these injuries and the frequent lack of obvious physical deformity, early diagnosis of SC dislocations can be challenging[19]. Consequently, establishing specific sports as frequently implicated mechanisms appropriately increases clinical suspicion for this rare injury pattern in these specific patient populations at a greater risk of injury.

Aligning with trends of increased SC dislocations in adolescents identified in prior literature[7,11,16], the majority of SC dislocations in our study occurred in young males between 5-17 years of age. One cause of increased risk in these patient populations may lie in sports participation, as football and wrestling are male-dominated sports often played by high-school or college-aged athletes. However, biomechanical factors may also play a role. The medial clavicular epiphysis may remain unfused up until age 25, rendering younger patients at increased risk for epiphyseal disruption causing posterior displacement[11,14]. Clavicular physeal fractures are radiographically indifferentiable from SC dislocations and present with similar immediate complications[11,14]; subsequently, the role of the late-fusing clavicular physis in predisposing young patients to these injuries may denote other physis-related risk factors. Interestingly, a study by Laffosse *et al*[14] reports that the only statistically significant difference between epiphyseal disruption *vs* SC dislocations was in patient age: The average age for patients presenting with epiphyseal disruption was 16.9 and ranged from 15-20 years *vs* those with SC dislocation was 24.2 and ranged from 17-41. With the knowledge that contact sports are a common mechanism of injury, the tendency for SC dislocations to present in young males raises a question regarding the degree to which increased exposure from contact sport participation *vs* preexisting biomechanical factors drive this increased risk.

Although much of the anterior *vs* posterior dislocation data is unavailable in our study group, there were 64 patients with specified posterior dislocations, confirming that a minimum of 2.9% of the SC dislocations that presented to EDs occurred posteriorly, reflecting an unexpectedly high percentage of posterior SC dislocations in the last 20 years. Historically, posterior dislocations are exceptionally uncommon: the classic epidemiological case series by Cave *et al*[1] of 1603 shoulder girdle injuries included only one posterior SC dislocation; the 50-year case series by Nettles *et al*[15] reports only three posterior injuries out of 60 SC dislocations; and 1996 literature review by Wirth *et al*[10] yielded fewer than 110 cases of posterior dislocations worldwide. Possible explanations include improved imaging techniques leading to fewer missed posterior diagnoses, increased rates of injuries caused by the specific activities that accrue a high risk of posterior dislocations, or increased frequency of presentation of the more severe posterior dislocations to EDs while anterior dislocations present to lower acuity facilities, possibly as chronic injuries. Regardless, future data collection that includes dislocation direction at a multi-institutional level could help better elucidate these trends.

Regarding disposition, most patients presenting to EDs with SC dislocations are discharged directly from the ED. In concordance with our hypothesis, all patients in our study presented with documented posterior dislocations were admitted or transferred. The limited availability of anterior *vs* posterior dislocation data in NEISS renders it difficult to compare the rates of these injury patterns in our data set; however, anterior dislocations are well-documented to be more common and less severe than posterior dislocations, implying that 82% of patients who were discharged from the ED more likely sustained anterior rather than posterior dislocations. Furthermore, patients with contact sports-related mechanisms were significantly more likely to be admitted or transferred compared to those with injuries from non-contact sport mechanisms, suggesting that injuries from sports with physical contact require more resources and may be more severe than those from other athletic activities.

Limitations to the present study stem from the paucity of SC dislocations and the resultant low sample size. While the NEISS database enables a more comprehensive and nationwide pool of acute traumatic injuries, it does not capture patients who present to urgent care or outpatient facilities, which means that the incidence of anterior and/or chronic dislocations may be higher as any severe injuries that presented to those facilities would likely be transferred to an ED. Furthermore, injury details such as anterior *vs* posterior dislocations were rarely present. Regarding population estimates, calculations relied on available census data, which necessitated projection statistics for the 2020 year.

CONCLUSION

SC dislocations from sports continue to be rare with a stably low incidence over the past two decades, likely comprising a smaller proportion of shoulder dislocations than previously thought. Contact sports are a frequent source of injury, especially among school-aged and teenage males. Most patients are discharged directly from the ED; however, a substantial number are hospitalized, many of which had documented posterior dislocations. Ultimately, understanding the epidemiology and mechanism-related trends of acute SC dislocations is important given the potential severity of these injuries, concentration in a specific population, and uncertainty linked to rare presentation.

ARTICLE HIGHLIGHTS

Research background

Epidemiological characterization of acute sternoclavicular (SC) dislocations is sparse, with classic epidemiology of injury dating back to the 1950s.

Research motivation

Characterize the epidemiology of acute SC dislocations over the last two decades.

Research objectives

This study aims to describe the epidemiological trends of SC dislocations that present to United States Emergency Departments (EDs) related to sports participation.

Research methods

Data for this cross-sectional, descriptive epidemiological study were obtained from the National Electronic Injury Surveillance System database spanning two decades.

Research results

The incidence of SC dislocations nationwide was found to be 0.262 per 1000000 people and comprised 0.1% of shoulder and upper trunk dislocations. The majority of patients were male (91%, n = 1480) and between ages 5-17 (61%, n = 982), and most sustained injuries in contact sports (59%, n = 961) with football the most frequently implicated sport. Most patients (82%, n = 1337) were discharged from the ED. Patients with SC dislocations from contact sports had a significantly increased risk of hospital admission or transfer rather than discharge from the ED (incidence rate ratio = 1.46, CI: 1.32-1.61, P < 0.001).

Research conclusions

SC dislocations sustained during sports are rare. Ultimately, contact sports are a frequent source of injury and the majority of patients are discharged directly from the ED.

Research perspectives

Future research will further clarify incidence of anterior *vs* posterior SC dislocations and characterize trends in treatment over time.

FOOTNOTES

Author contributions: Sandler AB contributed to the data collection, statistical analysis, presentation of data, writing of manuscript, presentation of figures and tables, and revisions of manuscript; Baird MD and Scanaliato JP contributed to the statistical analysis, and the writing, editing, and revision of the manuscript; Harris AL contributed to the writing and editing of the manuscript; Raiciulescu S contributed to the statistical analysis and editing of the manuscript; Green CK and Dunn JC contributed to the editing of the manuscript; Parnes N contributed to the conception of the idea for the manuscript, oversight throughout the course of the study, and writing, editing, revisions of the manuscript.

Institutional review board statement: All data used in the above study were obtained from a free, publicly-accessible database: The National Electronic Injury Surveillance System.

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

Data sharing statement: Data were obtained from the United States Consumer Product Safety Commission at the following website: https://www.cpsc.gov/Research--Statistics/NEISS-Injury-Data.

Country/Territory of origin: United States

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ORIGINAL ARTICLE

Observational Study

Achieving high union rates after first metatarsophalangeal joint arthrodesis: Radiographic outcomes and technical pitfalls

Christian von Deimling, Timo Tondelli, Samuel Brunner, Octavian Andronic, Alexander David Graf

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Abstract

BACKGROUND

Fusion of the first metatarsophalangeal (MTP1) joint is a common surgery performed to correct hallux rigidus, hallux rigidus et valgus and other painful degenerative diseases of the MTP1.

AIM

To assess outcomes of our surgical technique including non-union rates, accuracy and aims of correction.

METHODS

Between September 2011 and November 2020 a total 72 of MTP1 fusions were performed using a low profile, pre-contoured dorsal locking plate and a plantar compression screw. Union and revision rates were analyzed with a minimum clinical and radiological follow up of at least 3 mo (range 3-18 mo). The following parameters were evaluated on pre- and postoperative conventional radiographs: Intermetatarsal angle, Hallux-valgus angle, dorsal extension of the proximal phalanx (P1) in relation to the floor and the angle between the Metatarsal 1 and the P1 (MT1-P1 angle). Descriptive statistical analysis was performed. Pearson analysis was used to assess for correlations between radiographic parameters and achievement of fusion.

RESULTS

An overall union rate of 98.6% (71/72) was achieved. Two out of 72 patients did not primarily fuse with one patient suffering from a non-union, whilst the other demonstrating a radiological delayed union without clinical symptoms, with eventually complete fusion after 18 mo. There was no correlation between the measured radiographic parameters and the achievement of fusion. We believe the reason for the non-union was mainly attributed to the patient's incompliance without wearing the therapeutic shoe leading to a fracture of the P1. Furthermore,

we didn`t find any correlation between fusion and the degree of correction.

CONCLUSION
With our surgical technique, high union rates (98%) can be achieved using a compression screw and a dorsal variable-angle locking plate to treat degenerative diseases of the MTP1.

Key Words: Arthrodesis; First metatarsophalangeal joint; Dorsal plate; Arthrodesis

Core Tip: The most important findings in this study are that metatarsophalangeal joint fusion using a compressions screw and a dorsal plate can achieve union rates close to 100% even in patients that are diabetic or smoke. Furthermore, we didn't find any correlation between the degree of correction and risk of nonunion.

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INTRODUCTION

Arthrodesis of the metatarsophalangeal (MTP1) joint is a common surgery performed to correct hallux rigidus, hallux rigidus et valgus and other painful degenerative diseases of the MTP1. Furthermore, it is a salvage procedure for failed hallux valgus surgery. High patient satisfaction and union rates have been reported in the literature with union rates ranging from 77% to 100%[1-4]. Nevertheless, nonunion of the arthrodesis has been purported as a common complication with unsatisfying results often leading to revision surgery[5,6].

A wide range of fixation methods has been published showing that biomechanically the most stable construct is a combination of a compression screw and a dorsal locking plate[2,7,8]. Commonly a dorsal plate fixation is used as it offers superior strength and sagittal plane rigidity allowing for immediate weight bearing[9,10]. In our own institution we have been using the combination of a compression screw with a dorsal locking plate for more than 10 years. The technique is similar to the technique published by Kumar *et al*[11] with slight variations.

The given literature about radiologic outcomes after arthrodesis of the first ray is limited. Therefore, the aim of this study was to retrospectively assess our own patient collective regarding non-union rate, degree of correction, complications, look for independent risk factors of failure and describe our own surgical technique using a compression screw and a dorsal plate while giving some insightful tips on how to avoid classical pitfalls.

MATERIALS AND METHODS

This retrospective study was approved by the ethics commission board of northwest- and central-Switzerland and was conducted entirely at the authors institution: BASEC Nr 2021-00837. Patients recruited have provided written informed consent.

Study cohort

Out of the institution's database every MTP1 arthrodesis that was executed between September 2011 and November 2020 was identified. The consecutive cohort consisted of 9 male patients and 62 female patients with 34 left and 38 right feet. The average age was (70 years, range 32-90). All patients underwent fusion of the MTP1 by using a compression screw and a low-profile dorsal locking plate. An anatomical, variable-angle dorsal locking plate 2.4/2.7 mm (DePuy-Synthes, Johnson&Johnson) was used. Pre and postoperatively weight bearing radiographs (anterior-posterior, oblique and lateral) were obtained. All Patients with a minimum follow-up of 3 mo and a complete radiographic data set as mentioned above were included in the study.

Surgical technique and postoperative protocol

A single surgeon (SB) performed all surgeries. A classical medial approach is used to expose the medial capsule. A longitudinal incision is used to divide the capsule. After opening the capsule, the capsule is partially released from the metatarsal head. Afterwards the joint is dislocated and a 1.6 mm Kirschner wire is inserted centrally into the first metatarsal head. Now spherical reamers are used to prepare a convex first metatarsal head and a concentric concave proximal phalanx (P1). Afterwards 1 mL demineralized bone matrix is applied (Osteosparx, SeaSpine Carlsbad, CA 92008) into the arthrodesis gap. Now the correct position of the arthrodesis is adjusted under fluoroscopy. The sagittal position is verified using a flat tray simulating a weight-bearing situation. Once the correct position is set, the joint is temporarily fixated with a Kirschner wire inserted from medial to lateral and proximal to distal direction already defining the position of the compression crew. Now the clinical and radiologic position of the arthrodesis is checked again. The reduction is secured with a 4.3 mm cannulated screw (Qwix, Integra) inserted over the wire. Afterwards any dorsal prominences are removed allowing for a good fit of the arthrodesis plate. The plate can be provisionally fixed using olive-Kirschner wires. After assuring the correct position of the plate standard variable-angle locking screws are used. Now, the implant position and length of the screws is checked again, and the correct position of the arthrodesis is verified under fluoroscopy. Subsequently, the wound is closed in layers with non-absorbable suture material for the skin. A sterile wound dressing and a flat operative shoe are applied.

Postoperatively, full weight bearing is allowed with wearing the flat operative shoe day and night for 6 wk[12,13]. At six weeks regular shoes were permitted. Clinical-radiological follow-up takes place after 6 wk and 3 mo.

Radiographic assessment

The following parameters were evaluated on pre- and postoperative conventional radiographs which are widely used and accepted as the standard of care and decision making[14]: Intermetatarsal angle (IMA), Hallux-valgus angle (HVA), dorsal extension of the P1 in relation to the floor and the angle between the Metatarsal 1 and the P1 (MT1-P1 angle) as shown in Figure 1. Measurements were always taken from recordings of the last available follow-up. All conventional radiographs were recorded during weight bearing. Imaging was analyzed in a blinded manner by two independent orthopedic surgeons on the picture archiving and communication system (PACS) using PACS measurement tools. Fusion was defined as patients being pain free at 3 mo and by vanishing of the gap within the arthrodesis in at least three cortices.

IMA: The IMA was measured using the long axis of the first and second Metatarsal. An angle of less than 9° was viewed as normal[15].

HVA: The HVA was assessed by using the long axis of the first Metatarsal in relation to the P1. A value of less than 15 was deemed physiologic[16].

Dorsal extension of P1 in relation to the floor: The Angle between the long axis of the P1 in relation to the floor was measured on lateral radiograph to assess the position of the arthrodesis.

Angle between the first MT1 and the P1 angle: The position of the P1 in relation to the MT1 was measured on a lateral standing weight bearing radiograph.

Statistical analysis

Descriptive analysis of patient characteristics and outcome parameters was performed. For continuous variables the mean and range are reported. Frequencies and percentages were used for dichotomous variables. Union rates are reported as frequencies and exact pearson-clopper 95% confidence intervals (CI) were calculated. The subgroup analyses of diabetics and smokers was done in a descriptive fashion due to the low number of observations. Statistical analyses were computed using Stata/IC 15.1 software (StataCorp LP, College Station, TX, United States).

RESULTS

Of 71 patients with 72 feet were included in the study with a minimum follow up of three months. There were 9 male and 62 female patients with an average age of 70.1 years (range 32-90). The body mass index averaged 26.5 kg/m^2 (range 17-38). Further patient characteristics are displayed in Table 1. Out of these, 71 patients showed a fused arthrodesis (98.6%) at the latest follow-up with one patient suffering from malunion. One patient finally fused after 18 mo showing a delayed union while being asymptomatic throughout the whole period. One patient did not stick to the postop rehab protocol due to a rapidly increasing dementia leading to a P1 fracture. In consideration of the patient's underlying disease and freedom from symptoms, revision surgery was not performed. In one case the locking mechanism of the locking screws failed leading to relapse in valgus and pronation of the first toe which eventually fused in that position. In total three patients developed a symptomatic adjacent joint

Table 1 Demographics and comorbidities

Classification	
Age, years (Avg, range)	70.1 (range 32-90)
Gender	9 males; 62 females
BMI, kg/m^2 (Avg, range)	26.5 (range 17-38)
Surgical side	38 right; 34 lefts
Follow-up, months (Avg, range)	3 (60-108)
Previous surgeries	4
Diabetes Mellitus	8
Smoker (Avg PY, range)	13 (28, range 20-40)
Rheumatic disease	12
Immunosuppression	6

Avg: Average; BMI: Body mass index; PY: Pack years.

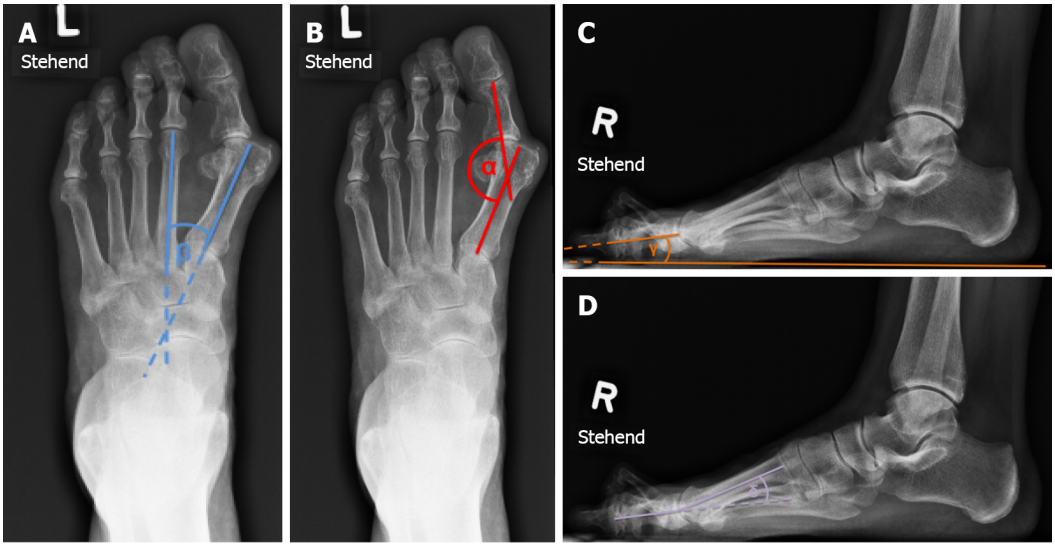

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Figure 1 The radiographic measurements: α = intermetatarsal angle, β = Hallux-valgus angle, γ = P1-Floor, δ = Mt1-P1 angle. A: The radiographic measurements of the intermetatarsal angle; B: The radiographic measurements of the Hallux-valgus angle; C: The radiographic measurements of P1-Floor angle; D: The radiographic measurements of the Mt1-P1 angle.

degeneration over time (15-37 mo). In one case the first tarsometatarsal joint (TMT I) and in two cases the interphalangeal (IP) joint was affected all requiring a TMT or IP joint arthrodesis over time. The preoperative HVA was in average 25.2 (range 14-64) with a correction down to 12 in average (range 2-27) while the preoperative IMA was 13.48 (range 4.5-24) with a postoperative correction to 9.2 in average (range 3.5-15). The preoperative MT1-P1 angle was 8.7 (range -28.05 to 55) with postoperative values of in average 16.89 (-4.05 to 34.5) which was already shown. All radiographic parameters are in detail displayed in Table 2. All patients with diabetes and smoking fused without showing signs of delayed healing or wound healing disorders. Only one patient developed a postoperative wound infection, which ultimately required a skin graft. Preoperatively the patient had a duplex ultrasound which did not show diminished perfusion. During the wound healing disorder another angiography was performed which showed a long-distance stenosis of the superficial femoral artery and the popliteal artery which was treated by balloon dilatation. Another wound healing disorder appeared that was successfully treated with oral antibiotics

Table 2 Pre- and postoperative radiographic parameters

	Preoperative (Avg, range)	Postoperative (Avg, range)
Hallux-Valgus-angle	25.21 (14-64)	12 (2-27)
Intermetatarsal-angle	13.48 (3.5-15)	9.2 (3.5-15)
P1-floor	3.33 (-38.05-18.55)	1.23 (-15.35-18.9)
MT1-P1	8.37 (-28.05-55)	16.89 (-4.05-34.5)

Avg: Average.

DISCUSSION

Arthrodesis of the MTP1 is a highly successful surgery to treat degenerative diseases of the MTP1. It has already been shown that using a construct of a compression screw and dorsal locking plate offers biomechanically the most stable construct[10]. In our own cohort, union rate was 98.6% (CI: 90.3-99.6) with one nonunion and one delayed union which we counted as a union as it finally fused. One malunion appeared due to failure of the locking mechanism. This patient had a known osteoporosis and suffered over the course of time of insufficiency fractures of the ipsilateral second and third metatarsal as a sign of lowered bone density. The clear nonunion was most likely attributed to a rapidly progressing dementia with incompliance regarding the postop protocol. In a big systemic review with 2656 joint included Roukis found an overall nonunion incidence of 5.4% with a symptomatic nonunion in only 1.8% which is consistent with our own data[17]. Interestingly in our own data, there was no association of nonunion or wound healing disorders with diabetes or smoking[18]. All patients with a nonunion or delayed union were non-diabetic and did not smoke. We used the P1-floor angle to radiologically assess the sagittal position of the great toe as already described[1,19]. A valgus of 5-20 degrees in the ap view has been recommended as a desired result in an earlier publication[16]. In our own cohort we measured an average postoperative valgus of 12 (range 2-27) which is again, consistent with recently published data[20]. The postoperative IMA was 9.2 (3.5-15) which can be deemed as borderline if you apply the cut-off values as mentioned above. Correspondingly McKean *et al*[21] showed that a complete correction of the IMA cannot be achieved in patients undergoing MTP1 fusion for severe HV deformity without an additional first metatarsal osteotomy[21]. We didn`t find any correlation between the amount of correction and risk of nonunion which is most likely attributed to the small numbers as according to Weber *et al*[18] negative influencing factors were the presence of preexisting diseases, higher grades of osteoarthritis, and a relative increased dorsiflexion position of the great toe after surgery[18].

The MT1-P1 angle was used to assess the sagittal position of the first ray. In our opinion this needs to be done intraoperatively using a flat tray as mentioned above and recommended by Drittenbass *et al*[20] simulating a weight-bearing situation as the MT1-P1 is strongly influenced by the position of the first metatarsal which differs in flatfoot, cavo-varus or other foot deformities reflected by the wide postoperative range and has to be taken into account intraoperatively[20]. Accordingly, we observed a wide range of the MT1-P1 angle in our own cohort with an average value of 16.89 (-4.05 to 34.5). This has already been published long ago deeming an average value of 12 degrees (range 0-32) as physiologic [22,23].

Strengths of the present study are more certainly that a SB performed all surgeries, and the same implant and fixation technique were used in all cases. Limitations of this study include the short period of follow up and the lack of clinical scores to correlate radiological and clinical outcome. Future studies should particularly correlate radiological data with clinical scores to confirm their clinical relevance and superiority.

CONCLUSION

We were able to show that with our surgical technique, high union rates (98%) can be achieved using a compression screw and a dorsal variable-angle locking plate to treat degenerative diseases of the MTP1 even in diabetic and smoking patients.

ARTICLE HIGHLIGHTS

Research background

Fusion of the first metatarsophalangeal joint (MTP1) is a common surgery performed to correct hallux rigidus, hallux rigidus et valgus and other painful degenerative diseases of the MTP1. High patient satisfaction and union rates have been reported in the literature with union rates ranging from 77% to 100%. In our own cohort we were also able to show high fusion rates.

Research motivation

Analyze our own cohort regarding union rate and radiologic outcome.

Research objectives

The main objective of this study as to asses our own patient collective regarding fusion rate and radiologic outcome including degree of correction.

Research methods

Out of the institution's database every MTP1 arthrodesis that was executed between September 2011 and November 2020 was identified. The consecutive cohort consisted of 9 male patients and 62 female patients with 34 left and 38 right feet. Patients were followed and pre and postoperatively weight bearing radiographs (anterior-posterior, oblique and lateral) were analyzed for fusion rate and various radiologic parameters.

Research results

Of 71 patients showed a fused arthrodesis (98.6%) at the latest follow-up with one patient suffering from malunion. One patient finally fused after 18 months showing a delayed union while being asymptomatic throughout the whole period. The preoperative Hallux-valgus angle was in average 25.2 (range 14-64) with a correction down to 12 in average (range 2-27) while the preoperative intermetatarsal angle was 13.48 (range 4.5-24) with a postoperative correction to 9.2 in average (range 3.5-15). The preoperative MT1-P1 angle was 8.7 (range -28.05 to 55) with postoperative values of in average 16.89 (-4.05 to 34.5) which was already shown.

Research conclusions

We were able to show that with our surgical technique, high union rates (98%) can be achieved using a compression screw and a dorsal variable-angle locking plate to treat degenerative diseases of the MTP1 even in diabetic and smoking patients.

Research perspectives

Future studies should particularly correlate radiological data with clinical scores to confirm their clinical relevance and superiority.

FOOTNOTES

Author contributions: von Deimling C wrote the manuscript, performed the data acquisition; Tondelli T contributed to the statisics, data acquisition; Andronic O main responsibility for the study plan and design; Brunner S and Graf AD are senior author.

Institutional review board statement: This retrospective study was approved by the ethics commission board of northwest- and central- Switzerland and was conducted entirely at the authors institution: BASEC Nr 2021-00837.

Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: SB is in the advisory board of DePuy Synthes and receives advisory fees.

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Observational Study

Chondroitin sulfate and glucosamine combination in patients with knee and hip osteoarthritis: A long-term observational study in Russia

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Abstract

BACKGROUND

Oral treatment of glucosamine (GA) combined with chondroitin sulfate (CS) was reportedly effective for pain relief and function improvement in osteoarthritis patients with moderate to severe knee pain in clinical trials. While the effectiveness of GA and CS on both clinical and radiological findings has been demonstrated, only a few high-quality trials exist. Therefore, controversy regarding their effectiveness in real-world clinical practice remains.

AIM

To investigate the impact of GA + CS on clinical outcomes of patients with knee and hip osteoarthritis in routine clinical practice.

METHODS

A multicenter prospective observational cohort study included 1102 patients of both genders with knee or hip osteoarthritis (Kellgren & Lawrence grades I-III) in 51 clinical centers in the Russian Federation from November 20, 2017, to March 20,

2020, who had started to receive oral capsules of glucosamine hydrochloride 500 mg and CS 400 mg according to the approved patient information leaflet starting from 3 capsules daily for 3 wk, followed by a reduced dosage of 2 capsules daily before study inclusion (minimal recommended treatment duration is 3-6 mo). Changes in subscale scores [Pain, Symptoms, Function, and Quality of Life (QOL)] of the Knee Injury and Osteoarthritis Outcome Score (KOOS)/Hip Disability and Osteoarthritis Outcome Score (HOOS) questionnaires during the observational period (up to 54-64 wk with a total of 4 visits). Patients' treatment satisfaction, data on the combined oral use of glucosamine hydrochloride and CS, concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs), and adverse events (AEs) were also evaluated.

RESULTS

A total of 1102 patients with knee and hip osteoarthritis were included in the study. The mean patient age was 60.4 years, most patients were women (87.8%), and their average body mass index was 29.49 kg/m^2. All subscale scores (Pain, Symptoms, Function, and QOL) of the KOOS and HOOS demonstrated clinically and statistically significant improvements. In patients with knee osteoarthritis, the mean score increases from baseline to the end of Week 64 were 22.87, 20.78, 16.60, and 24.87 on Pain, Symptoms, Physical Function (KOOS-PS), and QOL subscales ($P < 0.001$ for all), respectively. In patients with hip osteoarthritis, the mean score increases were 22.81, 19.93, 18.77, and 22.71 on Pain, Symptoms, Physical Function (HOOS-PS), and QOL subscales ($P < 0.001$ for all), respectively. The number of patients using any NSAIDs decreased from 43.1% to 13.5% ($P < 0.001$) at the end of the observation period. Treatment-related AEs occurred in 2.8% of the patients and mainly included gastrointestinal disorders [25 AEs in 24 (2.2%) patients]. Most patients (78.1%) were satisfied with the treatment.

CONCLUSION

Long-term oral GA + CS was associated with decreased pain, reduced concomitant NSAID therapy, improved joint function and QOL in patients with knee and hip osteoarthritis in routine clinical practice.

Key Words: Glucosamine; Chondroitin sulfate; Knee osteoarthritis; Hip osteoarthritis; Knee injury and osteoarthritis outcome score; Hip disability and osteoarthritis outcome score

Core Tip: Long-term 64-wk treatment by oral capsules of glucosamine hydrochloride 500 mg and chondroitin sulfate 400 mg three times a day for the first 3 wk, then twice daily, was associated with clinically significant improvements in all subscale scores (Pain, Symptoms, Function, and Quality of Life) of the Knee Injury and Osteoarthritis Outcome Score/Hip Disability and Osteoarthritis Outcome Score and a decreasing number of patients with knee and hip osteoarthritis receiving any non-steroidal anti-inflammatory drugs in real-world clinical practice. Incidence of drug-related adverse events was low, and their nature was consistent with known safety profile of glucosamine hydrochloride and chondroitin sulfate combination.

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INTRODUCTION

Osteoarthritis (OA), the most common musculoskeletal disease worldwide, is associated with significant morbidity and mortality[1]. According to the 2017 Global Burden of Disease study, OA is the 12th leading cause of years lived with disability (YLDs) of all ages. YLDs due to OA increased substantially by 31.5% from 2006 to 2016 in the world[2]. This burdensome syndrome has become more common due to the combined effects of the aging population, the increasing proportion of obese individuals worldwide, and the increasing number of joint injuries. By estimate, 250 million people are currently suffering from OA worldwide[3]. In an epidemiological study, approximately 13% of the Russian population over the age of 18 suffered from knee or hip OA[4].

Knee or hip OA is one of the most frequent and burdensome joint diseases, with knee OA being more common than hip OA. The clinical manifestations and symptoms of OA include pain, stiffness and impaired joint function, gradual pain onset, crunching, muscle atrophy, joint deformation, and joint enlargement[5]. By estimate, OA treatment costs in some high-income countries were 1%-2.5% of the gross domestic product, with hip and knee replacements accounting for the major share of such healthcare costs[3].

Management guidelines for OA patients by the Osteoarthritis Research Society International (OARSI) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases recommend a combination of non-pharmacological and pharmacological interventions[6,7]. Non-pharmacological options include exercise therapy, walking aids, weight loss, physical therapy, patient education, and self-help programs. Non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, opioids, duloxetine, intra-articular injections of corticosteroids and hyaluronic acid are the most common medicinal treatment products. Long-term usage of symptomatic slow-acting drugs for OA (SYSADOAs) is also considered a treatment option for symptomatic OA by several medical associations[7-10]. SYSADOAs reportedly had a structure-modifying effect in OA, based on their ability to activate anabolic processes in the cartilage matrix, suppress the activity of lysosomal enzymes, and stimulate chondrocyte function[11]. Regarding structure-modifying effects, standalone therapies of glucosamine (GA) as well as chondroitin sulfate (CS) achieved a statistically significant reduction in joint space narrowing[12].

The SYSADOA class comprises many products (GA, CS, diacerein, and unsaponifiables of soy and avocado oils), with various degrees of clinical efficacy. The most commonly investigated and recommended SYSADOAs are GA, CS, and their combinations. The increase in effectiveness of the combination of GA and CS as compared to each drug alone could be explained by the differences in their mechanisms of action[11]. However, their efficacy in clinical studies remains inconsistent for various reasons[7,13-17].

While many randomized controlled trials (RCTs) showed a significant treatment effect and remarkable safety for GA and CS, controversy regarding their relative effectiveness as compared to placebo or other treatments, their cost-effectiveness, and the need for insurance coverage of the cost of the therapy remains[18-20]. A recent meta-analysis[21] demonstrated clinical and radiological effectiveness of GA and CS. However, only a few high-quality trials exist, and the validity of these results was limited by a high risk of bias introduced in the studies[21]. Efficacious GA and CS treatment dosages, regimen of administration and treatment duration to provide symptom- and structure-modifying effects are not well investigated and properly justified[21], which emphasizes the importance of obtaining additional data on the effectiveness and safety of SYSADOA treatment in long-term studies, particularly in real-world clinical practice. The lower satisfaction with effectiveness of medication was strongly associated with treatment adherence[22].

Currently, GA and CS combination have been registered as an over-the-counter medicinal product in some countries (Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Mongolia, Russian Federation, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan). GA and CS combination showed anti-inflammatory, analgesic, and chondroprotective activities in several clinical studies, including randomized studies[23,24]. Data on efficacy and safety of GA and CS combination therapy in routine clinical practice, particularly among patients with knee and hip OA receiving a long-term treatment, are of important practical interest.

This observational study aimed to assess pain dynamics, daily functional activity of joints, quality of life, and treatment satisfaction in patients with knee and hip OA, who received long-term GA and CS combination in routine clinical practice, and to collect data on the characteristics of OA patients receiving GA and CS combination treatment.

MATERIALS AND METHODS

Study design

This multicenter prospective observational cohort study was conducted in 51 clinical centers in the Russian Federation from November 20, 2017, to March 20, 2020. Patients with OA who had been prescribed GA and CS combination by a doctor during routine care or bought the medicine in a pharmacy on their own care were invited to participate in the study. The study planned to enroll no less than 1100 participants with OA (Kellgren & Lawrence stages I-III) in 80 centers, who were treated with GA and CS combination (capsules, 500 mg + 400 mg) for no longer than 2 wk at the time of study enrollment.

Patients used GA and CS combination according to the approved patient information leaflet, starting from 3 capsules daily for 3 wk, followed by a reduced dosage of 2 capsules daily. Theraflex® [capsules, glucosamine hydrochloride 500 mg and CS 400 mg, (GA + CS)] was authorized in Russia in 2008 for treatment of OA (grades I-III).

Inclusion criteria were as follows: Patients aged 45-75 years with hip or knee OA of stages I-III according to the Kellgren & Lawrence classification; patient who started GA + CS treatment (capsules, 500 mg + 400 mg) no longer than 2 wk before study enrollment; and patients who personally signed and dated informed consent. For OA of several joints or bilateral knee or hip OA, only one "target" joint, in which the patient experienced the most pronounced pain at the time of study enrollment, was selected for evaluation.

Patients were considered ineligible for the study if: They had participated in any other studies involving interventions other than standard clinical practice; they had hip or knee OA stage 0 or stage IV; they had received GA + CS or other slow-acting drug for symptomatic treatment within the past 5 mo; they had received intra-articular corticosteroid injections within the past 3 mo, or hyaluronic acid injections, and/or intra-articular lower extremity autologous platelet-rich plasma injections within the past 6 mo; and women who were pregnant or breastfeeding.

Observational visits were scheduled based on routine clinical practice and GA + CS prescription by a consulting physician. The study protocol included an initial visit, two follow-up visits (Weeks 16-24 and Weeks 36-44 after GA + CS treatment initiation), and a final visit (Weeks 56-64 after treatment initiation). Once consent was obtained, patient demographics, lifestyle, medical history, and OA grades according to the Kellgren & Lawrence classification were recorded. During all visits, data on GA + CS usage were collected, patients' basic vital signs and body mass index (BMI) were recorded, a physical examination was performed, and concomitant therapy and adverse events (AEs) were noted. Patients completed the Knee Injury and Osteoarthritis Outcome Score (KOOS) or the Hip Disability and Osteoarthritis Outcome Score (HOOS) questionnaires (depending on selected "target" joint). HOOS is used to evaluate patients' opinions about their hip joint and related problems. This scale is intended for adults with hip joint disability with or without osteoarthritis[25]. KOOS is used to evaluate the opinion of patients about their knee and related problems. It can be used for short-term and long-term monitoring[26]. HOOS and KOOS are widely used questionnaires for patient reported joint-specific assessment of symptoms and functions in subjects with knee/hip injury and osteoarthritis. Both questionnaires are available on-line.

KOOS/HOOS consist of 5 subscales: Pain, other Symptoms, Function in daily living (ADL), Function in sport and recreation (Sport/Rec) and knee/hip related Quality of life (QOL). Standardized answer options are given (5 Likert boxes) and each question gets a score from 0 to 4. Questionnaire scores range from 0 to 100 with a score of 0 indicating the worst possible knee/hip symptoms and 100 indicating no knee/hip symptoms. To simplify the process of completing the questionnaires and reduce the amount of information provided, the subscales "Function in daily living" and "Function in sport and recreation" of the KOOS/HOOS questionnaires were replaced by the KOOS Physical Function (KOOSPS) and the HOOS Physical Function (HOOSPS) short forms, respectively.

Additionally, during the post-baseline visit, patients were asked to rate their satisfaction with the treatment on a 5point scale (very satisfied - 5, satisfied - 4, neither satisfied nor dissatisfied - 3, dissatisfied - 2, very dissatisfied - 1).

An interim analysis after completion of follow-up visits on Week 16-24 by the first 550 enrolled patients was performed during the study. Its main purpose was to investigate changes in pain, functions of daily living, and quality of life in patients with knee and hip OA after the first treatment course with GA + CS. A report on the results of the interim analysis was presented at the European League Against Rheumatism online congress in 2020[23].

This study was approved by the Intercollegiate Ethics Committee of the Russian Federation (protocol number 08/17, dated on September 14, 2017) and by the Bayer Protocol Review Committee (held on June 14, 2017). Patients provided informed consent for data collection before starting any study-related procedures. Study was registered on ClinicalTrials.gov resource before patient enrollment with the study Identifier NCT03330288 on November 6, 2017[27].

Outcomes

Changes in parameters of the KOOS/HOOS subscales were assessed as the primary outcome of the study. Other outcomes, such as patient satisfaction with the study treatment, data on the use of GA + CS, frequency of concomitant use of analgesics and other pain medications, were also evaluated as additional study outcomes.

Data source

Data for the study were collected through clinical interviews with patients and from source documents available at the center. Source documents were original documents, data, and records, which could include laboratory data/information or assessment checklists, pharmacy records, *etc.* The KOOS/HOOS and treatment satisfaction questionnaires were completed by the patients themselves with touch-screen tablets provided to them.

Statistical analysis

Statistical analysis was performed using SAS 9.4 software package for Windows (SAS Institute Inc., Cary, NC, United States). Since the study was observational, descriptive analysis was used to process

the data. All variables were analyzed in a full analysis set (FAS) that included all screened patients who received at least one dose of GA + CS and who had data to evaluate at least one efficacy and/or safety parameter. Categorical data were expressed as absolute numbers and percentages, and continuous data were expressed as mean values with standard deviations or 95% Wald confidence intervals (CI). The Student's paired *t*-test and the Bonferroni-Holm correction for *P* value were used in the analysis of the dynamics of KOOS and HOOS scales. The null hypothesis was tested: No changes on the visits. According to the results of testing, the hypothesis is rejected on all visits. The analysis of treatment satisfaction was carried out using median values and 25 and 75 quantiles.

RESULTS

Patient characteristics

A total of 1111 participants were screened over the course of the study, of which 1102 participants were enrolled. The study group included male and female patients aged 45-75 years with knee (824 participants) or hip (278 participants) OA.

A total of 38 patients (3.4%) discontinued the study prematurely. The main reason was loss of contact with patient (33 patients), the remaining 5 patients discontinued participation by withdrawal of consent due to treatment switch to another SYSADOA, planned hip arthroplasty, or patient inability to visit the study center. A total of 1102 patients received at least one dose of GA + CS and were included in the FAS population for efficacy and safety analysis. Among these patients, 97.1% completed the visit for Weeks 16-24, and 96.6% completed visits for Weeks 36-44 and Weeks 56-64 (Figure 1).

Patient demographics and baseline characteristics were summarized in Table 1. Most patients (74.8%) had knee OA. Approximately, 87.8% of patients were women, 99.6% were Caucasians, and their mean age was 60.4 years. Notably, the average BMI of patients was 29.49 kg/m^2, and most patients were obese or overweight.

At study enrollment, data on concomitant diseases were collected. The most common diseases were cardiovascular diseases (52.6%), metabolic and nutritional disorders (34.3%), and gastrointestinal disorders (22.1%). Hypertension (44.6%), obesity (23.2%), chronic gastritis (15.6%), varicose veins (9.3%), and type 2 diabetes mellitus (8.4%) were most often reported. Treatment of concomitant diseases was the main reason for the prescription of concomitant therapy during the observation period. At least one concomitant treatment was reported by 813 (73.8%) patients, the most commonly used concomitant medications were selective betaadrenergic blockers, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers (in 19%, 13.9% and 12.9% of patients, respectively).

Changes in the KOOS scale

According to the KOOS questionnaire, patients with knee OA noted a significant improvement during the observation period. The mean score increases from baseline to the end of Week 64 were 22.87 (95%CI: 21.56-24.18), 20.78 (95%CI: 19.43-22.13), 16.60 (95%CI: 15.59-17.61), and 24.87 (95%CI: 23.41-26.34) on Pain, Symptoms, Physical Function (KOOS-PS), and Quality of Life subscales, respectively, ($P < 0.001$ for all). Notably, for all KOOS subscales, the largest score increases were achieved by Week 16-24 (observation for 4-6 mo), and the achieved effects further remained at the mean values for all subscales with a tendency to increase ($P < 0.001$ for all) (Table 2, Figure 2).

The most important questions (pain frequency and knee stiffness) of the KOOS questionnaire were analyzed separately. By the end of the 64-week observation period, the percentage of patients who reported pain frequency as "daily" or "always" decreased from 62.7% to 12.9% (Figure 3A). The percentage of patients who reported knee stiffness in the morning as "moderate", "severe" or "extremely severe" decreased from 55.3% to 18.1%, and the percentage of patients with knee joint stiffness in the evening decreased from 60.9% to 18.6%. A significant improvement of quality of life was observed. According to answers to the question of how much the patient's life was complicated by knee joint problems, the percentages of patients reported "not at all" and "slightly" increased from 1.9% to 28.7%, and from 19.5% to 38.5%, respectively, while the percentages of patients with "moderate", "severe, and "extremely severe" decreased from 47.0% to 27.0%, 27.7% to 4.8%, and 3.9% to 1.0%, respectively.

Changes in the HOOS scale

Patients with hip OA showed positive dynamics in all HOOS subscales during the observation period. The mean increases from baseline to the end of Week 64 were 22.81 (95%CI: 20.47-25.16), 19.93 (95%CI: 17.49-22.36), 18.77 (95%CI: 16.61-20.93), and 22.71 (95%CI: 20.14-25.28) on Pain, Symptoms, Physical Function (HOOS-PS), and Quality of Life subscales, respectively. Similar to changes in the KOOS scale, the highest score increases in the HOOS subscales were achieved by Week 16-24 with a tendency to increase during further follow-up ($P < 0.001$ for all) (Table 3, Figure 4).

Similar to patients with knee OA, the percentage of subjects with less frequent and less severe symptoms, problems, or difficulties in the specified joint during the observation period increased among patients with hip OA. By the end of the 64-week follow-up, the percentage of patients with

Table 1 Main characteristics of the study population, *n* (%)

	Knee osteoarthritis (*n* = 824)	Hip osteoarthritis (*n* = 278)	All (*n* = 1102)
Age, (yr), mean (SD)	60.4 (6.9)	60.3 (7.2)	60.4 (7.0)
Gender			
Female	728 (88.3)	240 (86.3)	968 (87.8)
Male	96 (11.7)	38 (13.7)	134 (12.2)
Ethnicity			
Caucasian	820 (99.5)	278 (100.0)	1098 (99.6)
Black	1 (0.1)	0	1 (0.1)
Asian	3 (0.4)	0	3 (0.3)
BMI, mean (SD)	29.77 (5.5)	28.66 (5.3)	29.49 (5.5)
Scale of stages of osteoarthritis according to Kellgren & Lawrence			
Stage 1	81 (9.8)	35 (12.6)	116 (10.5)
Stage 2	617 (74.9)	211 (75.9)	828 (75.1)
Stage 3	125 (15.2)	32 (11.5)	157 (14.2)
No data available	1 (0.1)		1 (0.1)

BMI: Body mass index.

Table 2 Change in Knee Injury and Osteoarthritis Outcome Score subscale scores (Full analysis set)

Subscale	Knee osteoarthritis (*n* = 824) – KOOS scale					*P* value[a]
	Visit 1, baseline, *n* = 824	Visit 2, week 16-24, *n* = 798	Visit 3 week 36-44, *n* = 794	Visit 4, week 56-64, *n* = 794	Changes from baseline on visit 4	
Pain	61.48 (60.36-62.61)	79.59 (78.48-80.70)	82.50 (81.45-83.56)	84.24 (83.15-85.34)	**22.87** (21.56-24.18)	**< 0.001**
Symptoms	62.25 (61.02-63.48)	77.65 (76.46-78.84)	81.09 (79.97-82.21)	82.80 (81.66-83.93)	**20.78** (19.43-22.13)	**< 0.001**
Functional activity of the joint	61.46 (60.73-62.18)	72.48 (71.63-73.34)	75.78 (74.86-76.69)	78.03 (77.06-78.99)	**16.60** (15.59-17.61)	**< 0.001**
Quality of life	44.99 (43.83-46.16)	61.40 (60.10-62.69)	65.91 (64.54-67.27)	69.92 (68.45-71.39)	**24.87** (23.41-26.34)	**< 0.001**

[a]with Holm-Bonferroni method. Mean data are presented (95%CI). CI: Confidence interval; KOOS: Knee Injury and Osteoarthritis Outcome Score.

Table 3 Change in Hip disability and Osteoarthritis Outcome Score subscale scores (Full analysis set)

Subscale	Hip osteoarthritis (*n* = 278) – HOOS scale					*P* value[a]
	Visit 1, baseline, *n* = 278	Visit 2, week 16-24, *n* = 272	Visit 3, week 36-44, *n* = 271	Visit 4, week 56-64, *n* = 270	Changes from baseline on visit 4	
Pain	60.97 (58.93-63.02)	76.36 (74.34-78.38)	80.89 (78.95-82.84)	83.63 (81.64-85.62)	**22.81** (20.47-25.16)	**< 0.001**
Symptoms	61.17 (59.08-63.26)	73.73 (71.62-75.84)	78.17 (76.21-80.14)	81.19 (79.21-83.16)	**19.93** (17.49-22.36)	**< 0.001**
Functional activity of the joint	65.57 (63.62-67.52)	78.46 (76.72-80.21)	81.59 (79.93-83.26)	84.11 (82.45-85.76)	**18.77** (16.61-20.93)	**< 0.001**
Quality of life	46.79 (44.72-48.85)	60.75 (58.50-63.01)	65.41 (63.09-67.72)	69.33 (66.83-71.82)	**22.71** (20.14-25.28)	**< 0.001**

[a]with Holm-Bonferroni method. Mean data are presented (95%CI). CI: confidence interval; HOOS: Hip disability and Osteoarthritis Outcome Score (HOOS).

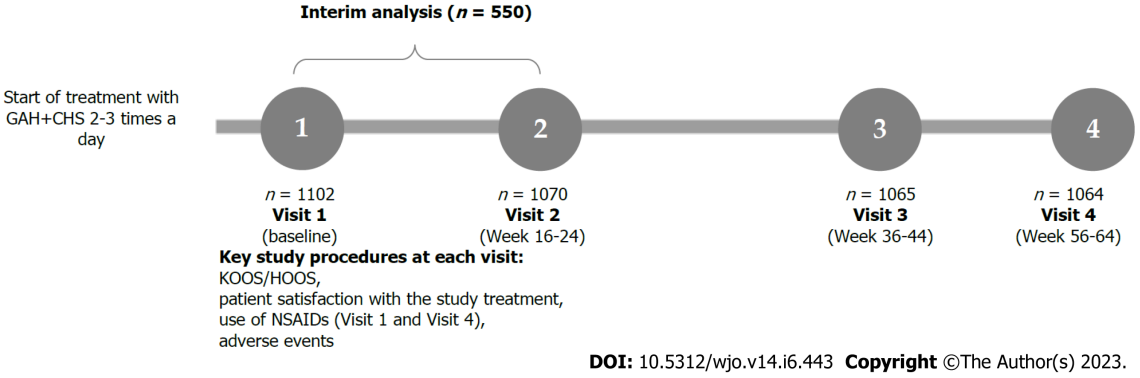

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Figure 1 Study design profile and recruitment of patients. Explanations for the participants excluded from the study were given in the Results section of this manuscript. GAH+CHS: 500 mg glucosamine hydrochloride and 400 mg chondroitin sulfate in one capsule; HOOS: Hip Disability and Osteoarthritis Outcome Score; KOOS: Knee Injury and Osteoarthritis Outcome Score; NSAID: Non-steroidal anti-inflammatory drugs.

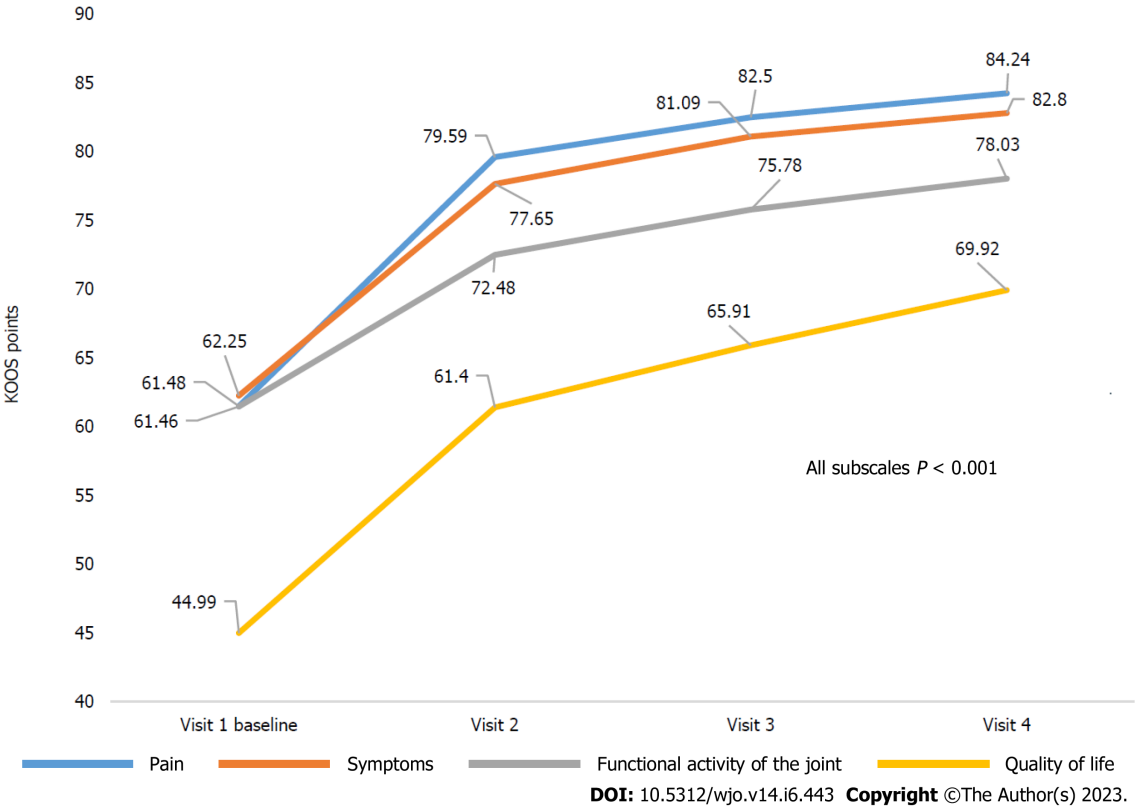

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Figure 2 Dynamics of Knee Injury and Osteoarthritis Outcome Score subscale scores. KOOS: Knee Injury and Osteoarthritis Outcome Score.

"daily" or "always" pain frequency decreased from 64.7% to 13.7% (Figure 3B), and those of patients with "moderate", "severe", or "extremely severe" morning hip stiffness and evening knee stiffness decreased from 55.4% to 15.9%, and from 61.9% to 17.0%, respectively. The percentages of patients who answered "not at all" and "slightly" in response to the HOOS question on complications due to hip joint problems increased from 1.8% to 23.7%, and from 22.7% to 41.5%, respectively, while the percentages of patients with "moderate", "severe", and "extremely severe" complications decreased from 46.4% to 28.1%, 25.5% to 4.8%, and 3.6% to 1.9%, respectively.

Duration of GA + CS usage

During the observation period, most patients (749/1102, 68%) were treated with GA + CS capsules for more than 6 mo. Treatment duration was 3-6 mo for 261 patients (23.7%), 1-3 mo for 78 patients (7.1%), and less than 1 mo for 14 patients (1.3%). A total of 1006 (91.3%) patients complied with the recommendations for the use of GA + CS.

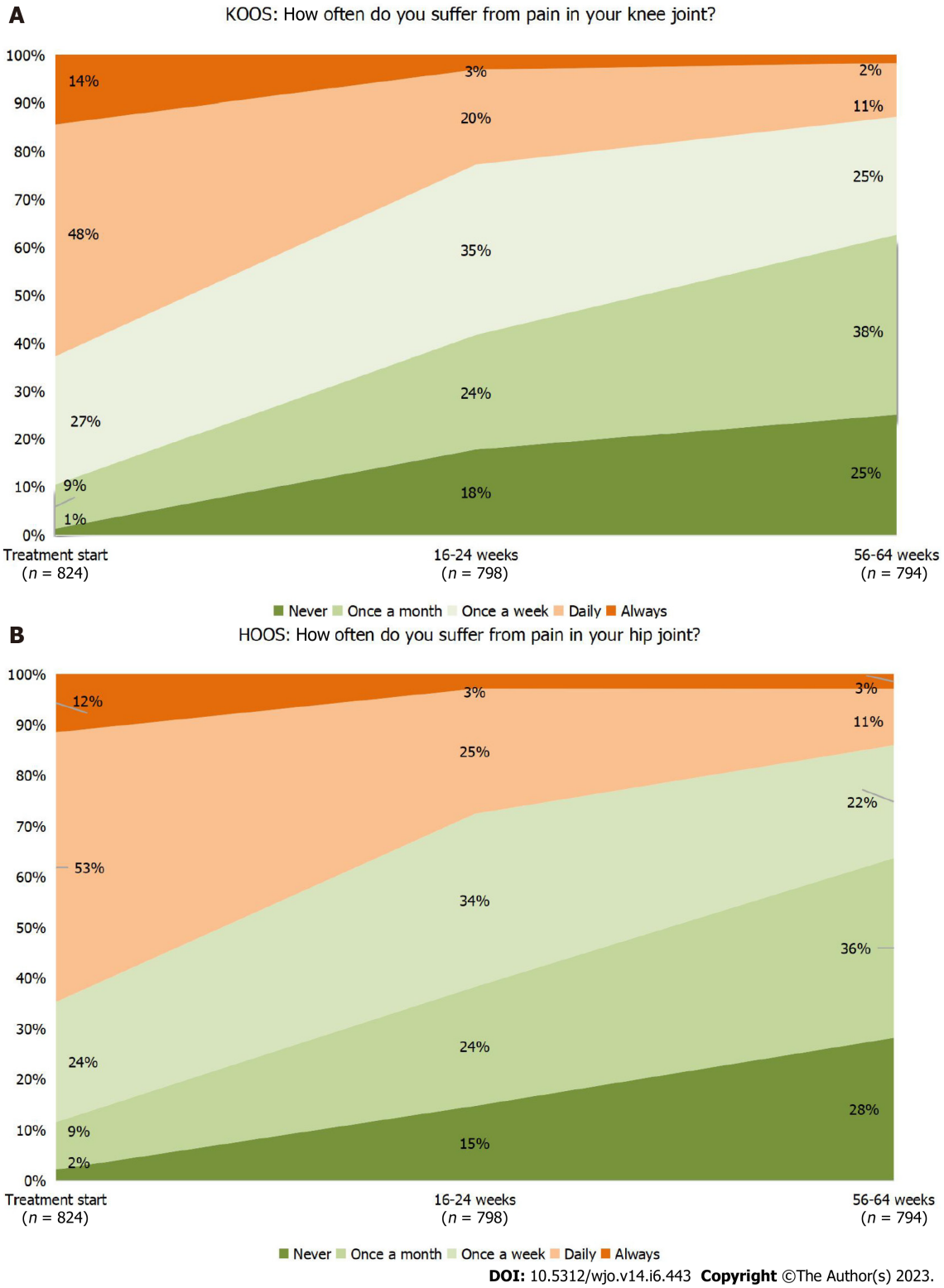

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Figure 3 Dynamics of pain during the study (analysis of "Pain Frequency" questions in Knee Injury and Osteoarthritis Outcome Score and Hip Disability and Osteoarthritis Outcome Score). A: Knee osteoarthritis; B: Hip osteoarthritis. HOOS: Hip Disability and Osteoarthritis Outcome Score; KOOS: Knee Injury and Osteoarthritis Outcome Score.

Patient satisfaction with treatment

The patient satisfaction response rates of "satisfied" or "very satisfied" on Visits 2, 3, and 4 were 78%, 79.9%, and 78.1%, respectively. Notably, over the visits, the proportion of patients who gave a rating of "very satisfied" tended to increase. In this regard, at Visit 2, 218/1070 (20.4%) patients rated treatment satisfaction as "very satisfied". This rating was given by 261/1065 (24.5%) patients and 312/1064 (29.3%) patients at Visits 3 and 4, respectively. The results of patients with knee OA and hip OA were generally comparable.

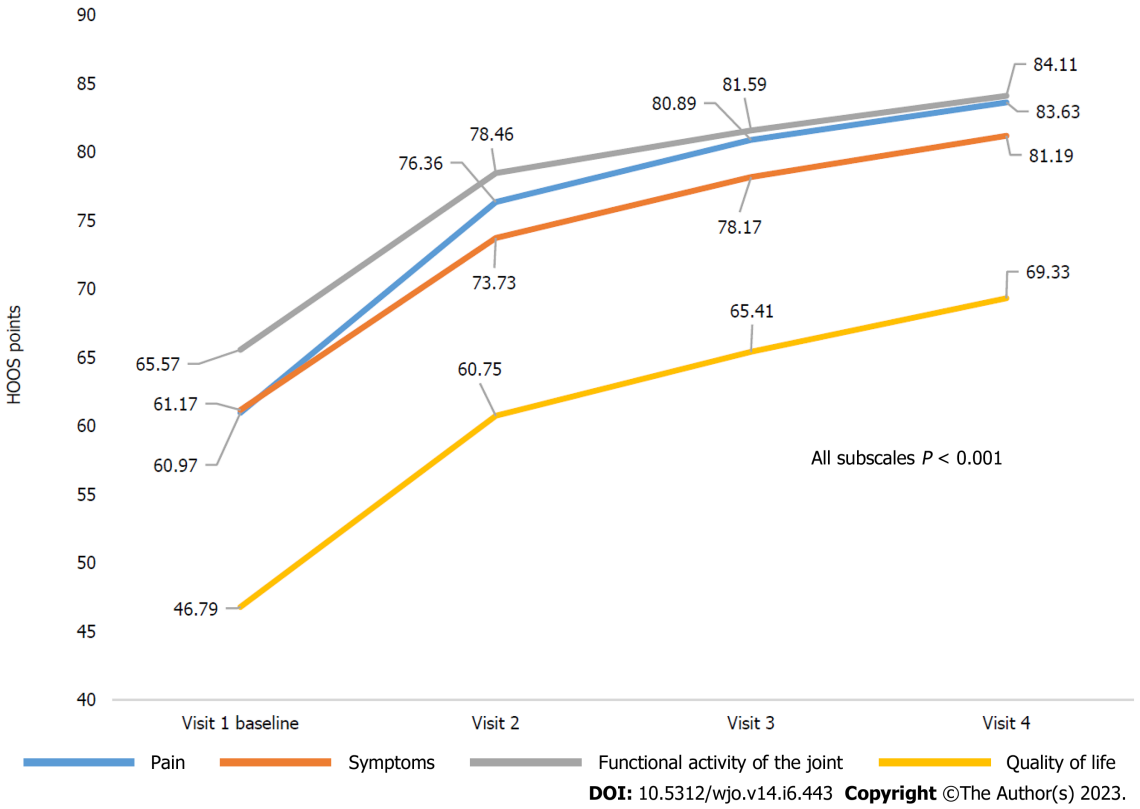

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Figure 4 Dynamics of Hip Disability and Osteoarthritis Outcome Score subscale scores. HOOS: Hip Disability and Osteoarthritis Outcome Score.

Concomitant analgesics therapy

At the end of each patient's observation period, the investigators were asked for their opinion on the need for concomitant analgesic therapy for patients during the study. According to the data at the initiation of GA + CS treatment, 200/1102 patients (18.1%) with knee or hip OA received regular NSAID/analgesic therapy, and 276 patients (25.0%) received analgesic therapy episodically. For the majority of these cases, oral treatment was used (375 patients). However, some patients required only topical anti-inflammatory products (45 patients) or a combination of topical and oral analgesics (56 patients).

At the end of the study, the number of patients using any types of analgesics or NSAIDs decreased from 43.6% to 12.68% ($P < 0.001$) in the knee OA group, and from 44.36% to 10.58% ($P < 0.001$) in the hip OA group (Figure 5). The majority of patients [953/1102 (86.5%) patients] did not require analgesic therapy by NSAIDs at the end of follow-up, showing significant reduction in the need of concomitant NSAIDs or analgesics therapy. Notably, a decrease in the need for the use of topical and oral analgesic therapy was observed in both knee OA and hip OA groups ($P < 0.001$ for both) (Figure 5).

Adverse events

During the study, 307 AEs were reported in 190 (17.2%) participants. The most common AEs for systemorgan classes of MedDRA were: "Musculoskeletal and connective tissue disorders" (5.3%), "Gastrointestinal disorders" (4.7%), and "Infections and infestations"4.4%). The most common AEs by the Preferred Term included OA (worsening of the main diagnosis) (1.2%), upper abdominal pain (1.3%), upper respiratory tract infections (2.3%), and headache (1.3%). In most patients, AEs were mild [108 patients (9.8%)] or moderate [78 patients (7.1%)].

AEs considered by the investigators as "related to the study product" were reported for 31 (2.8%) patients (a total of 33 AEs) and mainly included gastrointestinal disorders [25 AEs in 24 (2.2%) patients]. The most common AE was upper abdominal pain [12 (1.1%) patients].

The dosage of GA + CS was reduced in 7 (0.6%) patients due to AEs (upper abdominal pain, diarrhea, dyspepsia, flatulence, stomach upset, hypothyroidism secondary to diffuse nodular goiter, and hyperuricemia). In 19 (1.7%) patients, AEs led to the cancellation of therapy with GA + CS. The most common cause was gastrointestinal disorders [12 (1.1%) patients]. Additionally, AEs, such as myalgia, cerebrovascular disorder, hypertension, essential hypertension, angina pectoris, peripheral edema, and hip arthroplasty were recorded.

Serious AEs (SAEs) were reported in 14 (1.3%) patients, including atrial fibrillation (2 patients), cholecystectomy, coronary bypass, hip arthroplasty, knee arthroplasty, hemorrhoids, ischemic thrombotic stroke, radicular pain syndrome, cholelithiasis, foot fracture, and myositis (one patient for

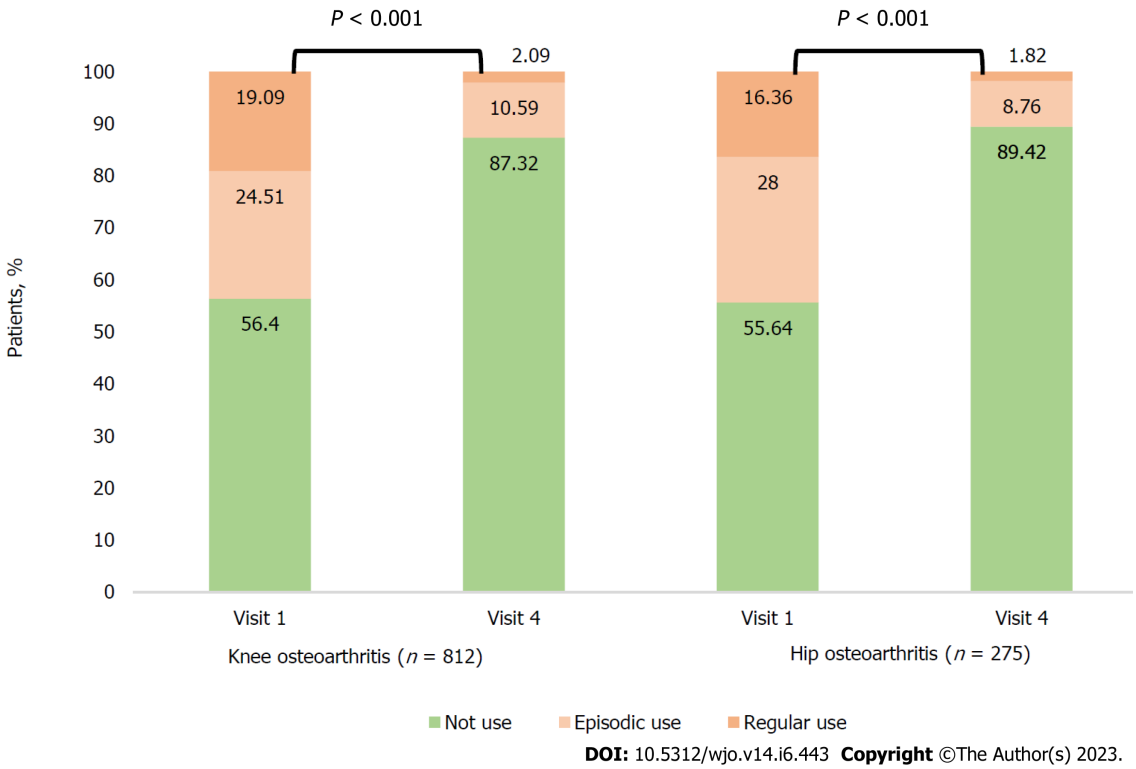

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Figure 5 The need for concomitant symptomatic therapy with non-steroidal anti-inflammatory drugs for target joints at baseline and at the end of the observation period.

each SAE). Additionally, one patient had several cardiac-related SAEs (atrial fibrillation, angina pectoris, chronic heart failure, ischemic cardiomyopathy, myocardial ischemia, and tachycardia) and another patient had gastrointestinal disorders (gastric ulcer and gastric ulcer bleeding, which was fatal). None of the SAEs were considered "related to the study product" by the investigator.

DISCUSSION

OA of knee and hip joints is one of the most common causes of disability and chronic pain worldwide. OA also implies significant medical and social costs, both directly due to treatment and indirectly because of reduced productivity and early retirement[3].

The main objectives of OA medication treatment are to alleviate pain, support quality of life, and maintain functional independence. Additionally, patients and doctors are concerned about possible adverse events caused by long-term use of NSAIDs[28,29]. The meta-analysis of the preferences of OA patients demonstrated, that patients evaluate side effects in the first place, when choosing medications, and the effectiveness of treatment significantly less affects the choice of therapy[29].

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SYSADOAs, including the combination of GA and CS, have been observed as effective and safe. SYSADOAs exert a delayed effect that persists after they are discontinued. These drugs have a symptomatic effect and could potentially slow down OA progression by influencing several pathways in the pathogenesis of the disease[30]. The effectiveness of GA or CS as monotherapies has been confirmed by several studies, which provided the prerequisites for the combination therapy[31,32]. In an experimental model, the combination of GA and CS increased the production of glycosaminoglycans in chondrocytes by 96.6% as compared to a 32% increase with the administration of each agent alone [33].

One of the most recent RCTs showed that combination of GA and CS was non-inferior to celecoxib in terms of reduction of pain, stiffness, and functional limitation after 6 mo in patients with painful knee OA, with a good safety profile[14]. In contrast, there are studies demonstrating inconsistent effects of GA and CS for OA treatment. For example, one of the largest studies [Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT)] showed no difference among the response rates, following the criteria recommended by OARSI, of CS alone, GA alone, and their combination in all OA patients[34]. However, a potentially high clinical efficacy was demonstrated in patients with moderate to severe knee

pain. The proportion of patients whose pain syndrome had decreased by ≥ 20% by Week 24 was higher in the combination therapy group than in the placebo group (79.2% *vs* 54.3%, $P = 0.002$)[34]. Notably, a significant effect was demonstrated for the combination treatment, but not for the monotherapy of GA or CS[34]. The safety of GA and CS in OA has also been confirmed in a recent meta-analysis[35].

The aim of this prospective multicenter observational cohort study was to assess changes in pain, functions of daily living, and quality of life in patients with knee and hip OA who received long-term treatment with GA + CS (capsules, 500 mg + 400 mg) in a real-world clinical setting, using the KOOS and HOOS questionnaires. We consider that the initial characteristics of patients and the treatment results are consistent with the data accumulated to date on the effectiveness of the drug.

During this real-world clinical study, patients with knee OA and hip OA showed positive dynamics in all subscales of the KOOS and HOOS questionnaires (increases in the mean scores relative to the baseline values) at each visit during the observation period, with the most pronounced changes observed during the visit after the first treatment course of GA + CS (week 16-24). Hereafter, the effect achieved by the therapy was maintained with a tendency to increase during the entire observation period (Visit 3/week 36-44, Visit 4/week 56-64). Importantly, mean score increases in all KOOS subscales exceeded 8-10 points, which were consistent with the Minimal Clinically Significant Change (MCSC) according to Roos *et al*[36]. For the HOOS questionnaire, the mean score increases across all subscales were also higher than 8-10 points. While the MCSC score for the HOOS questionnaire currently remains under assessment, the results obtained in this study on the HOOS questionnaire could be considered clinically significant according to literature data[37,38]. It's also worth noting that positive dynamics was observed for each question of the KOOS and HOOS questionnaires. In this regard, the proportion of patients with less frequent and less intense symptoms and difficulties associated with OA increased.

Data on patients' satisfaction with the long-term treatment also demonstrated beneficial efficacy and safety profile. At the end of the treatment, almost 80% patients with knee or hip OA were "very satisfied" or "satisfied". Satisfaction with the result of treatment is an important guideline in the choice of therapy tactics. The Guidance for Osteoarthritis by The National Institute for Health and Care Excellence (NICE) says that OA patients may be able to self-manage their condition effectively after getting information and guidance on management strategies. So, healthcare professionals should focus on the person's needs, so there are some situations in which planned follow-up may be necessary[39].

In general, during the observation period, patients showed a decrease in the need for concomitant pain therapy. Initially, 18.1% of the patients received regular analgesic therapy, and 25.0% of the patients received this therapy on demand (episodically). In most cases, systemic oral drug products were taken. By the end of the observation period, most patients (86.5%) did not require analgesic therapy with NSAIDs. This decrease in the need of analgesics over the observation period might be attributed to the overall improvements in functionality and well-being of the joints.

Notably, patients complied with the recommendations for the treatment duration of GA + CS. According to the evaluation results of treatment duration, therapy lasted for more than 6 mo in most patients (68.0%), 3-6 mo in 23.7%, 1-3 mo in 7.1%, and up to 1 mo in 1.3%. Therefore, the majority of patients (91.7%) generally complied with the treatment recommendations given in approved local patient information leaflet (minimal recommended treatment duration is 3-6 mo).

The baseline characteristics of our patients were consistent with the population of patients with knee and hip OA. Most patients (75.1%) had secondstage OA according to the Kellgren & Lawrence classification. The most frequent comorbidities were primary arterial hypertension (44.6%) and obesity (23.2%).

AEs associated with GA + CS usage were registered only in 31 patients (2.8%), and mainly included gastrointestinal events, which was consistent with available information on the side effects of GA + CS. SAE was reported in 14 (1.3%) patients, which could be explained by the prevalence of older people with many comorbidities in the study population (average patient age: 60.4 years). However, no SAEs were related to GA + CS therapy.

Notably, usage of patient-reported outcomes (KOOS and HOOS questionnaires) is one of the strengths of this study. Patient used touch-screen tablets to report their daily functionality and quality of life during OA treatment. Currently, data regarding patient-reported outcomes in long-term observation of OA patients are lacking.

Limitations

This study had several limitations. First, it was not possible to directly assess the effectiveness of GA + CS, since the study was observational in its nature and did not include a control group. However, long-term follow-up of patients up to 64 wk greatly offsets this limitation and increases value of received real-world data. Additionally, the standard clinical setting implied certain limitations. For example, the inability to control the use of concomitant treatment and the inability to obtain data at all time points, which could adversely affect data interpretation. To simplify the process of completing the questionnaires and reduce the amount of information provided, the subscales "Everyday Life" and "Sports and Health Activities" of KOOS/HOOS questionnaires were replaced by the KOOS-PS and HOOS-PS short forms, respectively. Nonetheless, these scales demonstrated changes in OA symptoms, improvements in functionality of the joints and quality of life, and safety.

CONCLUSION

In the framework of routine clinical practice, after long-term treatment with a fixed combination of GA and CS, a decrease in pain syndrome and significant improvements in the functional state and quality of life of patients were observed. There was a significant reduction in the need for concomitant usage of analgesics. Most patients (approximately 80%) were satisfied with the treatment. The results of this real-world clinical study confirmed the potential benefit of the combination of GA and CS for the treatment of knee and hip OA.

Long-term supplementation with GA and CS combination could be considered a standard pharmacological option on top of non-pharmacological treatment measures during any disease stage. The results of this study were considered during the preparation of national clinical guidelines on the treatment of knee and hip OA in Russia[8,9].

ARTICLE HIGHLIGHTS

Research background

High prevalence of osteoarthritis (OA) forces healthcare professionals to look for efficient and safe long-term treatment options. Combined oral treatment with glucosamine (GA) and chondroitin sulfate (CS) was shown to be efficient for pain relief and function improvement in OA patients with moderate to severe knee pain in clinical trials. There is still need in additional data regarding their effectiveness in routine clinical practice.

Research motivation

Considering high prevalence of OA and its frequent co-existence with concurrent diseases, as well as the absence of proven long-term disease-modifying treatment options, the authors aimed to evaluate the effectiveness and safety of long-term therapy of GA and CS in the framework of real clinical practice. One of the key questions was to assess the effectiveness of this therapy in the treatment of the two most common OA affected joints – knee and hip. It was important to assess the dynamics of OA symptoms, including patients who were using non-steroidal anti-inflammatory drugs (NSAIDs), and assessment of the following need of concomitant analgesic therapy.

Research objectives

The main objective of the study was to evaluate dynamics of pain syndrome, functions of living, quality of life and satisfaction of patient as well as of actual study product utilization by patients with OA for an observation period up to 64 wk. The study was also aimed to evaluate the HCP approach to the treatment and management of patients with OA to understand the place of the combination of GA and CS in their recommendations and formed the basis for the development of clinical practice guidelines.

Research methods

An open-label multicenter non-interventional prospective cohort study enrolled patients with Hip or Knee OA stage I to III who started a treatment with combination of GA and CS to evaluate health status by physical examination and validated patient questionnaires for an observation period up to 64 wk. Patients visited clinical sites up to 4 study visits. During all visits data was collected by Investigators within the routine clinical practice. In addition, during each visit patient reported outcomes were generated, assessing Knee or Hip OA outcome, as well as a simple patient satisfaction questionnaire. Depending on the target joint, one of the questionnaires, either the Knee injury and Osteoarthritis Outcome Score (KOOS) or the Hip Osteoarthritis Outcome Score (HOOS) was used.

Research results

Mean improvement on Pain subscale in patients with knee and hip OA was 22.87 and 22.81 respectively, on the Symptoms subscales – 20.78 and 19.93, on the Physical Function subscale – 16.60 and 18.77, and on the Quality-of-Life subscale – 24.87 and 22.71 from baseline to the end of observation (up to 64 wk). Number of patients using any NSAIDs decreased from 43.1% to 13.5% by the end of the observation period. Treatment-related AEs were reported for 2.8% of patients and mainly included gastrointestinal disorders [25 AEs in 24 (2.2%) patients]. Most patients (78.1%) were satisfied with the treatment. Most patients (91.3%) generally complied with the recommended duration of treatment (not less than 3 mo per year).

Research conclusions

This observational study showed that long-term oral treatment with GA + CS is associated with decrease of pain, improvements of joint function, quality of life and decrease of concomitant usage of NSAIDs in patients with knee and hip OA in routine clinical practice. Treatment with GA + CS combination showed low incidence of drug-related AEs, and high level of patients' satisfaction with the

treatment along with high compliance with long duration of the treatment.

Research perspectives

In the long term perspective, this study will contribute to the enhancement of guidelines for the treatment of OA and improve the long-term outcomes for patients with OA. Authors believe, that application of the results of this study will help to reduce the medicinal load on the patient with analgesics and NSAIDs, which ultimately can reduce the number of concomitant adverse events and increase the safety profile of the therapy.

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FOOTNOTES

Author contributions: Lila AM and Alekseeva LI were the guarantors and designed the study, and reviewed study protocol. Baranov AA, Taskina EA, Kashevarova NG, Lapkina NA, and Trofimov EA participated in the acquisition, analysis, and interpretation of the data. Alekseeva LI and Taskina EA drafted the initial manuscript; Lila AM, Baranov AA, Taskina EA, LapkinaNA, and Trofimov EA critically revised the article for important intellectual content.

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SYSTEMATIC REVIEWS

Cost-effectiveness of patient specific *vs* conventional instrumentation for total knee arthroplasty: A systematic review and meta-analysis

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Abstract

BACKGROUND

Over the past years, patient specific instrumentation (PSI) for total knee arthroplasty (TKA) has been implemented and routinely used. No clear answer has been given on its associated cost and cost-effectiveness when compared to conventional instrumentation (CI) for TKA.

AIM

To compare the cost and cost-effectiveness of PSI TKA compared to CI TKA.

METHODS

A literature search was performed in healthcare, economical healthcare, and medical databases (MEDLINE, EMBASE, CINAHL, Web of Science, Cochrane Library, EconLit). It was conducted in April 2021 and again in January 2022. Relevant literature included randomised controlled trials, retrospective studies, prospective studies, observational studies, and case control studies. All studies were assessed on methodological quality. Relevant outcomes included incremental cost-effectiveness ratio, quality-adjusted life years, total costs, imaging costs, production costs, sterilization associated costs, surgery duration costs and

readmission rate costs. All eligible studies were assessed for risk of bias. Meta-analysis was performed for outcomes with sufficient data.

RESULTS

Thirty-two studies were included into the systematic review. Two were included in the meta-analysis. 3994 PSI TKAs and 13267 CI TKAs were included in the sample size. The methodological quality of the included studies, based on Consensus on Health Economic Criteria-scores and risk of bias, ranged from average to good. PSI TKA costs less than CI TKA when considering mean operating room time and its associated costs and tray sterilization per patient case. PSI TKA costs more compared to CI TKA when considering imaging and production costs. Considering total costs per patient case, PSI TKA is more expensive in comparison to CI TKA. Meta-analysis comparing total costs for PSI TKA, and CI TKA showed a significant higher cost for PSI TKA.

CONCLUSION

Cost for PSI and CI TKA can differ when considering distinct aspects of their implementation. Total costs per patient case are increased for PSI TKA when compared to CI TKA.

Key Words: Total knee arthroplasty; Patient specific instrumentation; Instrumentation for total knee arthroplasty; Cost-effectiveness; Systematic review

Core Tip: Patient specific instrumentation (PSI) for total knee arthroplasty (TKA) has become a frequently used technique for performing TKA. In the past decade the use of PSI TKA has not proven superior nor inferior when compared to conventional instrumentation (CI) for TKA in terms of prosthetic alignment, prosthetic survival, and patient satisfaction. However, PSI TKA has been associated with a higher healthcare cost. In this review, we critically analysed the cost of PSI TKA compared to CI TKA, focusing on all facets of their cost.

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INTRODUCTION

Total knee arthroplasty (TKA) has become a commonplace surgery worldwide. Indication for TKA is disabling osteoarthritis which is often accompanied by pain, reduced range of motion and intra-articular wear and tear[1]. New technology has emerged during the past decades to improve surgical techniques and equipment. Among these developments, patient specific instrumentation (PSI) for TKA was brought to the market, which could possibly prove superior to conventional instrumentation (CI) for TKA in terms of outliers in alignment. PSI may be used as a drill guide for pin placement and/or as cutting blocks to perform the femoral and tibial bony resections.

Numerous studies have been conducted on this subject with differing results[2-10]. For example, femoral and tibial implant alignment precision has shown improved[6], declined[7] or not differing when compared to CI TKA[2-5]. Decreased blood loss[4,8], shortened hospital stay[6], and reduced operating time[3,6,8] have been reported more consistently when using PSI TKA compared to CI TKA. These factors could be associated with decreased healthcare costs and an improved efficiency of patient care. Additionally, no difference in patient reported outcome measures between PSI TKA and CI TKA have been found in a 1-, 2-, 3- and 5-year follow-up study done by Schoenmakers *et al*[10]. Clinically, PSI TKA has thus far not proved to be superior to CI TKA. However, some logistic improvements have been suggested, which may lead to a decreased cost of surgery.

Studies on cost-effectiveness of PSI show mixed results[11,12]. The included outcomes of these studies differ and thus do not allow for a concluding statement on the cost-effectiveness of PSI TKA.

The aim of this study was to systematically review literature about the cost-effectiveness of PSI for TKA and perform a meta-analysis on the available data. Thereby, the aim was to provide an evidence-based answer on the cost-effectiveness of PSI TKA compared to CI TKA.

MATERIALS AND METHODS

Review and protocol

This systematic review was performed in accordance with PRISMA statement and in line with the five-step approach for constructing a review on cost-effectiveness by PeerJ[13], Moher *et al*[14], Shamseer *et al*[15], Van Mastrigt *et al*[16], Thielen *et al*[17], and Wijnen *et al*[18]. The following research question was postulated:

Is PSI TKA cost-effective when compared to CI TKA when used for adults with disabling osteoarthritis of the knee? All included articles were examined on methodological quality. The protocol for this systematic review and meta-analysis was registered in the PROSPERO database, in December 2021 (protocol number CRD42021269209)[19].

Search strategy and eligibility criteria

The following databases were systematically searched: OVID MEDLINE, EMBASE.com, CINAHL (*via* EBSCO), The Cochrane Library and The Cochrane Central of register for Controlled Trials (CENTRAL)/ Wiley, Web of Science/Clarivate Analytics and Econlit. Additionally, ongoing unpublished trials were identified on clinical trials.gov, the World Health Organization trial registry portal and PROSPERO. Reference lists of all papers about cost effectiveness of PSI TKA and/or CI TKA have been searched manually to ensure no papers were missed in the search. No search limitations were applied. The search strategy was in accordance with the Cochrane Highly Sensitive Search Strategy[20].

Studies meeting the following criteria were included into the review: (1) TKA for disabling osteoarthritis in adults; (2) PSI TKA and/or CI TKA; and (3) Cost-analysis and/or cost-effectiveness for TKA. Articles that included patients undergoing TKA for any other reason than osteoarthritis were excluded.

Study selection and data collection

All searched and eligible articles were independently reviewed by two reviewers (ID, LG) using RefWorks[21]. The studies searched in the databases were de-duplicated and selected titles were examined on titles and abstracts based on the eligibility criteria named above. Thereafter the reviewers examined the full text independently and decided whether articles should be included or excluded. Disagreement regarding the inclusion or exclusion was resolved by discussion between the reviewers and if required a third reviewer (MS) was consulted. Once articles were included the two reviewers (ID, LG) objectively and independently extracted data from the included articles. The reviewers were blinded to each other's extractions. The following data items were obtained during the extraction process, if available: Study ID (author, year), number of patients (*n*), age of patients in years (mean), number of female and male patients, country of study conduction, study design, length of hospital stay, operation time, tray sterilization cost, PSI production cost, imaging cost, staff cost, hospital stay cost, data on Quality-Adjusted Life Years (QALYs) and Incremental Cost-Effectiveness Ratio (ICER). Other study results include length of hospital stay, operation duration, readmission rates and patient characteristics and the costs tied to these.

All costs were converted to 2018 United States Dollars using a web-based tool. This tool was developed by the Campbell and Cochrane Economics Methods Group and the Evidence for Policy and Practice Information and Coordinating Centre (v.1.6, updated last April 2019)[22]. If studies reported an index year, this year was used for conversion. This tool was able to adjust costs up to 2018. Studies performed after 2018 were therefor indexed to 2018 despite them reporting later index years. If studies did not specify an index year, it was set using the year in which the last patients were included. If this was not applicable due to study design, year of study receival (in revised form) was used.

Quality assessment

Included studies were assessed by the two reviewers separately (ID, LG) for quality and risk of bias (RoB). The assessment for RoB was performed using the Cochrane Risk of Bias Tool. For randomised studies the RoB Tool 2.0 was used, for non-randomised studies the RoB-I Tool was used. Both tools were retrieved from the Cochrane Handbook for Systematic Reviews of Interventions[23]. Evidence level of the included articles has been determined using the level of Evidence Guidelines from the Oxford centre for Evidence-Based Medicine[24].

To evaluate the methodological quality of economic evaluations the Consensus on Health Economic Criteria (CHEC) list was used[25]. The CHEC-list scores range from 0 to 19 (0 being the lowest score and 19 being the highest).

Agreement on RoB, methodological quality and evidence level was reached through discussion between the two reviewers (ID, LG) after separate and individual assessment was performed.

Statistical analysis and meta-analysis

Studies have been stratified by geographical location, year of conduction, study design, level of evidence, RoB and CHEC scores. All costs, including QALYs and ICER values, have been adjusted for inflation using a web-based tool by Campbell and Cochrane Economics Methods Group and the

Evidence for Policy and Practice Information and Coordinating Centre (v.1.6, updated last April 2019) [22]. Due to differing sourcing of costs and a variety of countries of study conduction, results were expected to show heterogeneity. Results are therefore not presented as means. The reported costs are presented in ranges.

Review Manager version 5.3 (2014) was used to perform a meta-analysis of the study data. For the meta-analysis, a fixed effects model was used and relative risk was reported with a 95% confidence interval (CI), which was used when there was similarity in included study execution. Mean difference was selected as the effect measure. Results were statistically significant if $P \leq 0.05$. To quantify the statistical heterogeneity in the studies, the I^2 value was used. I^2 values of > 75% were interpreted as high heterogeneity[26]. Only if studies were sufficiently clinically, methodologically, and statistically homogenous, the data was pooled in a meta-analysis.

Data which could be included into the meta-analysis but was presented as ranges with a 95%CI were converted to standard deviations.

RESULTS

Search results

An extensive overview of the search can be found in Supplementary Table 1. The first search was conducted on April 26, 2021. The second and last search was conducted on January 24, 2022. The systematic search of the databases resulted in 16454 studies. The manual search of the relevant reference lists resulted in 6 additional examined studies. De-duplication was performed which resulted in a remainder of 10366 studies. These were screened on titles and abstracts by the two independent reviewers. Of these studies, 15 possible relevant titles had unavailable abstracts. They were sought for retrieval by a clinical epidemiologist (MH). Six of these titles were not retrieved. Out of all screened studies, 81 articles were eligible for full text analysis. After full-text analysis, 28 articles were included into the study. Three more studies were included after reference-list analysis. A second search was conducted with the exact search terms on January 24, 2022, to include any new literature. One additional study was eligible for inclusion. This resulted in the inclusion of a total of 32 studies. A full overview of the study selection procedure is shown in the PRISMA-flowchart in Figure 1. An overview of the included studies is presented in Table 1.

Study traits

The characteristics and patient demographic of the 32 included studies are summarized in Supplementary Table 2[11,12,27-56].

Of the included studies three were randomised controlled trials[27,38,44], twenty-one were retrospective studies[11,12,28-31,33,34,36,37,40-43,46,49-52,56], seven were prospective studies[32,35,39,45,47,48,55] and one was a theoretical cohort study[54]. Publication years ranged from 1998 to 2020. Of the included studies sixteen were cost-effect analyses, fifteen were financial studies, and two studies used financial decision models.

Eleven studies directly compared PSI TKA to CI TKA. Eight papers compared CI TKA to another type of TKA (robot-assisted, unicondylar, single-use). Six papers only analysed CI TKA. Six papers compared CI TKA to total hip arthroplasty. One single paper compared PSI TKA to CI TKA and single-use instruments for TKA.

Twelve studies assessed costs from a societal perspective[12,32-35,37,39,43,46,53-55], all other studies assessed costs from a hospital perspective. Studies obtained cost estimates by either using their own hospital data set, diagnosis-related group codes, Medicare data (for studies conducted in the United States) or other national cost databases.

The main outcome measure was QALYs for sixteen studies, TKA procedure related costs for eleven studies, and surgical instrumentation and sterilization costs for five studies.

In all studies determining cost-effectiveness based on QALYs, quality of life before and after TKA was determined using health-related quality of life (HRQoL) scores. Thirteen studies used the EQ-5D, SF-6D, SF-12, SF-36, 15D HRQoL or WOMAC to determine QALY gain for TKA. Three other studies determining QALY gain for TKA used a Markov model design.

The total sample size consisted of 19331 patients and 19360 performed TKAs. Of these, 3994 PSI TKAs and 13267 were CI TKAs. All other 2099 TKAs were either unicondylar, computer-assisted, single-use or robot-assisted TKAs.

Methodological quality of included studies

All three randomised studies had some concerns for RoB[27,38,44]. This was mainly caused by the presence of randomization bias. Thirteen non-randomised studies were assessed, of which eleven had a moderate risk of bias[11,31,36,41,42,48,49,51,52,55,56]. One single study showed a low risk of bias[40] and one study showed serious risk of bias[34]. The main domains in which studies showed moderate risk of bias were the possible presence of bias in measurement of outcome and bias in the selection of participants. The 17 remaining studies could not be assessed for risk of bias as they did not compare two

Table 1 Included articles and article attributes

Ref.	Country of conduction	Study design	Studied TKA types	Type of economic analysis
Attard *et al*[44], 2019	United Kingdom	RCT	PSI TKA *vs* CI TKA *vs* Single use inserts for TKA	Financial study
Barrack *et al*[31], 2012	United States	Retrospective	PSI TKA *vs* CI TKA	Financial study
Cotter *et al*[42], 2022	United States	Retrospective	CI TKA *vs* other[1] TKA	Financial study
Dakin *et al*[43], 2012	United Kingdom	Retrospective RCT-analysis	CI TKA	Cost-effectiveness analysis
Dakin *et al*[33], 2020	United Kingdom	Retrospective	CI TKA *vs* Total hip arthroplasty	Cost-effectiveness analysis
DeHaan *et al*[49], 2014	United States	Retrospective	PSI TKA *vs* CI	Financial study
Elmallah *et al*[29], 2017	United States	Retrospective comparative cohort	CI TKA *vs* Total hip arthroplasty	Cost-effectiveness analysis
Goldberg *et al*[30], 2019	United States	Retrospective	CI TKA *vs* other TKA	Financial decision model
Jenkins *et al*[32], 2013	United Kingdom	Prospective	CI TKA *vs* Total hip arthroplasty	Cost-effectiveness analysis
Konopka *et al*[37], 2018	United States	Retrospective	CI TKA *vs* Total hip arthroplasty	Cost-effectiveness analysis
Krummenauer *et al*[35], 2009	Germany	Prospective	CI TKA	Cost-effectiveness analysis
Lionberger *et al*[27], 2014	United States	RCT	PSI TKA *vs* CI TKA	Financial study
Losina *et al*[46], 2009	United States	Retrospective population analysis	CI TKA	Cost-effectiveness analysis
Moerenhout *et al*[36], 2021	Switzerland	Case control, retrospective chart	PSI TKA *vs* CI TKA	Financial study
Mont *et al*[48], 2012	United States	Prospective controlled trial	CI TKA *vs* other TKA	Financial study
Navarro Espigares and Hernández Torres[47], 2008	Spain	Prospective cohort	CI TKA *vs* Total hip arthroplasty	Cost-effectiveness analysis
Nunley *et al*[11], 2012	United States	Retrospective	PSI TKA *vs* CI TKA	Financial study
Peersman *et al*[53], 2014	Belgium	Retrospective	CI TKA *vs* other TKA	Cost-effectiveness analysis
Räsänen *et al*[45], 2007	Finland	Prospective	CI TKA *vs* Total hip arthroplasty	Cost-effectiveness analysis
Rorabeck and Murray[50], 1996	Canada	Retrospective	CI TKA	Financial study
Schilling *et al*[28], 2017	Australia	Retrospective	CI TKA	Cost-effectiveness analysis
Siegel *et al*[40], 2015	United States	Retrospective	CI TKA *vs* other TKA	Financial study
Slover *et al*[54], 2006	United States	Theoretical cohort	CI TKA *vs* other TKA	Cost-effectiveness analysis
Slover *et al*[12], 2012	United States	Retrospective	PSI TKA *vs* CI TKA	Financial decision model
Stan *et al*[34], 2015	Romania	Retrospective	CI TKA *vs* other TKA	Cost-effectiveness analysis
Teeter *et al*[38], 2019	Canada	RCT	PSI TKA *vs* CI TKA	Financial study
Thienpont *et al*[41], 2015	Belgium	Retrospective	PSI TKA *vs* CI TKA	Financial study
Thomas *et al*[56], 2022	United States	Retrospective	PSI TKA *vs* CI TKA	Financial study
Tibesku *et al*[51], 2013	Germany	Retrospective	PSI TKA *vs* CI TKA	Financial study
Waimann *et al*[39], 2014	United States	Prospective	CI TKA	Cost-effectiveness analysis
Watters *et al*[52], 2011	United States	Retrospective	PSI TKA *vs* CI TKA	Financial study

Xie *et al*[55], 2010	Singapore	Non-randomized prospective observational cohort	CI TKA *vs* other TKA	Cost-effectiveness analysis

[1]Other type of total Knee arthroplasty (TKA) includes robot-assisted, unicondylar or single-use TKA.
PSI: Patient specific instrumentation; CI: Conventional instrumentation; TKA: Total knee arthroplasty; RCT: Randomised controlled trial.

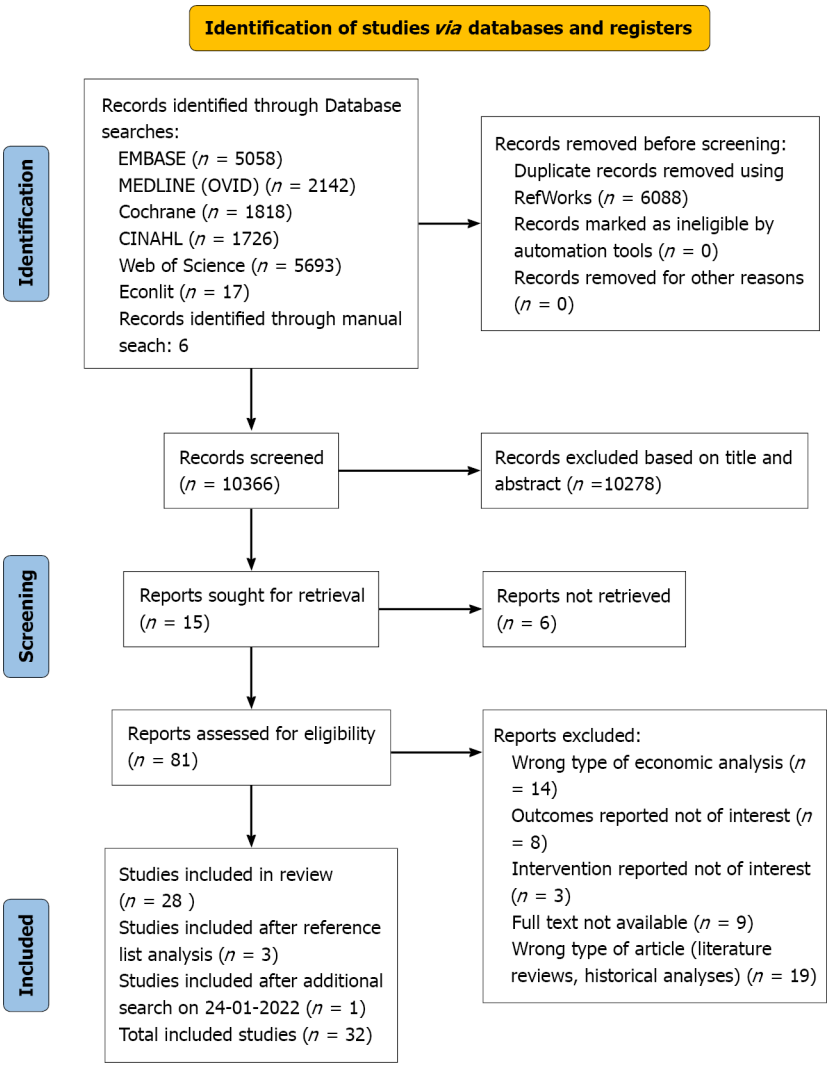

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Figure 1 PRISMA-flowchart of searches in databases and registers. This figure was generated using the PRISMA-diagram provided in the PRISMA statement.

or more interventions or used an economical model without patient population (*e.g.* Markov-model) to calculate cost-effectiveness[12,25,26,28-30,32,33,35,37,39,43,45-47,50,53,54].

The three included randomised studies have an evidence level of II[27,38,44]. One single study, a case control study, has a level of evidence of IV[36]. All other included studies have an evidence level of III [11,25,26-30,31,32,34,37,39-43,45-55]. The level of evidence and RoB of the included studies have been summarized in Supplementary Table 3.

Economic quality of the included studies according to the CHEC-score were moderate. CHEC-scores ranged from 11 to 17, with an average of 14. CHEC-scores are not available for two of the included studies (Rorabeck and Murray[50], Nunley *et al*[11])[11,50]. The scoring-system was not applicable for studies in which no costing-models or mean costs were used and/or presented. Basis for lower CHEC-scores was due to inappropriate study design for an economic analysis, a lack of incremental analysis of costs and outcomes, a lack of sensitivity analysis of costs and outcomes, a lack of discounting of costs for appropriate index years and a lack of analysis on ethical aspects of intervention costs. A summary of CHEC scores per study can be found in Supplementary Table 4.

Study results

Reported costs and inflation-adjusted costs, are summarized in Supplementary Table 5.

Imaging costs

Imaging costs were defined as all imaging needed for patients preoperatively. For CI TKA, this included standard X-ray imaging of the affected knee. Imaging costs for CI TKA ranged from $52.51 to $901.48 [39,42,50,54]. Imaging for PSI TKA was defined as MRI-imaging needed to model the PSI. The reported costs ranged from $226.79 to $13942.40[12,27,31,41,44,49,51]. A single study directly compared imaging costs for PSI TKA and CI TKA[51]. The study reported an increased imaging cost of $12091 for PSI TKA.

PSI TKA production costs

PSI production costs were defined as the cost of producing the PSI model. Costs were reported to range from $377.98 to $119.35 per model[12,31,44,49,51,52]. The types of PSI models used in the included studies were the patient-specific cutting blocks from MyKnee (Medacta), KneePlan (Symbios), Visionaire (Smith & Nephew's) and Zimmer-Biomet's Signature knee system. For CI TKA, no additional production costs were reported.

Sterilization costs

Sterilization costs were defined as the cost of sterilizing surgical instrument trays per surgical case. Studies have reported a decrease in tray usage when TKA is performed using PSI. The amount of trays needed for CI TKA in all studies ranged from 6 to 34 trays per patient case[41,48,51,52]. For PSI TKA the amount of trays needed per patient case ranged from 1 to 5 trays[41,49,51,52].

A decrease of 4 trays per case have been reported in two studies when using PSI TKA[49,51]. A decrease of 5 trays per case have been reported in two other studies when using PSI TKA[41,52]. Tray sterilization costs ranged from $353.89 to $1533.32 per case for CI TKA[30,41,42,44,51,52]. For PSI TKA, tray sterilization costs ranged from $67.60 to $495.50 per case[36,44,49,52]. In three studies costs of tray sterilization between PSI TKA and CI TKA were directly compared. All three studies reported cost decrease when using PSI TKA[44,51,52]. However, they do not report the amount of decrease in a monetary value.

Operating room time and costs

Operating room (OR) time was defined as time from patients entering the OR to leaving the OR, patient preparation time combined with surgery time, and time from the start of the patient case to the start of the next patient case.

When using CI TKA, studies reported mean OR times that ranged from 63.10 ± 38.02 min to 141.3 ± 22.1 min[11,41,42,44,49,51,52]. When using PSI TKA, studies reported mean OR times that ranged from 58.10 ± 23.04 min to 148.2 ± 16.2 min.

Six studies directly compared mean OR time differences between CI and PSI TKA. One study reported a prolonged mean OR time of 2 min, resulting in associated $1985 in costs when using PSI TKA [41]. The remaining five studies reported a reduced mean OR time when using PSI TKA[40,44,49,51,52]. Time savings reported in these studies ranged from 5 min to 30 min when using PSI TKA.

Additionally, five studies reported the comparison of OR time and their associated costs between CI TKA and PSI TKA. One study does not give exact OR times for CI or PSI TKA. They reported that PSI TKA usage is associated with a mean OR time decrease of 11 min which translated to saving $226.54 per patient case[31]. The three remaining studies observe a decrease in mean OR time when using PSI TKA [49,51,52]. The decrease in mean OR time per patient case for PSI TKA was reported to be between 13 and 30 min[49,51,52]. The associated decrease in cost is respectively between $117.36 and $1416.38[49,51, 52].

Readmission rates

One study reports lower readmission rates when using PSI TKA compared to CI TKA[56]. Patients who received a TKA using PSI had statistically significant ($P \leq 0.05$) lower readmission rates at 30 d (2.03% *vs* 2.92%), 60 d (2.65% *vs* 4.02%), 90 d (3.19% *vs* 4.62%), and at one year (6.46% *vs* 8.76%).

Total TKA costs

Total costs for TKA were defined as the sum of costs per patient case for OR time, inpatient stay, sterile processing, surgeon cost, imaging costs, PSI production, TKA implant, and/or postoperative care.

Nine studies solely reported total costs for CI TKA[28-30,32,39,42,43,47,55]. The reported mean cost for CI TKA ranged from $1391 to $29163.16 per patient case.

One study solely reported total cost for PSI TKA[27]. The reported mean cost for PSI TKA was $12642.27 per patient case.

Four studies compared mean PSI TKA costs directly to mean CI TKA costs[38,51,52,56]. In three of the comparing studies, PSI TKA was more costly than CI TKA[38,51,52]. In one study PSI TKA was less costly than CI TKA[56].

The first study found a mean costs per patient case of $9337.17 ± 5446.83 for CI TKA compared to $13352.33 ± 10783.22 for PSI TKA[38]. The following studies found these mean costs per patient case to be respectively; $8177.77 compared to $8264.76[51], $2989.46 compared to $3608.84[52], and $16379.17 (16182.84-16577.55) compared to $15246.19 (15067.24-15427.18)[56]. An overview of total TKA costs for PSI and CI is presented in Figure 2.

QALY gain

QALY gain was determined as the amount of QALYs gained in a certain number of years after TKA. Seven studies reported data on this for CI TKA[28,29,34,35,37,45,46], no studies reported data on QALY gain for PSI TKA. QALY gain was determined using the EQ-5D in three studies and the SF-12, SF-6D, 15D HRQol and SF-36 were used in the remaining four studies. QALY gain per year for CI TKA was reported as; 0.77/1 year[28], 0.768/1 year[29], 2.6/1 year[34], 0.17/1 year[37], 0.359/1 year[45], 2.93/0.25 years[35] and 1/7.957 years[46].

Cost per QALY

Costs per QALY were determined in eight of the included studies. QALY outcomes were based on EQ-5D in four studies[34,35,43,47], EQ-5D-3L in two studies[32,33], 15D HRQoL in one study[45] and a Markov model in one other study[12].

One study compared PSI and CI TKA directly[12]. PSI TKA costs $4700/QALY compared to $2900/QALY for CI TKA. Costs per QALY gained determined for CI TKA ranged from $1275.84 per QALY to > $20000 per QALY[32-35,43,45,47].

ICER per QALY

ICER per QALY was defined as the price per QALY gained for TKA. Four studies presented data on this for CI TKA[29,46,53,55]. No studies presented this data for PSI TKA. ICER per QALY ranged from $20090.25/QALY to $76384.09/QALY.

Meta-analysis

A meta-analysis was performed using the data on total cost for PSI TKA and CI TKA. Two studies were included into the meta-analysis[38,56]. Two other studies (Tibesku *et al*[51], Watters *et al*[52]) comparing total cost for both techniques could not be included into the analysis due to lack of ranges or standard deviation[51,52].

The forest plot is presented in Figure 3. Study heterogeneity was high, with an I^2 of 78% (P = 0.03). The overall effect was in favour of CI TKA, with a significant mean difference of $1132.98 [850.00-1383.32] 95%CI (P > 0.00001) less when compared to PSI TKA.

DISCUSSION

The goal of this systematic review was to assess the cost-effectiveness of PSI TKA compared to CI TKA. Additionally, results were pooled into a meta-analysis. The study aimed to combine the most accurate results available on this topic to produce a clear answer as to whether PSI TKA is a cost-effective alternative to CI TKA.

The main conclusion is that there is a lack of literature on PSI TKA when it comes to data on QALYs and ICER. Furthermore, data on costs of PSI TKA and CI TKA show heterogeneity. Due to this, no definite conclusion can be drawn on the cost-effectiveness of PSI TKA when directly compared to CI TKA. This systematic review has shown that PSI TKA costs less when considering OR time and tray sterilization. PSI TKA costs are increased when considering imaging, production, and costs per total patient case.

There was a large heterogeneity in costs due to differences in calculation methods of costs and patient charges per study. Additionally, country of study conduction has an impact on prices. Furthermore, differences in patient population (such as age, comorbidities, anatomic variance of knee joints) per study could influence the cost outcome. In this systematic review costs were directly compared, but the abovementioned factors should be considered when interpreting the outcome of these comparisons. For example, studies performed in the United States often reported much higher costs than studies performed in Europe.

A meta-analysis was performed, the results were heterogeneous and therefore did not provide conclusive evidence. Furthermore, no meta-analysis could be performed on the QALY or ICER data as no studies were found that directly compared these for PSI TKA and CI TKA. In the future, studies should directly assess and directly compare cost-effectiveness using QALYs and ICER.

Multiple studies have investigated whether PSI TKA is superior to CI TKA when it comes to prosthetic placement, peri- and post-operative outcomes. Schotanus *et al*[57] described that PSI TKA was ready for primetime after performing a comparative study with CI TKA. The study compared four different PSI TKA systems to CI TKA in a total of 117 knees. PSI TKA was showed to have a lower number of significant outliers[57]. Predescu *et al*[58] performed a comparative study, where PSI and CI

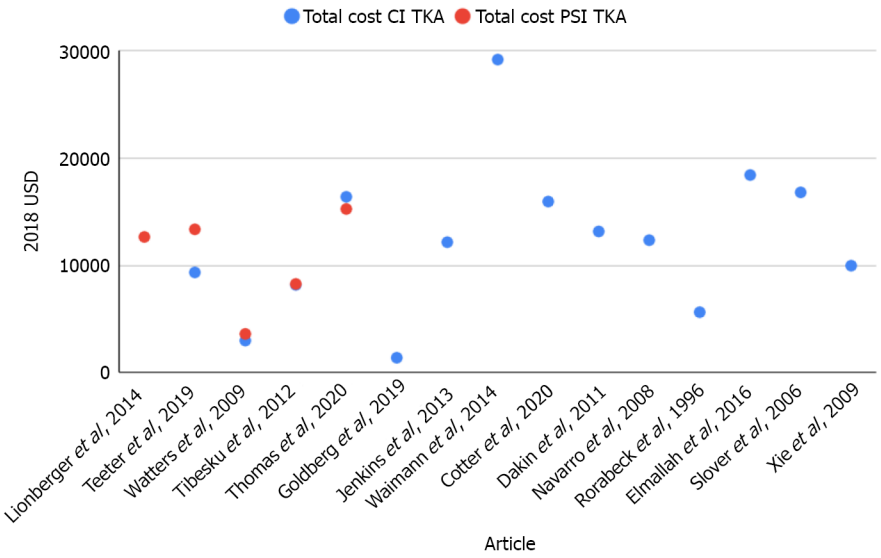

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Figure 2 Scatter plot of total cost for patient specific instrumentation total knee arthroplasty and conventional instrumentation total knee arthroplasty per study. Total costs for patient specific instrumentation (PSI) total knee arthroplasty (TKA) and conventional instrumentation (CI) TKA per paper. This figure present costs without variance. The figure shows the heterogeneity of total cost per patient case for PSI TKA and CI TKA when compared in multiple different studies. When directly compared PSI TKA costs more per patient case in three[38,51,52] out of four[56] studies. PSI: Patient specific instrumentation; TKA: Total knee arthroplasty; CI: Conventional instrumentation; USD: United States Dollars.

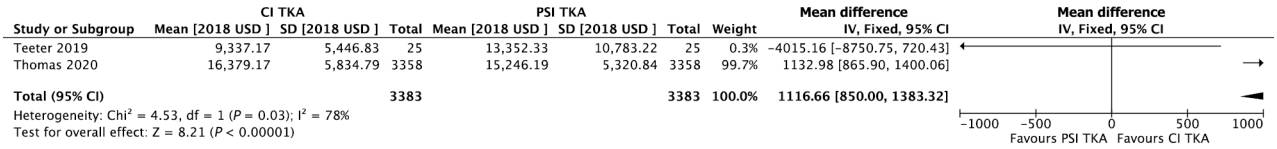

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Figure 3 Forrest plot of meta-analysis of total cost of patient specific instrumentation total knee arthroplasty compared to conventional instrumentation total knee arthroplasty. PSI: Patient specific instrumentation; TKA: Total knee arthroplasty; CI: Conventional instrumentation; USD: United States Dollars. This figure has been generated using Review Manager version 5.3 (2014).

TKA were compared in a population of 80 patients. They found that PSI TKA did not prove superior however posed as an alternative for CI TKA or computer assisted TKA[58]. Furthermore, Sassoon *et al* [59] described in their systematic review that PSI TKA has not reliably demonstrated improvement of postoperative limb or component alignment[59]. Despite this, PSI TKA has remained popular due to its relatively easy production and especially its usefulness as an additional planning tool in anatomically challenging cases. This systematic review shows that in most cases, more costs are associated with the use of PSI TKA. The results of this review could be taken into consideration when making decisions on whether and when to use PSI TKA.

One single study included into this systematic review determined additional costs for readmission rates related to either PSI or CI use for TKA[55]. The results from this study showed that CI TKA was associated with higher readmission rates, which is associated with increased costs of $6753 ± 175[60]. Thus, more investigation into cost-effectiveness related to readmission rates could be useful for future decision-making regarding instrumentation choices in general. This should also be reconsidered now that robotics are being introduced for TKA at a rapid pace, which entails the additional necessary costs [61].

Results from this systematic review were extracted from a variety of countries. As a result of this, pricing may vary for developing countries or countries with different types of health care pricing systems.

In regards to study quality, multiple studies received sponsoring or funding through prosthetic and/or orthopaedic manufacturers[28,30,33,41,42,46,50]. Minimal influence on the results is expected due to these sponsorships since not all authors were associated with the sponsorships, nor did they receive any payment for the conducted study. Additionally, variety in definition of utilities per study should be considered as pricing may not be based on the exact same parameters per case. Therefore, not all costs in this systematic review should be considered as directly comparable to any or every country. However, these costs are an indication of true cost of PSI and CI TKA worldwide.

This systematic review provided a detailed overview of relevant literature on costs and cost-effectiveness of PSI compared to CI TKA. Systematic reviews on PSI TKA which investigate facets of its costs, such as tray sterilization, are available[59]. However, this systematic review aimed to present relevant literature on all facets of costs associated with PSI TKA and CI TKA.

The strength of this systematic review is its methodological quality. It was executed in accordance with the five-step approach for constructing a review on cost-effect by Van Mastrigt *et al*[16] and the PRISMA statement[13-18]. Furthermore, a large patient population and all the attributed costs for CI and PSI TKA were analysed.

Its limitation is, however, the possibility of biased results due to exclusion of non-full texts.

CONCLUSION

This study showed that costs for PSI TKA and CI TKA can differ when considering different aspects of their implementation in a hospital setting. A comprehensive overview of the contributing components to the pricing of CI and PSI TKA is provided. When considering total costs, PSI TKA is more costly when directly compared to CI TKA.

ARTICLE HIGHLIGHTS

Research background

Over the years, extensive research into the clinical outcomes of patient specific instrumentation (PSI) for total knee arthroplasty (TKA) compared to conventional instrumentation (CI) for TKA have been performed. Clinically, the instrumentation techniques are considered equal. However, decreased operating time and sterilization tray usage have been reported when using PSI TKA. These factors could influence the healthcare cost.

Research motivation

Multiple studies into the cost and cost-effectiveness of PSI and CI TKA have been performed since its introduction. Most studies consider specific aspects of their costs, such as: Additional imaging costs, PSI production costs, operating time costs, and tray sterilization costs. Furthermore, studies on Quality Adjusted Life Years (QALY) and Incremental Cost Effectiveness Ratio (ICER) for PSI and CI TKA have been performed. Despite the abundance of research, no clear overview or comparison has been presented. The motivation for this systematic review was to give a clear overview of the cost and cost-effectiveness of PSI TKA compared to CI TKA.

Research objectives

The objective of this research was to present the different aspects of cost of PSI TKA and CI TKA. Furthermore, cost-effectiveness was investigated. By doing this, the secondary objective was to advise orthopaedic surgeons in their decision making when choosing either PSI TKA or CI TKA.

Research methods

A systematic literature search was performed in healthcare, economical healthcare, and medical databases (MEDLINE, EMBASE, CINAHL, Web of Science, Cochrane Library, EconLit). Relevant literature included randomised controlled trials, retrospective studies, prospective studies, observational studies, and case control studies. Data extraction was performed to obtain the following results: ICER, QALYs, total costs, imaging costs, production costs, sterilization associated costs, surgery duration associated costs and readmission rates and associated costs. Meta-analysis was performed for outcomes with sufficient data.

Research results

Thirty-two studies were included into the systematic review. Two were included in the meta-analysis. 3994 PSI TKAs and 13267 CI TKAs were included in the sample size. We found that when considering mean OR time and its associated costs and tray sterilization per patient case, PSI TKA costs less than CI TKA. PSI TKA is more costly compared to CI TKA when considering imaging and production costs. Considering total costs per patient case, PSI TKA is more expensive in comparison to CI TKA. Meta-analysis comparing total costs for PSI TKA, and CI TKA showed a significant higher cost for PSI TKA.

Research conclusions

This study showed that costs for PSI TKA and CI TKA can differ when considering different aspects of their implementation. When directly comparing PSI and CI TKA, results showed that total costs per patient case are more for PSI TKA.

Research perspectives

Based on the results presented, we recommend orthopaedic surgeons worldwide make careful decisions when deciding on which instrumentation technique to use for TKA. In anatomically challenging cases PSI is a helpful planning modality for TKA. However, this systematic review showed that the total cost of its implementation is higher per patient case. Surgeons are advised to take the cost-effectiveness and total cost into consideration.

FOOTNOTES

Author contributions: Dorling IM designed the research; Dorling IM and Geenen L performed the research; Heymans MJLF performed the systematic search; Dorling IM and Geenen L performed the data analysis; Most J, Boonen B, and Schotanus MGM supervised the research and revised the manuscript; Dorling IM wrote the paper.

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SYSTEMATIC REVIEWS

Return to sport following toe phalanx fractures: A systematic review

Greg A J Robertson, Amit Sinha, Thomas Hodkinson, Togay Koç

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Abstract

BACKGROUND

Evidence-based guidance on return to sport following toe phalanx fractures is limited.

AIM

To systemically review all studies recording return to sport following toe phalanx fractures (both acute fractures and stress fractures), and to collate information on return rates to sport (RRS) and mean return times (RTS) to the sport.

METHODS

A systematic search of PubMed, MEDLINE, EMBASE, CINAHL, Cochrane Library, Physiotherapy Evidence Database, and Google Scholar was performed in December 2022 using the keywords 'Toe', 'Phalanx', 'Fracture', 'injury', 'athletes', 'sports', 'non-operative', 'conservative', 'operative', 'return to sport'. All studies which recorded RRS and RTS following toe phalanx fractures were included.

RESULTS

Thirteen studies were included: one retrospective cohort study and twelve case series. Seven studies reported on acute fractures. Six studies reported on stress fractures. For the acute fractures (n = 156), 63 were treated with primary conservative management (PCM), 6 with primary surgical management (PSM) (all displaced intra-articular (physeal) fractures of the great toe base of the proximal phalanx), 1 with secondary surgical management (SSM) and 87 did not specify treatment modality. For the stress fractures (n = 26), 23 were treated with PCM, 3 with PSM, and 6 with SSM. For acute fractures, RRS with PCM ranged from 0 to

100%, and RTS with PCM ranged from 1.2 to 24 wk. For acute fractures, RRS with PSM were all 100%, and RTS with PSM ranged from 12 to 24 wk. One case of an undisplaced intra-articular (physeal) fracture treated conservatively required conversion to SSM on refracture with a return to sport. For stress fractures, RRS with PCM ranged from 0% to 100%, and RTS with PCM ranged from 5 to 10 wk. For stress fractures, RRS with PSM were all 100%, and RTS with surgical management ranged from 10 to 16 wk. Six cases of conservatively-managed stress fractures required conversion to SSM. Two of these cases were associated with a prolonged delay to diagnosis (1 year, 2 years) and four cases with an underlying deformity [hallux valgus (n = 3), claw toe (n = 1)]. All six cases returned to the sport after SSM.

CONCLUSION

The majority of sport-related toe phalanx fractures (acute and stress) are managed conservatively with overall satisfactory RRS and RTS. For acute fractures, surgical management is indicated for displaced, intra-articular (physeal) fractures, which offers satisfactory RRS and RTS. For stress fractures, surgical management is indicated for cases with delayed diagnosis and established non-union at presentation, or with significant underlying deformity: both can expect satisfactory RRS and RTS.

Key Words: Acute; Stress; Fracture; Toe; Phalanx; Return; Sport; Rate; Time

Core Tip: We performed a systematic review, assessing studies that recorded return rates (RRS) and return times (RTS) to sports following acute and stress fractures of the toe phalanges. Thirteen studies were included. Seven studies reported on acute fractures (n = 156); six studies on stress fractures (n = 26). For acute fractures, 63 underwent primary conservative management (PCM), 6 primary surgical management (PSM), and 1 sary surgical management (SSM). For stress fractures, 23 underwent PCM, 3 PSM, and 6 SSM. For acute fractures, PCM conferred acceptable RRS and RTS. PSM was indicated for displaced intra-articular proximal phalanx fractures. For stress fractures, PCM, when successful, conferred acceptable RTS. Significant delays to diagnosis or associated deformity often necessitated the conversion to SSM: this was invariably successful at returning athletes to sport.

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INTRODUCTION

Acute toe phalanx fractures are a relatively common injury, comprising 3%-4% of all traumatic fractures [1-4]. Most of these fractures occur within the first and fifth toes, with the majority being undisplaced or minimally displaced, and suitable for conservative management[5]. The functional results following these injuries have shown promising results[5].

While 16% of all acute toe fractures occur during sport, the incidence and outcome of these fractures in the athlete remain poorly defined[6]. Traumatic toe phalanx fractures have been found to comprise 4.5% of all sport-related fractures, and occur at an incidence of 0.06 per 1000 of the general population [6].

By comparison to acute fractures, the epidemiology of toe phalanx stress fractures is less well described[7]. While a significant proportion of these fractures are sport-related, the current literature on this injury type comprises a limited number of case series and case reports[7]. While there are emerging theories that link biomechanical deformities to their occurrence (*e.g.* hallux valgus and great toe proximal phalanx stress fractures), a comprehensive description of this fracture type has yet to be presented[8].

The most common causative sports for acute toe phalanx fractures are soccer, gymnastics, and judo [9]. The most common causative sports for stress-toe phalanx fractures are sprinting, soccer and long-distance running[7]. For acute toe phalanx fractures, the common sporting mechanisms of injury include tackle and dismount[9].

Regarding treatment, with the vast majority of acute toe phalanx fractures being undisplaced or minimally displaced and extra-articular, they are managed conservatively, with toe strapping and

protected weight-bearing[5,9]. Those that are significantly displaced or intra-articular, are often managed with closed +/- open reduction with k-wire or screw fixation[9]. Open fractures require fracture site washout +/- fixation[9]. Stress fractures of the toe phalanx are routinely managed conservatively in the first instance, with protected weight-bearing and avoidance of relevant sporting activities [7]. However, those with significantly delayed presentation (> 1 year) and established non-union, or those that are associated with a significant causative deformity, often require surgical intervention[7].

Despite this treatment framework, there is very limited information in the current literature to guide the optimal management of these fractures in the athlete[7,9-11]. Similarly, there is very limited published data, which illustrates the expected morbidity that such fractures will have on the athlete[7,9-11].

This systematic review aims to provide a comprehensive overview of the current literature which records return to sport following acute fractures and stress fractures of the toe phalanges in the athlete.

MATERIALS AND METHODS

Literature search

The authors performed a systematic analysis of the listed databases in December 2022: PubMed, MEDLINE, EMBASE, CINAHL, Cochrane Library, Physiotherapy Evidence Database (PEDro), and Google Scholar.

The search aimed to identify all peer-reviewed studies, which recorded return rates to sport (RRS) and return times to sport (RTS) in patients who sustained toe phalanx fractures. The search terms used were 'toe', 'phalanx', 'fracture', 'injury', 'athletes', 'sports', 'non-operative', 'conservative', 'operative', 'surgical', and 'return to sport'. All articles were considered, regardless of the date of publication or level of the sport.

The review was structured along the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines[12]. Two authors (X.X.X., X.X.X.) searched for and reviewed the articles. Table 1 records the inclusion and exclusion criteria. The QUOROM Process for the review is illustrated in Figure 1.

The authors excluded technical notes, case reports, instructional course reports, biomechanical reports, articles of expert opinion, and literature reviews, unless these manuscripts contained relevant patient data. Similarly, articles reporting on return to sport following toe sesamoid fractures were excluded. A stepwise process of article assessment was performed, first reviewing all the relevant titles, then abstracts, then full-length articles as required. Relevant reference lists and review studies were also assessed to locate further studies, which were appropriate for inclusion. Any disagreement in article inclusion was confirmed through consensus agreement or liaison with the senior author.

Data extraction

The recorded data from each study included: Demographic details, mechanism of injury (for acute fractures), duration of preceding symptoms (for stress fractures), pre-operative imaging investigations, fracture location, fracture nature (acute *vs* stress) and fracture severity, conservative and surgical treatment methods, RRS, RTS, return rates to pre-injury level of sport, complications, outcome scores recorded, and relevant predictive factors.

Acute fractures and stress fractures were grouped separately. For the acute fracture studies, some papers recorded the fractures with no differentiation regarding fracture type or location: These studies were grouped as 'general cohort' studies. Other studies specifically described the management of intra-articular (physeal) fractures of the base of the great toe proximal phalanx: These were grouped as 'Intra-Articular (Physeal) Base of Proximal Phalanx Fractures'.

Outcome measures

The primary outcome data was RRS and RTS. The secondary outcome data included 'return to pre-injury level of sport' rates and relevant complications.

Study definitions

RRS was defined as the percentage of athletes who successfully returned to sport with the designated treatment modality. Where conversion to a further treatment was required, with RRS not possible from the initial treatment method, this was recorded as a non-return to sport for the method in question. For conservative treatment, RTS was defined as the time from the commencement of conservative treatment to return to sport. For surgical treatment, RTS was defined as the time from the commencement of the relevant surgical treatment to return to sport[13].

If surgical management was chosen as the first-line treatment, this was referred to as 'primary surgical management' (PSM). If surgical management was chosen following failed conservative management, this was referred to as 'secondary surgical management' (SSM). Return times to sport for 'secondary surgical management' were recorded from the relevant surgical procedure.

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Acute toe phalanx fractures	Toe sesamoid fractures
Stress toe phalanx fractures	Toe joint dislocation without fracture
Elite or recreational athletes	Toe joint fracture dislocation
Return rate to sporting activity reported	Toe ligament injuries
Time to return to sporting activity reported	No sporting outcome data reported
Two or more injuries reported	Concomitant upper or lower limb fractures
Peer-reviewed journals	Reviews, case reports, abstracts, or anecdotal articles
English language	Animal, cadaver, or *in vitro* studies

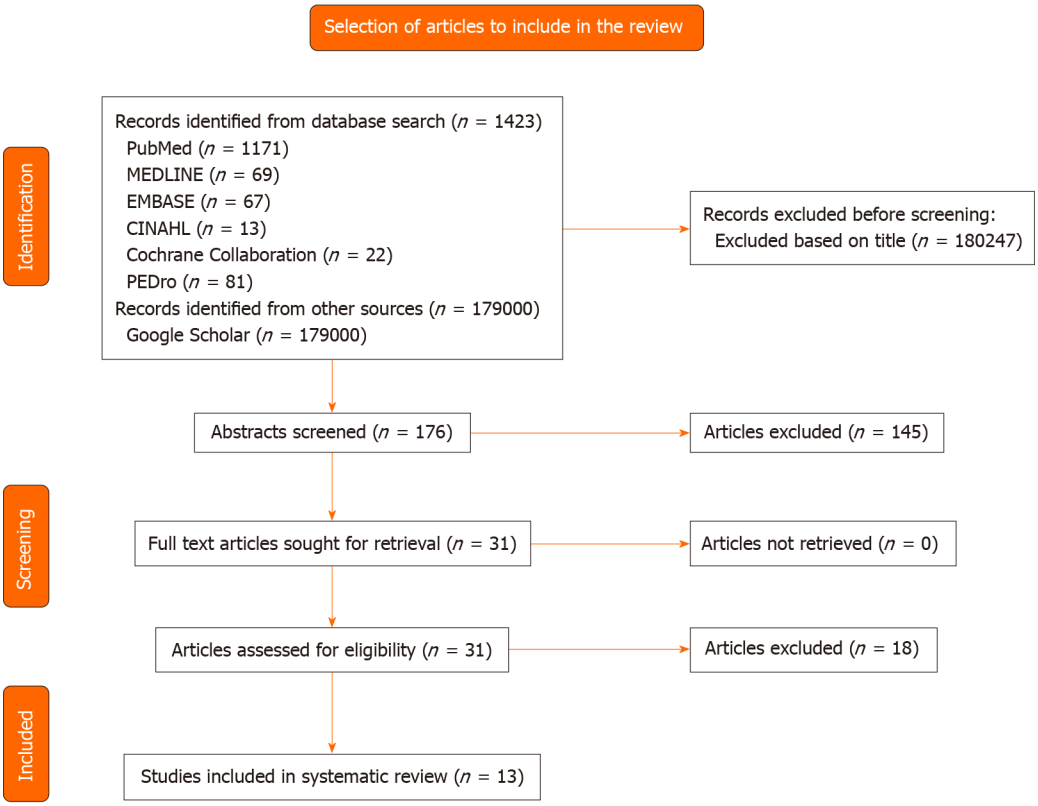

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Figure 1 Selection of articles to include in for inclusion in the review by in accordance with the PRISMA protocol[12].

Quality assessment

Study quality was quantified by the modified Coleman Methodology Score (CMS), as described by Coleman *et al*[14]. Study quality was also assessed by the Methodological Index for Non-Randomized Studies (MINORS) Score. Two of the authors calculated the modified CMS and the MINORS Score for each study (X.X.X, X.X.X). Inter-observer reliability of the modified CMS and MINORS scoring processes were quantified using the intra-class correlation co-efficient statistic. For the modified CMS, this was 0.98 (95%CI: 0.96-1.00). For the MINORS scores, this was 0.92 (95%CI: 0.89-0.94).

Statistics

There was insufficient data to perform data synthesis or meta-analysis comparisons within the data. Thus, the available data was presented as a systematic review, without the use of analytic statistics. The intra-class correlation co-efficient statistic was used to assess the inter-observer reliability of the Modified Coleman Scores and the Methodological Index for Non-Randomized Studies Scores using IBM SPSS Statistics, Version 27.0 (Armonk, NY, United States).

RESULTS

Search

The details of the review process for the included articles are provided in Figure 1. In total, 176 abstracts and 31 articles were reviewed.

Quality of the included studies

The mean CMS for all the studies was 49.6 (range 34-67)[8,15-26] (Tables 2 and 3). For the studies reporting on acute fractures, the mean CMS was 53.1 (range 39-67)[15-21] (Table 2). For the studies reporting on stress fractures, the mean CMS was 45.5 (range 34-55)[8,22-26] (Table 3).

The mean MINORS score for all the studies was 10.3 (range 8-18)[8,15-26] (Tables 2 and 3). For the studies reporting on acute fractures, the mean MINORS score was 12.1 (range 9-18)[15-21] (Table 2). For the studies reporting on stress fractures, the mean MINORS score was 8.2 (range 8-9)[8,22-26] (Table 3).

Patient demographics

13 relevant studies[8,15-26] were identified, (year of publication from 1986[22] to 2022[18]), which recorded return to sports data for patients who sustained toe phalanx fractures (Table 2). One of these studies was a retrospective cohort study[18], and 12 were case series[8,15-17,19-26].

There were 156 acute toe phalanx fractures and 26 stress fractures. Eight of the acute fractures were specifically described as intra-articular (physeal) (all great toe bases of the proximal phalanx). Of the acute fractures, 14 occurred in the great toe, 1 in the second toe, and 1 in the third toe, and the location was not specified for 140. Of the stress fractures, 22 occurred in the proximal phalanx of the great toe and 4 in the proximal phalanx of the second toe. Of the 26 stress fracture patients, 16 (of the 22 great toe proximal phalanx stress fracture patients) had associated 'hallux valgus' deformity, and 1 (of the 4-second toe proximal phalanx stress fracture patients) had associated 'claw toe' deformity (Table 3). Regarding the etiology of the deformities, only one case noted the deformity to have developed secondary to the stress fracture[26].

Of the 156 acute fractures, 129 (83%) occurred in male patients, 23 (15%) in female patients, and 4 (3%) failed to specify gender. None of the studies reported bilateral fractures. Follow-up data were available for 154 (99%) of the 156 acute fractures. The mean age at the time of injury ranged from 12.5 years[19,21] to 21.1 years[15], and the causative sports included soccer, gymnastics and judo (Table 2).

Of the 26 stress fractures, 10 (38%) occurred in male patients, and 16 (62%) in female patients. None of the studies reported bilateral fractures. Follow-up data were available for all 26 (100%) of the stress fractures. The mean age at the time of injury ranged from 13.7 years[23] to 29.0 years[24], and the causative sports included sprinting, soccer, long-distance running, rugby, Japanese Fencing/Kendo, triathlon, gymnastics, baseball and volleyball (Table 3). The recorded duration of symptoms before diagnosis ranged from 1 wk to 2 years[24,26].

Fracture nature and classification

Seven of the studies reported on acute toe phalanx fractures exclusively[15-21]. Three of these studies reported on acute intra-articular (physeal) fractures of the base of the great toe proximal phalanx specifically[19-21]. Six of the studies reported on stress-toe phalanx fractures exclusively[8,22-26].

Of the acute fracture studies, one 'general cohort' study used the AO classification to describe the fracture types[15]. All of the acute 'intra-articular (physeal) fracture' studies used the Salter-Harris Fracture Classification to describe the fracture types[19-21]. None of the stress fracture studies used classification systems to describe the fracture patterns[8,22-26].

Of the 156 acute fractures, 69 (44%) specified treatment modality. Of these, 63 (91%) were treated with 'primary conservative management', and 6 (9%) with 'primary surgical management'. One fracture was converted to 'secondary surgical management' after failed conservative treatment (Table 4). Of the 8 intra-articular (physeal) acute fractures, all (100%) specified treatment modalities: 6 (75%) underwent 'primary surgical management' and 2 (25%) underwent 'primary conservative management'. One intra-articular fracture was converted to 'secondary surgical management' after failed conservative treatment. This was following a re-fracture on return to sport (Table 4).

Of the 26 stress fractures, all (100%) specified treatment modality: 23 (88%) were treated with 'primary conservative management', and 3 (12%) were treated with 'primary surgical management' (Table 5). Six stress fractures were converted to 'secondary surgical management' after failed conservative treatment (Table 5). Of these six, two were associated with a delayed diagnosis (1 year and 2 years respectively), and 4 were associated with an underlying deformity [hallux valgus (n = 3), claw toe (n = 1)] (Table 5).

Choice of radiological imaging

Plain radiography was the diagnostic imaging modality used in acute fracture studies[15-21]. All the stress fracture studies used plain radiography as first-line diagnostic imaging[8,22-26]. In addition to this, one stress fracture study used magnetic resonance imaging/computed tomography Scan to aid diagnosis[26], and another study used Tc-99 Bone scanning as second-line imaging[22].

Table 2 Demographic data - acute fractures

Ref.	*n*	Study type	Mean age (yr)	Male:Female	Follow-up, %	Sport	Level of sport	Most common MOI	Location	Modified coleman score	MINORS score
General cohort											
Robertson *et al*[15], 2012	8	Case series	21.1	8:0	6 (75)	Soccer	General population	Tackle (50%)	Great toe (n = 6) 2nd Toe (n = 1); 3rd Toe (n = 1)	44	12
Larsson *et al*[16], 2016	18	Case series	N/A	18:0	18 (100)	Soccer	Elite/Professional	N/A	N/A	39	12
Chan *et al* [17], 2021	53	Case series	N/A	32:21	53 (100)	US Collegiate Sports	Collegiate	N/A	N/A	54	12
Diaz *et al* [18], 2022	69	RCS	N/A	69:0	69 (100)	Soccer	Elite	N/A	N/A	41	18
Intra-Articular (Physeal) base of proximal phalanx fractures											
Maffulli [19], 2001	2	Case series	12.5	2:0	2 (100)	Soccer (n = 1), Judo (n = 1)	Recreational	Tackle	Great toe proximal phalanx	65	9
Perugia *et al*[20], 2014	4	Case series	13-15	N/A	4 (100)	Gymnastics (n = 4)	Adolescent high level	Dismount	Great toe proximal phalanx	67	11
Bariteau *et al*[21], 2015	2	Case series	12.5	0:2	2 (100)	Gymnastics (n = 2)	Elite	Dismount	Great toe proximal phalanx	62	11

MOI: Mechanism of injury; RCS: A retrospective cohort study.

Table 3 Demographic data - stress fractures

Ref.	*n*	Study type	Mean age (yr)	Male:Female	Follow-up, %	Sport	Level of sport	Location	Associated deformity	Modified coleman score	MINORS score
Yokoe *et al* [22], 1986	3	Case series	16.3 (12-21)	1:2	3 (100)	Sprinting (n = 1), Rugby (n = 1), Kendo (n = 1)	Amateur	Great Toe Proximal Phalanx	Hallux valgus (n = 3)	34	8
Shiraishi *et al*[23], 1993	3	Case series	13.7 (12-17)	1:2	3 (100)	Volleyball (n = 1), Long Distance Running (n = 1), Soccer (n = 1)	Amateur	Great toe proximal phalanx		51	9
Yokoe *et al* [8], 2004	10	Case series	16.3 (12-21)	2:8	10 (100)	Sprinting (n = 6), Distance Running (n = 1), Basketball (n = 1), Rugby (n = 1), Kendo (n = 1)	N/A	Great toe proximal phalanx	Hallux valgus (n = 9)	35	8
Pitsis *et al* [24], 2004	2	Case series	29 (17-41)	0:2	2 (100)	Triathlon (n = 1), Gymnastics (n = 1)	Non-professional/Elite	Great toe proximal phalanx	Hallux valgus (n = 1)	46	8
Munemoto *et al*[25], 2009	4	Case series	14.5 (13-17)	2:2	4 (100)	Short track running (n = 3), Soccer (n = 1)	Amateur	Great toe proximal phalanx	Hallux valgus (n = 3)	55	8
Yamaguchi *et al*[26], 2017	4	Case series	14.8 (13-16)	4:0	4 (100)	Soccer (n = 3), Baseball (n = 1)	N/A	2nd toe proximal phalanx	Claw toe (n = 1)	52	8

Management

Acute fractures: Conservative management: There were 63 acute fractures treated with 'primary conservative management' (Table 4).

Table 4 Outcome data - acute fractures

Ref.	*n*	Treatment (%)	Return to sport (%)	Return to the same level of sport (%)	Return time to sport	Secondary surgery - return rate (RR)/Return time (RT)	Persisting symptoms (%)	Complications
General cohort								
Robertson *et al* [15], 2012	6	PCM (100)	3 (50)	3 (50)	7.0 wk (mean)		3 (50)	Nil
Larsson *et al* [16], 2016	18	N/A	N/A	N/A	26 d (mean)		N/A	1 re-fracture
Chan *et al*[17], 2021	53	PCM (100)	53 (100)	N/A	8.5 d (median)		N/A	1 re-fracture
Diaz *et al*[18], 2022	69	N/A	N/A		30 d (median)		N/A	Nil
Intra-articular (Physeal) base of proximal phalanx fractures								
Maffulli[19], 2001	2	PCM (50) PSM (50)	2 (100)	2 (100)	By 6 mo		0 (0)	0 (0)
Perugia *et al* [20], 2014	4	PSM (100)	4 (100)	4 (100)	By 3 mo		0 (0)	0 (0)
Bariteau *et al* [21], 2015	2	PCM (50) PSM (50)	1 (50) (PSM)	1 (50) (PSM)	5 mo	1 – RR 100%/RT 14 wk	0 (0)	1 re-fracture (PCM)

PCM: Primary conservative management; PSM: Primary surgical management.

Table 5 Outcome data - stress fractures

Ref.	*n*	Treatment (%)	Return to sport (%)	Return to the same level of sport (%)	Time to return to sport (mean)	Secondary surgery - return rate (RR)/Return time (RT)	Factors associated with secondary surgery	Persisting symptom (%)	Complications (%)
Yokoe *et al* [22], 1986	3	PCM (67) PSM (33)	3 (100)	N/A	PCM - 3 mo; PSM - N/A			0 (0)	0 (0)
Shiraishi *et al* [23], 1993	3	PCM (100)	3 (100)	3 (100)	6 wk			1 (33)	1 non-union for a patient who did not stop training (33)
Yokoe *et al* [8], 2004	10	PCM (100)	6 (60)	6 (60)	N/A	4 (40) – RR 100%	Hallux valgus deformity (n = 3)	0 (0)	3 delayed unions with PCM (50)
Pitsis *et al* [24], 2004	2	PCM (100)	0 (0)[a]	0 (0)[a]	N/A	1 (50) – RR 100%	2-yr delay to diagnosis	0 (0)	1 non-union with PCM (50)
Munemoto *et al*[25], 2009	4	PCM (50) PSM (50)	4 (100)	4 (100)	PCM - 8.5 wk, PSM - 10 wk			0 (0)	1 mild deformity with PCM (50)
Yamaguchi *et al*[26], 2017	4	PCM (100)	3 (75)	3 (75)	5 wk	1 (25) – RR 100%/RT 4 mo	1-yr delay to diagnosis/Claw toe deformity	0 (0)	1 non-union and claw toe deformity with PCM (25)

[a]1 no return due to fear of re-injury. PCM: Primary conservative management; PSM: Primary surgical management.

Only two of the 'general cohort' studies specified the type of management[15,17]. Both studies used conservative management for the fractures[15,17]. The type of conservative management was not described[15,17].

All the 'intra-articular (physeal) fracture' studies described the type of management selected[19-21]. Of the two which employed conservative management, the techniques included: heel weight-bearing in a forefoot offloading shoe for 6 wk, referral to physiotherapy at 6 wk, the commencement of training at 12 wk[19]; and 6 wk of non-weight bearing with immobilization, with a return to sport at 3 mo[21].

Surgical management: There were six acute 'intra-articular (physeal) fractures' treated with primary surgical management[19-21]. The described techniques included: open reduction with K-wire fixation (n

= 4), open reduction with screw fixation and cancellous bone graft (n = 1), and open reduction with no fixation (n = 1)[19-21]. One fracture was managed with secondary surgical management, using open reduction and screw fixation[21].

The post-operative regimes included heel weight-bearing in a forefoot offloading shoe for 6 wk, with the removal of K-wire and referral to physiotherapy at 6 wk, and commencement of training at 12 wk [19]; non-weight bearing with cast immobilization for 4 wk, with subsequent removal of K-wire at 4 wk and commencement of weight-bearing[20]; non-weight bearing in a moon boot orthotic for 6 wk, with progressive weight-bearing for the next 4 wk in the orthotic, then gradual weaning from the orthotic, with the commencement of impact activities at 10 wk post-op[21].

Stress fractures

Conservative management: There were 23 stress fractures treated with 'primary conservative management' (Table 5). All studies described the management techniques used[8,22-26].

The management techniques fell into three categories: cessation of sporting activities, with no formal immobilization or other restrictions, for 4 to 8 wk[22,23,25,26]; immobilization of the foot in a cast for 5 wk[25]; non-weight bearing on the affected side with crutches for 3 to 6 wk[24].

All regimes were then followed with a graduated return to sporting activities[8,22-26], which could be supplemented by shoes with shock-absorbing insoles[23], foot orthoses with medial arch support, and a metatarsal pad[26] or a 2nd to 5th metatarsal bar orthosis[24].

Surgical management: There were 3 stress fractures treated with 'primary surgical management' (Table 5). The reported techniques were: Open reduction with drilling, screw and K-wire fixation (n = 1), open reduction with drilling and screw fixation (n = 1), and osteotomy for hallux valgus correction (n = 1)[22,25]. There were 6 stress fractures treated with 'secondary surgical management' (Table 5). The reported techniques were: Open reduction internal fixation (n = 3), osteotomy for hallux valgus correction (n = 1), open reduction with scar tissue debridement, screw and K-wire fixation (n = 1), surgical excision of the non-union, open reduction with cancellous bone graft and screw fixation (n = 1) [8,24,26].

The post-operative regimes included: immediate weight-bearing, with the commencement of activities 8 wk post-operatively[25] (– 'primary surgical management'); non-weight bearing for 4 wk, with the removal of K-wire and commencement of heel weight-bearing at 4 wk, and commencement of mobilization exercises at 6 wk[26] (– 'secondary surgical management'); non-weight bearing for 6 wk, then partial weight bearing in a walker boot for 6 wk, then a graduated return to training[24] (– 'secondary surgical management').

Functional assessment

Two of the acute fracture studies used formal scores to record post-treatment outcomes[20,21]. These included: a 'Visual Analog Pain' scale, the 'American Orthopaedic Foot and Ankle Society (AOFAS) Hallux Metatarsal Phalangeal' scale, the 'Short Form-36 (SF-36) Physical Component Summary (PCS)' and the 'Short Form-36 (SF-36) Mental Component Summary (MCS)'[20,21].

None of the stress fracture studies used formal scores to record post-treatment outcomes[8,22-26].

Return rates to sports

Acute fractures: Conservative management: Four studies recorded RRS following conservative management of acute fractures[15,17,19,21]. The RRS ranged from 0 to 100%[15,17,19,21] (Table 4 and Figure 2A).

The return rates to pre-injury level sports for the conservatively-managed acute fractures ranged from 0% to 100%[15,19,21] (Table 4).

Surgical management: Three studies recorded RRS following PSM of acute fractures[19-21], and one study recorded RRS following SSM of acute fractures[21]. The recorded RRS were 100% for PSM[19-21], and 100%% for SSM[21] (Table 4 and Figure 2A).

The return rates to pre-injury level sports for the surgically-managed acute fractures were all 100% [19-21] (Table 4).

Stress fractures

Conservative management: Six studies recorded RRS following conservative management of stress fractures[8,22-26]. The RRS ranged from 0 to 100%[8,22-26] (Table 5 and Figure 2B).

The return rates to pre-injury level sports for the conservatively-managed stress fractures ranged from 0% to 100%[8,23-26] (Table 5).

Surgical management: Two studies recorded RRS following PSM of stress fractures[22,25], and three studies recorded RRS following SSM of stress fractures[8,24,26]. The recorded RRS was 100% for PSM [22,25], and 100% for SSM[8,24,26] (Table 5 and Figure 2B).

The return rates to pre-injury level sports for the surgically-managed stress fractures were 100%[25] (Table 5).

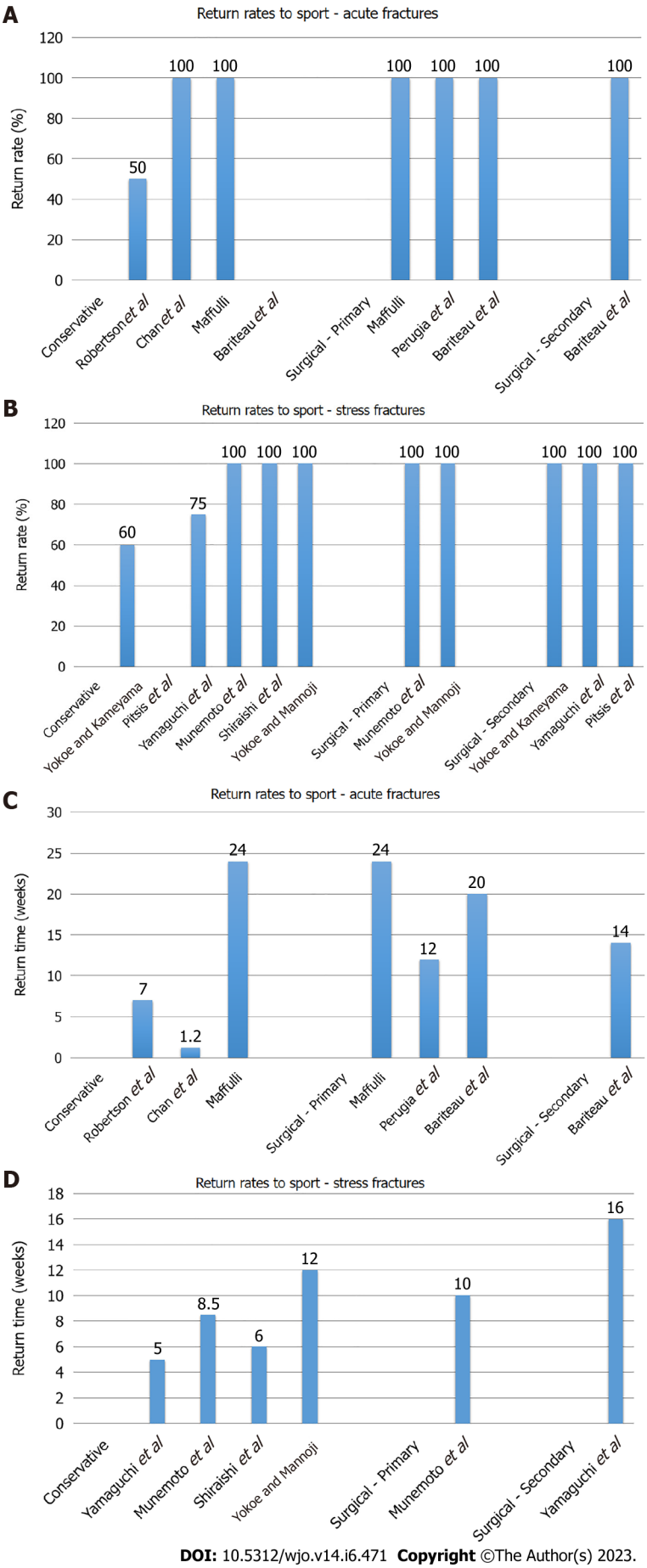

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Figure 2 Return rates to sport. A: Acute Fractures; B: Stress Fractures; C: Acute Fractures; D: Stress Fractures.

Return times to sports

Acute fractures: Conservative management: Three studies recorded RTS following conservative management of acute fractures[15,17,19]. The RTS ranged from 8.5 d to 6 mo[15,17,19] (Table 4 and Figure 2C).

Surgical management: Three studies recorded RTS following PSM of acute fractures[19-21], and one study recorded RTS following SSM of acute fractures[21]. The RTS ranged 3 to 6 mo for PSM[19-21], and was 14 wk for SSM[21] (Table 4 and Figure 2C).

Stress fractures

Conservative management: Four studies recorded RTS following conservative management of stress fractures[22,23,25,26]. The RTS ranged from 5 wk to 3 mo[22,23,25,26] (Table 5 and Figure 2D).

Surgical management: One study recorded RTS for PSM of stress fractures[25], and one study recorded RTS for SSM of stress fractures[26]. The recorded RTS for PSM was 10 wk[25], and for SSM was 4 mo[26] (Table 5 and Figure 2D).

Radiographic union

One of the acute fracture studies recorded radiographic union, with a 100% final union rate[21]. Five of the stress fracture studies recorded radiographic union[22-26]. Four of the studies reported a 100% final union rate[22,24-26], and one study reported a 67% final union rate[23].

Complications

Acute fractures: Three of the acute fracture studies recorded complications, which were re-fracture (Table 4).

Stress fractures: Five of the stress fracture studies recorded complications, which were delayed union with primary conservative management, non-union with primary conservative management, and residual deformity (Table 5).

Predictive factors

While the majority of sport-related toe phalanx fractures were treated with 'primary conservative management', acute intra-articular (physeal) fractures had high rates of 'primary surgical management', especially when displaced[19-21].

Sixteen of the twenty-two 'great toe' phalanx stress fractures had an associated hallux valgus deformity[8,22-25]. One of the four 'second toe' proximal phalanx stress fractures had an associated claw toe deformity[26].

Three of the four 'second toe' proximal phalanx stress fractures had a history of stress fractures at other locations, with two of the patients having a history of stress fractures at multiple locations[26].

Of the six stress fractures that required 'secondary surgical management', one-third of cases (n = 2) had a significant delay to diagnosis (1 year and 2 years respectively)[24,26], and two-thirds of cases (n = 4) had an associated deformity [hallux valgus (n = 3)/claw toe (n = 1)][8,26].

DISCUSSION

This systematic review found that the majority of sport-related toe phalanx fractures are treated with 'primary conservative management', with satisfactory results for RRS and RTS. For acute fractures, intra-articular (physeal) fractures, especially when displaced, had high rates of 'primary surgical management'. Such fractures had uniform good RRS, though had prolonged RTS, due to the required post-operative restrictions. For stress fractures, those with significantly delayed diagnosis or with significant underlying causative deformity were at risk of requiring surgical intervention. Again, such fractures, when treated surgically, demonstrated good overall RRS, though with prolonged RTS due to the required post-operative restrictions. However, given the limited, heterogenous data available, it was difficult to draw firm conclusions from this review.

The quality of the included studies in this review was lower than that of similar studies[13,27-31], with a mean CMS of 49.6. This was particularly true for the stress fracture studies, with a mean CMS of 45.5.

From the review data, it is difficult to conclude the optimal management of acute sport-related toe phalanx fractures[15-21]. The results appear to support 'primary conservative management' of extra-articular, non or minimally displaced fractures, with overall acceptable RRS and RTS[15-21]. 'Primary surgical management' should be reserved for extra-articular fractures which are significantly displaced, rotated, or open[9]. However, there is no evidence to guide such recommendations[15-21]. Surgery is also indicated for displaced, intra-articular (physeal) fractures[9]. There is moderate evidence to support this recommendation, with the need to restore joint surface congruency, especially in the adolescent athlete[19-21]. However, if these fractures are non or minimally displaced, they can be treated with

'primary conservative management'[19-21]. The review shows reasonable RRS and RTS for both primary conservative and surgical management of these fractures, however, surgical management has longer RTS, due to post-operative restrictions[15-21]. Refractures following 'primary conservative management' necessitating 'secondary surgical management' is associated with a notably prolonged RTS[21].

Regarding the optimal surgical technique for intra-articular fractures, several methods have been described, though the evidence is inadequate to conclude which is best[19-21]. Compared to K-wire fixation, screw fixation avoids the risk of pin-track infection and may allow for a quicker return to non-contact training activities (no risk of catching and dislodging the K-wire), but such theories are yet to be proved[19-21,32].

With a variety of rehabilitation techniques described, it is difficult to confirm which is the optimal method[15-21]. It would appear that heel weight-bearing in a forefoot offloading shoe can be recommended, both with 'primary surgical management' and 'primary conservative management'[15-21]. This avoids the need for complete non-weight bearing, allowing more muscle mass preservation[15-21]. Following such restrictions, for between 4 to 6 wk, a graduated return to activities can be commenced[15-21].

Reviewing the common sporting mechanisms of injury (tackle and dismount), it would appear there may be a future role for improved protective footwear, to reduce the incidence of traumatic toe phalanx fractures[15,19-21]. Modification of technique, especially in gymnastics, may also allow for future reduction in the incidence of such fractures. However, further research on this topic is required to confirm such theories[32].

Similar to acute fractures, with the limited, heterogeneous data available, it remains difficult to conclude the optimal management for sport-related, toe phalanx stress fractures[8,22-26]. Anatomically, these should be 'low-risk' stress fractures, so conservative management should form the first line of treatment[7,33,34]. This has been shown to provide acceptable RRS and RTS[8,22-26]. However, due to variations in the anatomy of the foot, some of these fractures can be associated with an underlying deformity (*e.g.* hallux valgus), which can create a biomechanically 'tension-sided', 'high risk' type[8,22,24-26,33,34]. For instance, with hallux valgus, it has been advocated that the medial-sided structures (medial collateral ligament and abductor hallucis) provide an adverse traction force, that potentiates a shear force during exercise, which propagates the stress fracture[8]. In such cases, 'primary surgical management' may be necessary to correct the fracture or the deformity[8,22].

Assessing the data available, it would appear that conservative management is acceptable first-line management for all toe phalanx stress fractures[8,22-26]. 'Primary surgical management', however, can be considered for cases with significant underlying deformity, especially when they show delayed healing with initial conservative management. It can also be considered for cases with significant delays to diagnosis (> 1 year), with evidence of established non-union at presentation[8,22-26]. Such 'primary surgical management' could prevent delayed recovery, due to unnecessary prolonged initial conservative management[8,22-26].

Regarding the optimal surgical technique, there is insufficient data to conclude this[8,22,24-26]. One may consider that the surgeon must correct any underlying significant deformity, at the time of surgical treatment[8,22,24-26]. However, the available data shows that this is not always necessary, to facilitate a successful, timely return to sport[8]. Deformity correction at the time of surgery may reduce the chance of recurrence of the stress fracture on return to sport[8]. However, the more complex surgical technique required may incur a higher risk of complications, prolonged post-operative immobilization and a prolonged return to sport[8]. As such, the optimal strategy for this problem remains to be defined[8]. With established non-unions, the adjunct of biological stimulus (*e.g.* bone grafting) should be considered [24].

Regarding the optimal rehabilitation with 'primary conservative management', it would appear that initial cessation of sporting activities for around 4 to 8 wk is an appropriate first-line plan[8,22-26]. If successful, this should be followed by a graduated return to sport[8,22-26]. For surgical management, heel weight-bearing in a forefoot offloading shoe for 6 wk, followed by a graduated return to sports is similarly an appropriate regime[8,22,24-26].

While modifiable predisposing factors have been extensively reviewed for stress fractures as a whole, with important findings such as sub-optimal physiological condition (*e.g.* female athlete triad), excessive repetitive training, and abnormal physiological load, there is limited information regarding this for toe phalanx stress fractures[7,8,22,24-26,34]. As discussed previously, the associated deformity is a significant predisposing factor for these fractures, and this should be actively sought and monitored appropriately[8,22,24-26]. Similarly, tight footwear, which exacerbates such deformities, should be avoided[8]. Further research is required to determine optimal methods by which to prevent such injuries in the future[8,22-26].

There are several limitations to this study. These are predominantly based on the limited, heterogeneous data on the topic[8,15-26].

The lack of available literature on toe phalanx fractures has been previously highlighted[5]. This is likely a consequence of most toe phalanx fractures being managed directly from emergency departments, with limited input from orthopedic services[35]. Future collection of data on this subject should be encouraged, through the relevant services, to increase the information on this topic.

Despite this, of the studies retrieved, several of those with high cohort numbers failed to stratify the fractures by toe or phalanx injured, or by treatment type received[16-18]. Such limitations prevent accurate analysis of these datasets and subsequently preclude data synthesis and meta-analysis of the available studies.

As such, it was not possible to draw firm conclusions on the optimal treatment and rehabilitation of these injuries, nor the expected RRS and RTS[8,15-26]. Further more detailed, research on this topic is required, stratifying outcome data by fracture location and a treatment selected.

CONCLUSION

There is limited information on return to sport following toe phalanx fractures. The majority of acute fractures are treated with 'primary conservative management', with overall satisfactory RRS and RTS. 'Primary surgical management' is reserved for significantly displaced fractures or displaced intra-articular fractures and has been found to achieve good RRS and RTS. Conservative management forms the first line of treatment for sport-related, toe phalanx stress fractures. When successful, this can result in appropriate RTS. Surgical management is indicated with associated deformity and delayed union, or with significantly delayed presentation and established non-union. In both instances, good RRS and RTS can be achieved. Further research is required to better define the optimal treatment and rehabilitation of sport-related, toe phalanx fractures.

ARTICLE HIGHLIGHTS

Research background

There is very little evidence available to guide the management of toe phalanx fractures in the athletic population.

Research motivation

This is the first systematic review to assess return to sport following toe phalanx fractures. It provides a comprehensive overview of the available literature, assessing both acute fractures and stress fractures.

Research objectives

To systemically review all studies recording return to sport following toe phalanx fractures (including acute fractures and stress fractures), and to collate information on return rates to sport (RRS) and return times (RTS) to the sport.

Research methods

A systematic search of all relevant scientific databases was performed followed by manual screening of articles according to the eligibility criteria.

Research results

Most toe phalanx fractures were treated conservatively. Surgical management was reserved for displaced or intra-articular acute fractures, as well as symptomatic stress fracture non-unions, and stress fractures with significant underlying deformity. RRS for both acute fractures and stress fractures managed conservatively ranged from 0% to 100%. RRS for both acute fractures and stress fractures managed surgically was 100%. RTS after conservative management ranged from 8.5 d to 6 mo for acute fractures, and 5 wk to 3 mo for stress fractures. RTS after surgical management ranged from 3 to 6 mo for acute fractures, and 10 wk to 4 mo for stress fractures.

Research conclusions

The majority of sport-related toe phalanx fractures (acute and stress) are managed conservatively with overall satisfactory RRS and RTS.

Research perspectives

Currently, the available literature regarding return to sport after toe phalanx fractures is limited, with most studies being low-volume case series. Further research is required to better define the optimal treatment and rehabilitation of sport related toe phalanx fractures.

FOOTNOTES

Author contributions: Robertson GAJ conceived the methodology for the manuscript, performed the literature search and analysis for the study and wrote the manuscript; Sinha A performed the literature search and analysis for the study, and reviewed and edited the manuscript; Hodkinson T advised on the study, and reviewed and edited the manuscript; Koç T advised on the study, and reviewed and edited the manuscript.

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META-ANALYSIS

Effectiveness of platelet-rich plasma in the treatment of Achilles tendon disease

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Abstract

BACKGROUND

The effectiveness of Platelet-Rich Plasma (PRP) in the treatment of patients with Achilles tendon rupture (ATR) and Achilles tendinopathy (AT) has been controversial.

AIM

To assess PRP injections' effectiveness in treating ATR and AT.

METHODS

A comprehensive review of relevant literature was conducted utilizing multiple databases such as Cochrane Library, PubMed, Web of Science, Chinese Science and Technology Journal, EMBASE, and China Biomedical CD-ROM. The present investigation integrated randomized controlled trials that assessed the effectiveness of platelet-rich plasma injections in managing individuals with Achilles tendon rupture and tendinopathy. The eligibility criteria for the trials encompassed publications that were published within the timeframe of January 1, 1966 to December 2022. The statistical analysis was performed utilizing the Review Manager 5.4.1, the visual analogue scale (VAS), Victorian Institute Ankle Function Scale (VISA-A), and Achilles Tendon Thickness were used to assess outcomes.

RESULTS

This meta-analysis included 13 randomized controlled trials, 8 of which were randomized controlled trials of PRP for AT and 5 of which were randomized controlled trials of PRP for ATR. PRP for AT at 6 wk [weighted mean difference (WMD) = 1.92, 95%CI: -0.54 to 4.38, I^2 = 34%], at 3 mo [WMD = 0.20, 95%CI: -2.65 to 3.05, I^2 = 60%], and 6 mo [WMD = 2.75, 95%CI: -2.76 to 8.26, I^2 = 87%) after which there was no significant difference in VISA-A scores between the PRP and control groups. There was no significant difference in VAS scores between the PRP group and the control group after 6 wk [WMD = 6.75, 95%CI: -6.12 to 19.62, I^2 = 69%] and 6 mo [WMD = 10.46, 95%CI: -2.44 to 23.37, I^2 = 69%] of treatment, and at mid-treatment at 3 mo [WMD = 11.30, 95%CI: 7.33 to 15.27, I^2 = 0%] after mid-treatment, the PRP group demonstrated better outcomes than the control group. Post-treatment patient satisfaction [WMD = 1.07, 95%CI: 0.84 to 1.35, I^2 = 0%], Achilles tendon thickness [WMD = 0.34, 95%CI: -0.04 to 0.71, I^2 = 61%] and return to sport [WMD = 1.11, 95%CI: 0.87 to 1.42, I^2 = 0%] were not significantly different between the PRP and control groups. The study did not find any statistically significant distinction between the groups that received PRP treatment and those that did not, regarding the Victorian Institute of Sport Assessment - Achilles scores at 3 mo [WMD = -1.49, 95%CI: -5.24 to 2.25, I^2 = 0%], 6 mo [WMD = -0.24, 95%CI: -3.80 to 3.32, I^2 = 0%], and 12 mo [WMD = -2.02, 95%CI: -5.34 to 1.29, I^2 = 87%] for ATR patients. Additionally, no significant difference was observed between the PRP and the control groups in improving Heel lift height respectively at 6 mo [WMD = -3.96, 95%CI: -8.61 to 0.69, I^2 = 0%] and 12 mo [WMD = -1.66, 95%CI: -11.15 to 7.83, I^2 = 0%] for ATR patients. There was no significant difference in calf circumference between the PRP group and the control group after 6 mo [WMD = 1.01, 95%CI: -0.78 to 2.80, I^2 = 54%] and 12 mo [WMD = -0.55, 95%CI: -2.2 to 1.09, I^2 = 0%] of treatment. There was no significant difference in ankle mobility between the PRP and control groups at 6 mo of treatment [WMD = -0.38, 95%CI: -2.34 to 1.58, I^2 = 82%] and after 12 mo of treatment [WMD = -0.98, 95%CI: -1.41 to -0.56, I^2 = 10%] there was a significant improvement in ankle mobility between the PRP and control groups. There was no significant difference in the rate of return to exercise after treatment [WMD = 1.20, 95%CI: 0.77 to 1.87, I^2 = 0%] and the rate of adverse events [WMD = 0.85, 95%CI: 0.50 to 1.45, I^2 = 0%] between the PRP group and the control group.

CONCLUSION

The use of PRP for AT improved the patient's immediate VAS scores but not VISA-A scores, changes in Achilles tendon thickness, patient satisfaction, or return to sport. Treatment of ATR with PRP injections alone improved long-term ankle mobility but had no significant effect on VISA-A scores, single heel lift height, calf circumference or return to sport. Additional research employing more extensive sampling sizes, more strict experimental methods, and standard methodologies may be necessary to yield more dependable and precise findings.

Key Words: Platelet-Rich plasma; Achilles tendon rupture; Achilles tendinopathy; Systematic evaluation; Randomized controlled trial

Core Tip: Achilles tendon rupture (ATR) and Achilles tendinopathy (AT) are commonly seen in orthopaedic outpatient clinics. The effectiveness of Platelet-Rich Plasma in the treatment of patients with ATR and AT has been controversial. This study aims to inform the decisions of physicians faced with challenges when making treatment choices.

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INTRODUCTION

Achilles tendon rupture (ATR) and Achilles tendinopathy (AT) are commonly seen in orthopaedic outpatient clinics. These conditions have serious complications and are treated clinically, mainly by conservative treatment. However, this treatment is ineffective and prone to recurrence[1]. The cause is

regular unreasonable or excessive exercise, which leads to repeated friction or overstretching of the Achilles tendon and its surrounding tissues beyond the repair capacity of the tendon itself, caused inflammatory reactions in the tendon tissue. Chronic inflammation leads to the tendon's collagen fibres and fatty tissue degeneration. This effect is diminished and can lead to spontaneous ATR[2].

The component of Achilles tendon tissue included tendon cells and fibrin collagen. Due to the lack of blood supply to the Achilles tendon, its healing rate is significantly lower than other damaged connective tissues[3].

AT and ATR are usually treated by surgical or non-surgical methods, which included non-steroidal anti-inflammatory drugs (NSAIDs), steroid hormone blocking treatment, low-frequency ultrasound stimulation, and hypothermia therapy. Steroid and lidocaine-blocking therapies brought excellent anti-inflammatory and analgesic results, which made it become the most popular treatments in physic therapist. However, collagen necrosis and decline in the Achilles tendon's mechanical properties may caused by repeated injections[4-6]. Gastric ulcers is one of likely complications of prolonged use of NSAIDs. Therefore, the clinical use of these drugs in the treatment of Achilles tendon rupture and AT has been controversial[7]. Growth factors have been identified to play a vital role in ATR, Therefore Certain researchers suggested the utilization of platelet-rich plasma (PRP) as a potential treatment for conditions affecting the Achilles tendon[8,9].

PRP injections, which are increasingly used in clinical practice, are platelet concentrates that often contain various growth factors within them. In some cases, an increase on following growth factors were noticed, including epidermal growth factor, platelet-derived growth factor (PDGF), transforming growth factor-b1, basic fibroblast growth factor, vascular endothelial growth factor, insulin-like growth factor and hepatocyte growth factor[10]. Therefore, platelet-rich plasma has attracted the curiosity of numerous researchers as a tissue regeneration-inducing factor[11-14]. Several current investigations have demonstrated that PRP is useful in the treatment of orthopedic injuries, including syndrome of the carpal tunnel[15-17], Rotator cuff rupture[18-20], AT[21,22], Achilles tendon injury[23], *etc*. Animal experimentation has demonstrated that PRP injections speed up the histopathological recuperation of the Achilles tendon, boost the overall strength of the tendon, relieve the inflammatory response, and facilitate tendon regeneration[24,25].

PRP has been shown to increase the histopathological recovery of the Achilles tendon in humans. However, the role of PRP in human Achilles tendon healing remains controversial[21,22,24-28]. Overall, additional research is required to investigate and uncover the efficacy of PRP treatment for individuals with AT to inform and guide clinical decision-making. This study aimed to determine whether PRP injection is viable for patients with AT. Treatment success depends on measuring Achilles tendon function scores, pain levels, return to sport rates, complication rates and the time taken to return to the pre-injury functional range. There are few studies on the effects of PRP injections on Achilles tendon disease. This study aims to inform the decisions of physicians faced with challenges when making treatment choices.

MATERIALS AND METHODS

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards, before initiating the investigation, we drafted a protocol delineating our objectives, criteria for eligibility literature search methodologies, statistical assessments, and outcome measures. The registration number for PROSPERO is CRD 42023388903.

Study design

This study employed meta-analysis to compile quantitative research on the efficacy of PRP for treating AT. The research was conducted in a structured manner, and the methodology employed in this study involved several steps. (1) A study strategy and criteria aligned with the study's objectives were developed; (2) The primary databases of interest were searched using specific search terms and formulas; (3) The studies were screened for eligibility based on the predetermined criteria; (4) The quality of the literature was evaluated using the Jadad scale to eliminate those of inferior quality; (5) Involves using a data extraction form to extract the required data meticulously; (6) Entails the utilization of Review Manager 5.4.1 for data examination; and (7) Involves analyzing and interpreting the results and marking decisions.

Data collection

The inclusion criteria were restricted to the following conditions: (1) The investigation focused on patients with AT or ATR; (2) The study intervention involved administering a local PRP injection to the experimental group; (3) Various outcome indicators, including the Victorian Institute Ankle Function Scale (VISA-A) score, visual analogue scale (VAS) for pain, variations in Achilles tendon thickness, rate of returning to sports activities, patient satisfaction, return to sport, ankle flexion, return to pre-injury heel-rise height, and incidence of adverse events, were utilized in this study; and (4) The focus of this research is on randomized controlled trials (RCTs) published prior to December 2022.

Exclusion criteria

The study excluded trials with the following criteria: (1) Non-randomized trials; (2) A follow-up duration of less than 6 wk; (3) No control group; (4) Used PRP with other drugs; and (5) Did not report results.

Search method

Searches were conducted in Cochrane Library, PubMed, Web of Science, Chinese Science and Technology Journal, EMBASE, and China Biomedical CD-ROM without restriction on language. The search terms were "PRP", "Platelet Concentrate", "platelet gel", "ATR", "Achilles tendon injury", "AT", and "AT", all the full text from 1966 to 2022 was download, carefully read.

Literature screening

At least two individuals conduct separate literature searches using predetermined keywords and formulas to access databases. The literature screening process outcomes were then consolidated through literature management tools, with duplicate papers being eliminated and insignificant literature being excluded based on title lists. Potentially appropriate research was downloaded and thoroughly read, with the final choice of literature determined by inclusion and exclusion criteria. In the event of divergent results, a third person was invited for Arbitration and selection.

Quality evaluation of the included studies

The present study conducted a methodological analysis of previous research about the research design protocol, randomization approach concealment, blinding implementation, and the incidence of missed visits. The Jadad scale was employed for this purpose. The total score achievable on this scale was seven. Research studies that obtained a cumulative score ranging from one to three were categorized as low-quality, while those that obtained a cumulative score ranging from four to seven were classified as high-quality. Studies with a score ≥ three or higher were deemed eligible for participation in this investigation[29-31].

Statistical analysis

Review Manager 5.4.1 (Revman 5.4) served as the statistical tool for this investigation. Following the evaluation criteria, all admissible data from the literature were extracted and inserted into Revman 5.4 for analysis. The risk difference or the odds ratio was used to describe count data (such as adverse events and return to sport rate).

All metrics (such as VISA-A score, ankle mobility, VAS score, *etc.*) were reported as weighted mean difference (WMD)[32]. The study assessed heterogeneity utilizing the I^2 index, which served as an indicator of the degree of heterogeneity. Studies with I^2 values below 31% were deemed homogeneous, while those with I^2 values above 56% were considered more heterogeneous. Studies with I^2 values between 56% and 70% could not be excluded from heterogeneity. When I^2 values were below 50%, the fixed-effects model Peto method was employed to combine effect sizes. Conversely, when I^2 values exceeded 50%, the random-effects model DerSimonian-Laird method was utilized for calculation. In cases where there was significant heterogeneity among groups, meta-analysis was abandoned in favor of descriptive analysis.

RESULTS

A total of 16 publications were screened, and 3 were excluded through further evaluation: 1 trial design protocol with no outcome indicators. One was a retrospective case-control study and not a true RCT trial. 1 had no primary outcome indicators. A total of 13 publications were included in the final results (Figure 1).

All 13 RCTs, comprising 857 cases, were included in this study. All trials were published in full text, with 13 being in English and none in Chinese. Eight trials included 526 subjects in a randomized controlled trial of PRP for AT, and five included 349 subjects in a randomized controlled trial of PRP for ART. All had modified Jadad scores greater than 3. Saline were used in eight studies as a control group, and blank controls were used in five studies; 12 were double-blind RCTs, and one was a single-blind RCT; the basic characteristics of the related literature are listed in Table 1. Every included studies were compared at baseline, and there found no significant differences in age, weight, gender and treatment between the two comparable groups. Regarding the risk of bias, Figures 2 and 3 shows the assessment results of the included studies.

Results of the analysis of AT

VISA-A rating: The VISA-A score changes were accurately and fairly stated in 8 articles, including 526 patients. The combined statistic was calculated using a random effects model due to statistical heterogeneity between studies (I^2 = 76%, P = 0.00001), The study revealed that the VISA-A score was greater in

Table 1 Characteristics of randomized controlled studies included in this meta-analysis

Ref.	Sample size (I/C)	Achilles tendon lesion	Location	Control	Follow-up	PRP injection frequency/interval/dose (mL)
de Vos *et al*[42], 2010	27/27	C-AT (> 2 mo)	Netherlands	Saline	6, 12, 24 wk	Once/-/4
de Jonge *et al*[41], 2011	27/27	C-AT (> 2 mo)	Netherlands	Saline	6, 12, 24, 48 wk	Once/-/4
Kearney *et al*[50], 2013	9/10	C-AT (> 8 mo)	United Kingdom	Blank	6 wk, 3 mo, 6 mo	Once/-/3 to 5
Krogh *et al*[22], 2016	12/12	C-AT (mean 33 mo)	Denmark	Saline	3, 6, 12 mo	Once/-/6
Boesen *et al*[21], 2017	19/19	C-AT (> 3 mo)	Denmark	Saline	6, 12, 24 wk	4 times/2-wk/4
van der Vlist *et al*[53], 2020	39/41	C-AT (> 6 mo)	Netherlands	Saline	2, 6, 12, 24 wk	Once/-/NR
Thermann *et al*[51], 2020	17/19	C-AT (> 6 mo)	Italy	Blank	6 wk, 3, 6, 12 mo	Once/-/NR
Kearney *et al*[52], 2021	121/119	C-AT (> 3 mo)	United Kingdom	Blank	2 wk, 3, 6 mo	Once/-/3
Schepull *et al*[28], 2011	15/14	A-ATR (< 3 d)	Sweden	Blank	6, 12 mo	Once/-/10/4
De Carli *et al*[49], 2015	15/15	A-ATR	Italy	Blank	1, 3, 6, 24 mo	2 times/2-wk/4
Zou *et al*[27], 2016	16 /20	A-ATR (< 3 wk)	China	Placebo	3 wk, 3, 6, 12, 24 mo	Once/-/NR
Keene *et al*[33], 2019	107/109	A-ATR (< 12 d)	United Kingdom	Placebo	4, 7, 13, 24 wk	Once/-/4
Boesen *et al*[34], 2020	19/19	A-ATR (< 3 d)	Denmark	Saline	8 wk, 3, 6, 12 mo	Once/-/4

PRP: Platelet-Rich Plasma; AT: Achilles tendinopathy; ATR: Achilles tendon rupture.

the PRP group as compared to the placebo group [WMD = 1.20, 95%CI: -0.94 to 3.34, P = 0.27]. No important statistical improvement was observed in the VISA-A score among those who had PRP therapy (Figure 4).

Change in Achilles tendon thickness: Changes in Achilles tendon thickness were accurately and appropriately reported by 98 individuals across 3 articles. Due to statistical heterogeneity among studies (I^2 = 61%, P = 0.08), we applied a model with random effects to calculate the pooled statistic, which indicated that the PRP group had thicker Achilles tendons than the placebo group [WMD = 0.34, 95%CI: -0.04 to 0.71, P = 0.08], a difference not supported by statistical evidence. This indicates no significant improvement in AT thickness in the PRP group (Figure 5).

VAS score: Changes in VAS score were accurately and appropriately reported by 93 individuals across 3 articles. The result shows there was a statistical heterogeneity among those studies (I^2 = 56%, P = 0.02), we used a random effects model to determine the pooled statistic, the result indicated that the VAS scores in PRP group was greater than the placebo group [WMD = 11.74, 95%CI: -7.45 to 16.02, P < 0.00001], with a significant statistical difference. According to this result, PRP treatment group brings significantly promotions on VAS scores compare to the placebo group (Figure 6).

Patient satisfaction: Enhancements in patient satisfaction were accurately and appropriately reported by 222 patients across four studies. Because there was heterogeneity among due to the heterogeneity among the research papers (I^2 = 0%, P = 0.68), the study employed a fixed-effects approach to determine the paired statistic. The findings indicate that the level of patient satisfaction was higher in the group that received platelet-rich plasma compared to the group that received a placebo [Relative risk (RR) = 1.07, 95%CI: 0.84 to 1.35, P = 0.58], but there was no statistically significant difference between the two groups. According to this information, the level of patient satisfaction did not substantially increase in the PRP group compared to the placebo group (Figure 7).

Return to sport rate: 199 patients accurately and reasonably described their exercise resumption rates across 4 publications. The results indicated no statistical heterogeneity among studies (I^2 = 0%, P = 0.54), in present study we used a fixed-effects approach to determine the combined statistic, the result indicated that the ratio of return to exercise in the PRP-treated group (experimental group) was greater than in the placebo group (control group) [RR = 1.11, 95%CI: 0.87 to 1.42, P = 0.40]. This suggests that

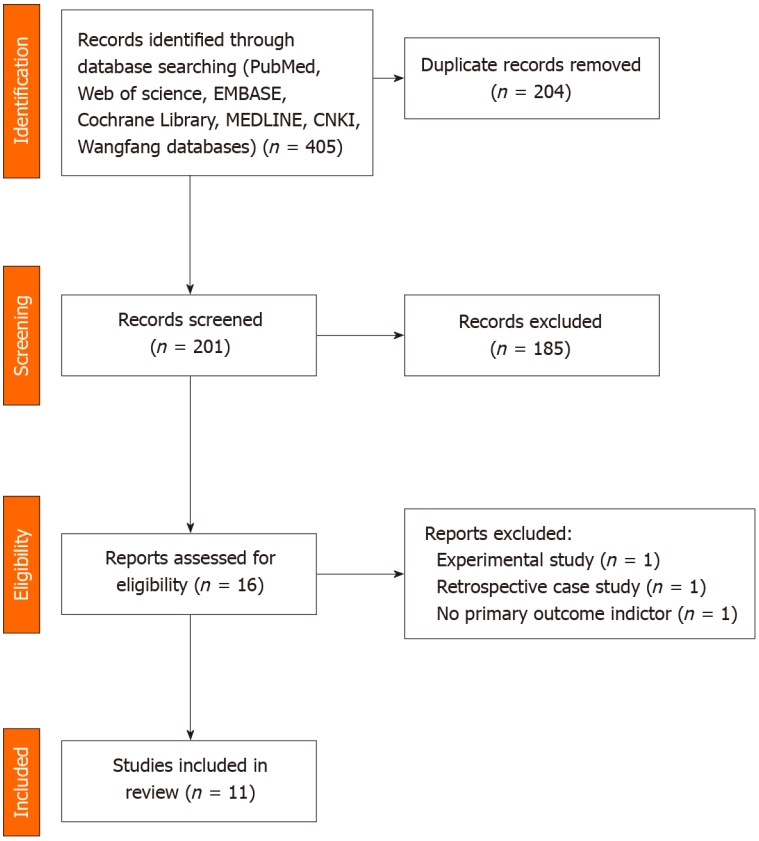

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Figure 1 Flow diagram of study selection.

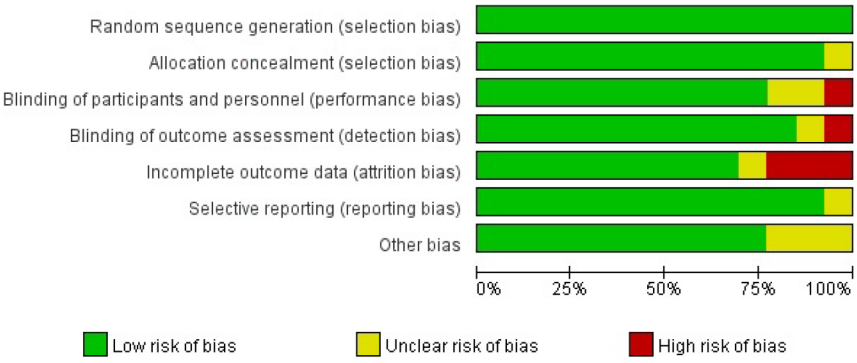

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Figure 2 Proportional risk of bias graph: Judgement of the percentage of bias items arising from all included studies.

the PRP therapy group did not substantially increase the patient's return to activity rate compared to the placebo group (Figure 8).

Results of the analysis of the effectiveness of PRP in the treatment of ATR

VISA-A Rating: In total, 274 patients from three different articles gave an accurate and credible description of the value of the change in their VISA-A score. Because the statistical result shows no heterogeneity among the studies (I^2 = 39%, P = 0.13), we used a fixed-effects approach to generate the paired statistic. This result indicated that the PRP group had smaller VISA-A Scale scores compared to the placebo group [WMD = -1.28, 95%CI: -3.32 to 0.75, P = 0.22]; there was also no significant difference among both groups statistically (Figure 9).

Single-foot heel height: In three articles, 259 patients accurately and adequately defined the height of a single heel lift. Because the statistical result shows no heterogeneity among those studies (I^2 = 0%, P = 0.90), we used a fixed effects approach to determine the overall statistic, the results revealed that the

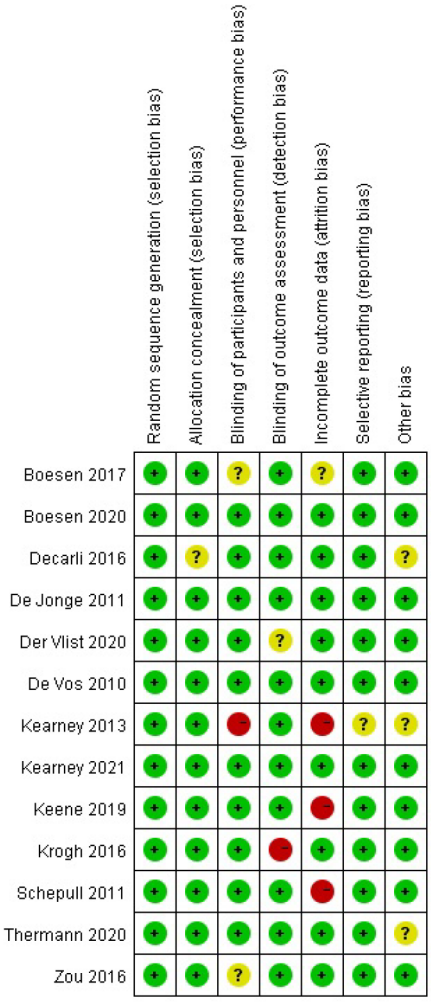

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Figure 3 Risk of bias summary diagram: Assessment of specific items of bias arising from all included studies.

PRP group had a smaller single heel lift height compared to the placebo group. [WMD = -3.51, 95%CI: -7.69 to 0.66, P = 0.10], there was no statistical difference. This result suggested that the PRP group did not substantially enhance the single heel lift height among individuals with ATR (Figure 10).

Calf circumference: Two papers accurately and reasonably reported the calf circumference measurements of 75 patients. The statistical result shows no heterogeneity among those studies (I^2 = 24%, P = 0.27), we used fixed-effects approach to determine the paired statistic, the result indicated that calf circumference in the PRP group was greater compared to the placebo group [WMD = 0.17, 95%CI: -1.05 to 1.38, P = 0.79], there was no statistical difference. This suggests that the PRP therapy did not substantially improve calf circumference length in patients with ATR (Figure 11).

Ankle mobility: Ankle mobility was accurately and fairly assessed in 103 patients across 3 articles. The statistical result shows no heterogeneity among each study (I^2 = 81%, P < 0.0001), we used a random effects approach to determine the paired statistic, the result demonstrated that ankle mobility in the PRP group was lower compared to the placebo group [WMD = 0.93, 95%CI: -1.60 to -0.26, P = 0.007], the statistically difference was significant. This indicates that the PRP therapy did not substantially increase ankle mobility in individuals with ATR (Figure 12).

Return to sport rate: Two studies included 68 patients who accurately and sufficiently reported the ratio of their return to exercise. The statistical result shows no heterogeneity among those studies (I^2 = 0%, P = 1.00), we used a fixed-effects approach to determine the paired statistic, the outcome showed that there was no statistically significant difference in the ratio of return to sport in the PRP group and the placebo group [RR = 1.20, 95%CI: 0.77 to 1.87, P = 0.42]. This suggests that the PRP the therapy did not substantially increase the return-to-sport rate among individuals with ATR (Figure 13).

Incidence of adverse events: A total of 2 publications with 305 patients correctly and reasonably described the incidence of adverse events. The statistical result shows no heterogeneity among the

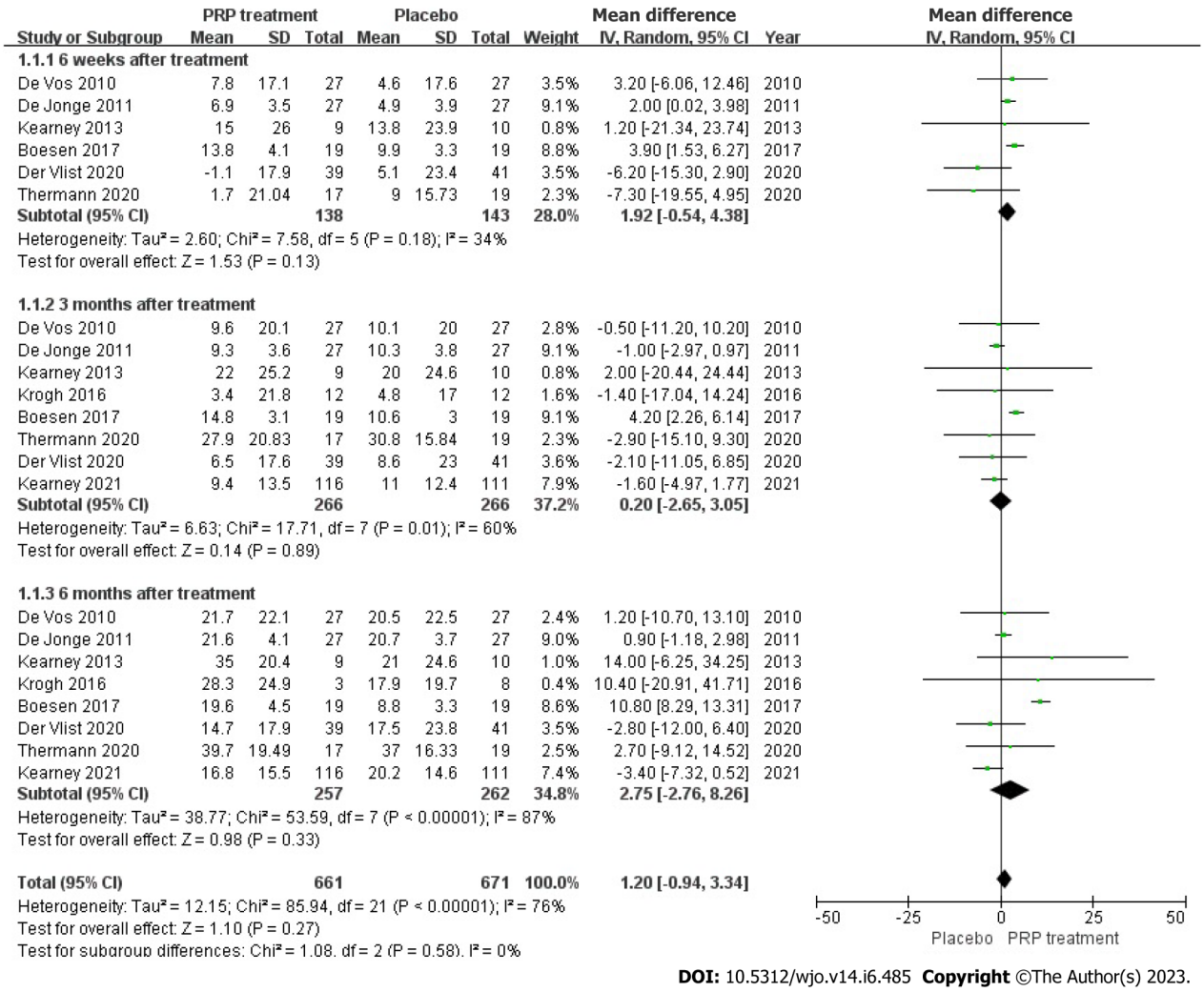

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Figure 4 Forest plot of change values for Victorian Institute Ankle Function Scale scores. PRP: Platelet-Rich Plasma.

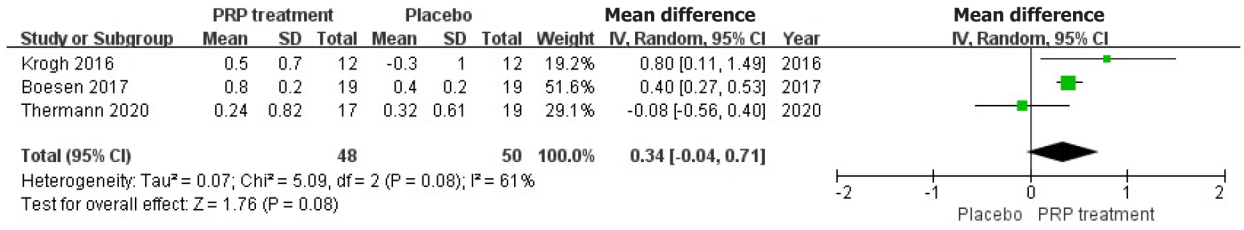

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Figure 5 Forest plot of Achilles tendon thickness variation. PRP: Platelet-Rich Plasma.

studies (I^2 = 0%, P = 0.66), we used a fixed-effects approach to determine the paired statistic, the PRP group's Achilles tendon re-rupture was greater than the placebo group [RR = 1.21, 95%CI: 0.43 to 3.47, P = 0.71]; no statistical difference existed. The prevalence of pain and distress in the PRP-treated group was greater compared to the placebo group [RR = 1.02, 95%CI: 0.51 to 2.01, P = 0.96]; however, the difference between the groups was not statistically significant. The results showed no statistically significant difference between the PRP-treated group and the control group in terms of re-rupture rate of the Achilles tendon, infection, and incidence of pain and discomfort (Figure 14).

DISCUSSION

PRP is a platelet-rich plasma obtained by centrifugation of whole blood from animals or humans, to

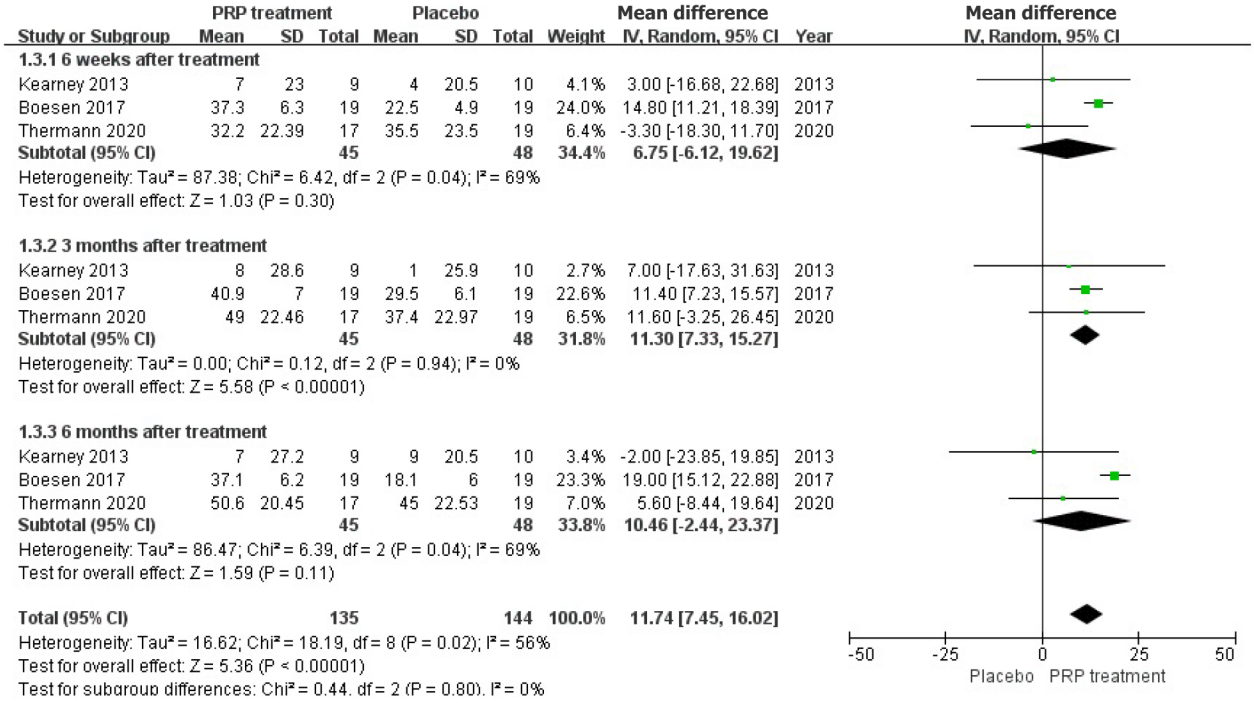

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Figure 6 Forest plot of change in visual analogue scale scores. PRP: Platelet-Rich Plasma.

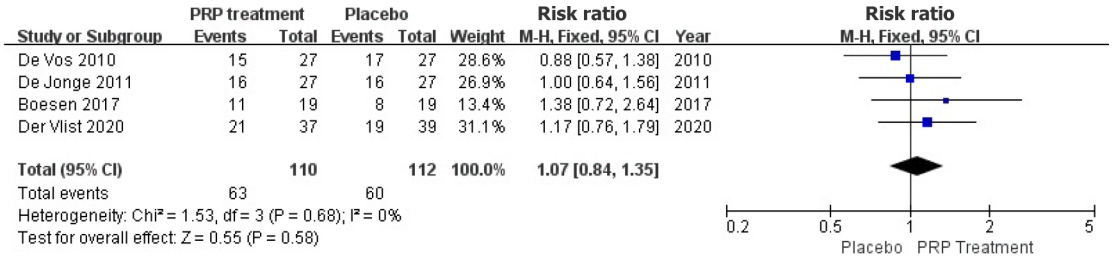

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Figure 7 Forest plot of change in patient satisfaction. PRP: Platelet-Rich Plasma.

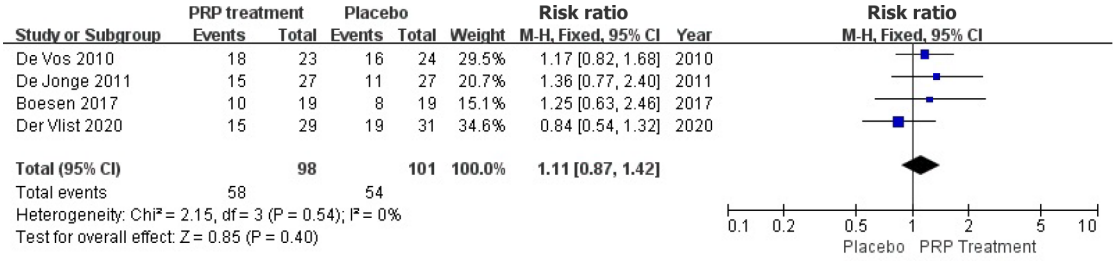

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Figure 8 Forest plot of patient return to exercise rate. PRP: Platelet-Rich Plasma.

which thrombin is added to turn it into a gel, and the platelet concentration of PRP increases on average by a factor of two to six. Platelets contain high levels of growth factors such as growth-like insulin growth factor, PDGF, epidermal growth factor (EGF). Transforming growth factor-β, vascular EGF, *etc.* Theoretically, when platelet concentrates are activated, PRP injections can release supraphy siological concentrations of various autologous growth factors with healing and regenerative abilities for treating musculoskeletal disorders[33,34]. Theoretical In vitro and *in vivo* experiments have also demonstrated the mechanobiological properties of PRP to promote the healing of tendon injuries[24,35-37]. Li *et al*[38] demonstrated that PRP heals tendon tissue by reducing the number of cells, decreasing the number of blood vessels, promoting type I collagen deposition and increasing the glycosaminoglycan content. PRP

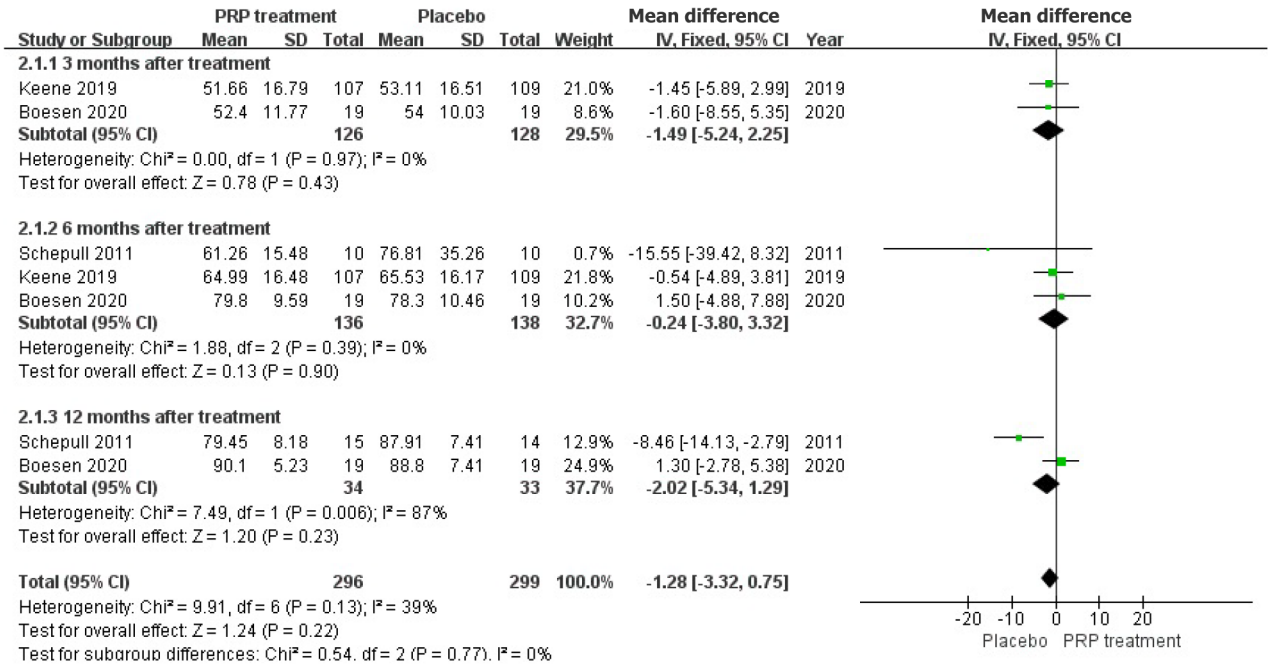

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Figure 9 Forest plot of Victorian Institute Ankle Function Scale scores in patients with Achilles tendon rupture. PRP: Platelet-Rich Plasma.

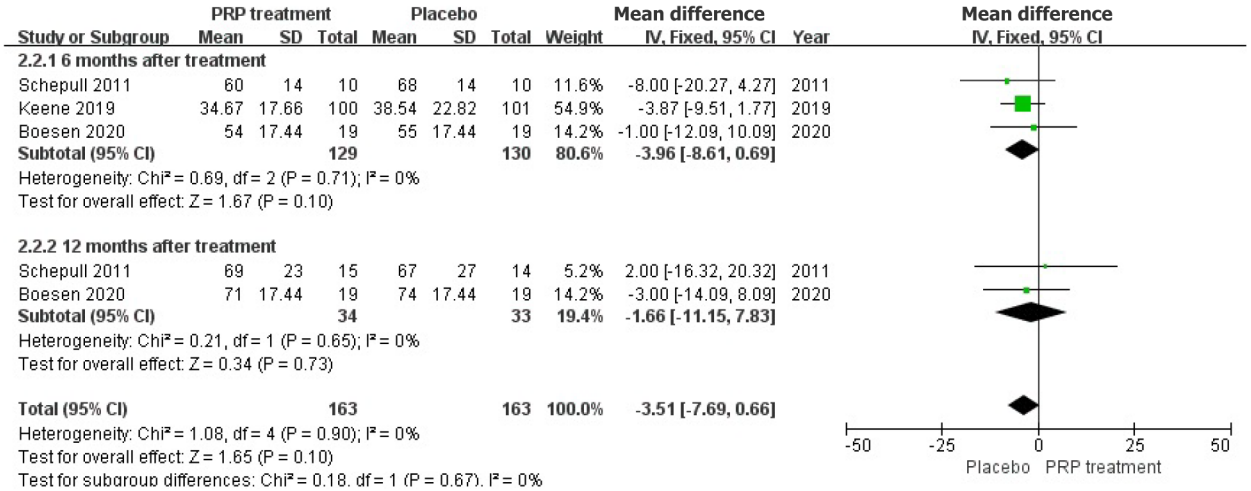

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Figure 10 Forest plot of single heel lift height in patients with Achilles tendon rupture. PRP: Platelet-Rich Plasma.

is also derived from the patient's own body. Furthermore, PRP is derived from the patient himself and is administered after a short period of *in vitro* centrifugation. PRP therapies have achieved satisfactory clinical results; however, there are no consistent results on their overall efficacy and inconsistencies in patient outcomes, and new insights challenge the usefulness of PRP for clinical use[39,40].

AT develops from many factors, and this disorder's exact mechanism is unknown. Most studies suggest that AT is primarily caused by anatomical abnormalities resulting from overexertion, incorrect exercise training, stiffness and weakness of the limbs. Various factors first lead to local inflammation of the Achilles tendon. These effects lead to degenerative changes and eventually to partial or complete Achilles tendon rupture. This meta-analysis found that the use of PRP for AT did not significantly change patients' VISA-A scores, patient satisfaction, return to sport rates, or Achilles tendon thickness compared to controls, and interestingly, patients' VAS scores at 3 mo were significantly improved compared to controls but did not significantly change long-term clinical outcomes. (This is similar to De Jonge's findings.) The randomized controlled trial by de Jonge *et al*[41] showed that PRP injections did not significantly improve pain and function in patients with tendonitis compared to placebo injections in patients with chronic Achilles tendonitis after 1 year of PRP treatment, and there was no advantage in ultrasound findings. deVos *et al*[42] conducted a randomized controlled trial utilizing a double-blind

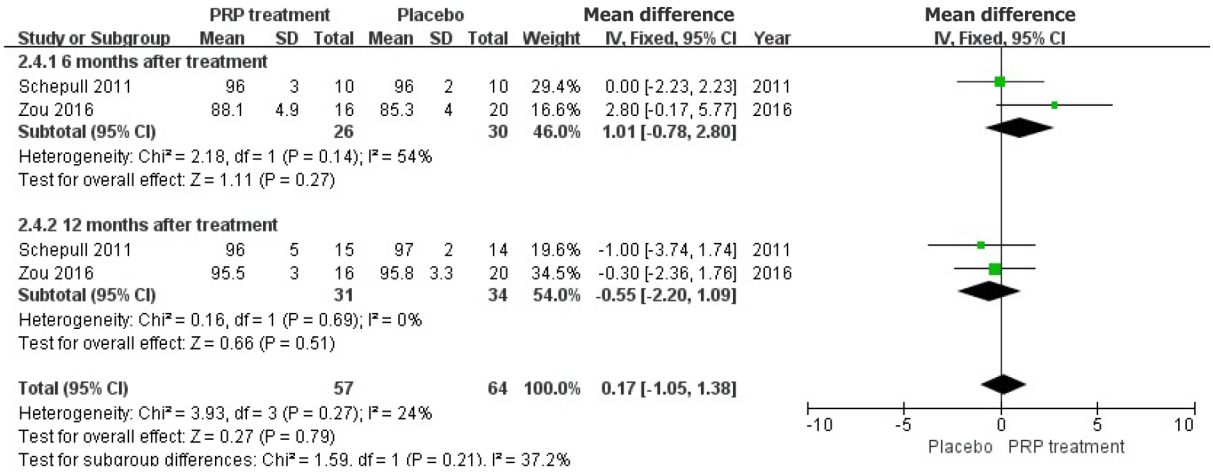

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Figure 11 Forest plot of calf circumference in patients with Achilles tendon rupture. PRP: Platelet-Rich Plasma.

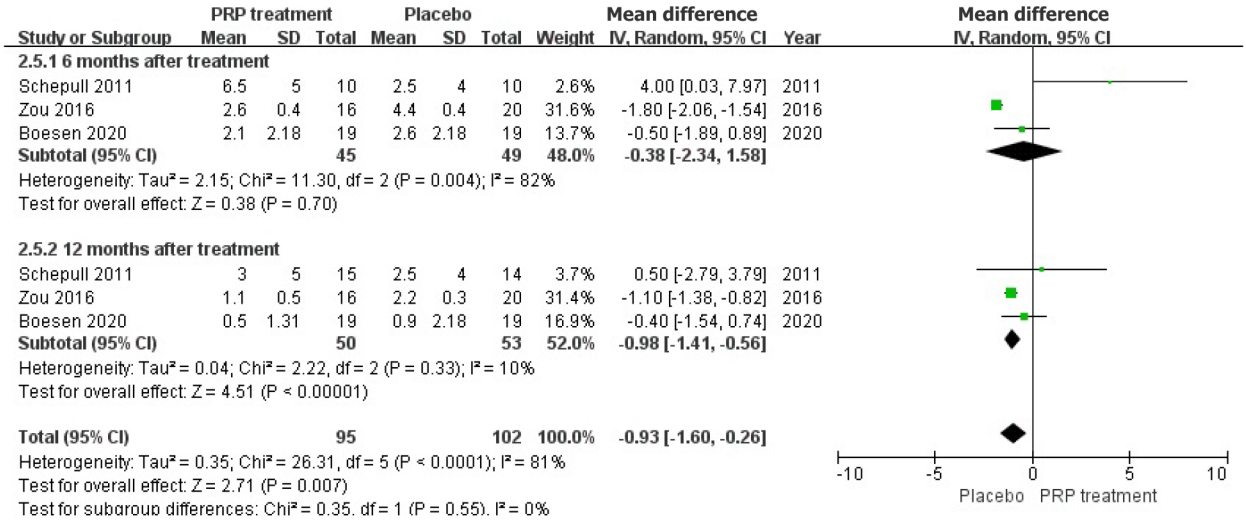

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Figure 12 Forest plot of ankle mobility in patients with Achilles tendon rupture. PRP: Platelet-Rich Plasma.

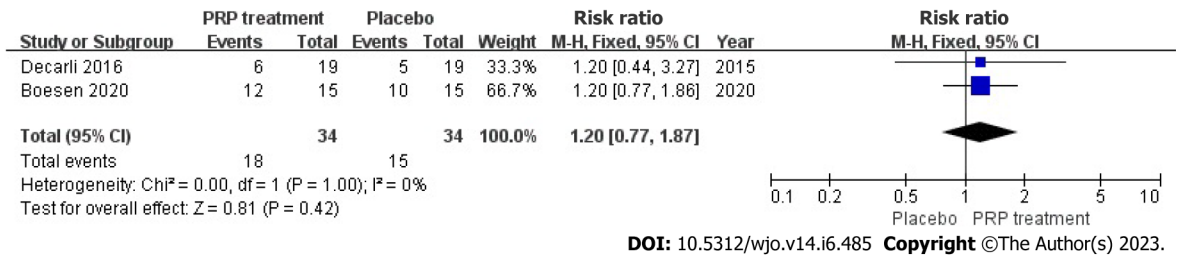

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Figure 13 Forest plot of return to sport rates in patients with Achilles tendon rupture. PRP: Platelet-Rich Plasma.

method. The study involved 54 patients with chronic inflammatory Achilles tendon disease, all receiving PRP treatment. The study demonstrated that the administration of PRP therapy did not result in significant alterations in the ultrasound echo structure or neovascularisation scores associated with Achilles tendon injuries[42]. Neither study described a clinical benefit of PRP injection over placebo. The study by Krogh *et al*[22] also concluded that PRP injection had no additional value in treating AT. However, this study raises concerns about the quality of the method. Patients were blinded, but the outcome assessors were aware of the interventions implemented. Furthermore, they reported a 54% decline rate three months after PRP, making it almost impossible to observe a potential late effect of PRP. Interestingly Boesen *et al*[21] reported a significant improvement in VISA-A scores in the PRP

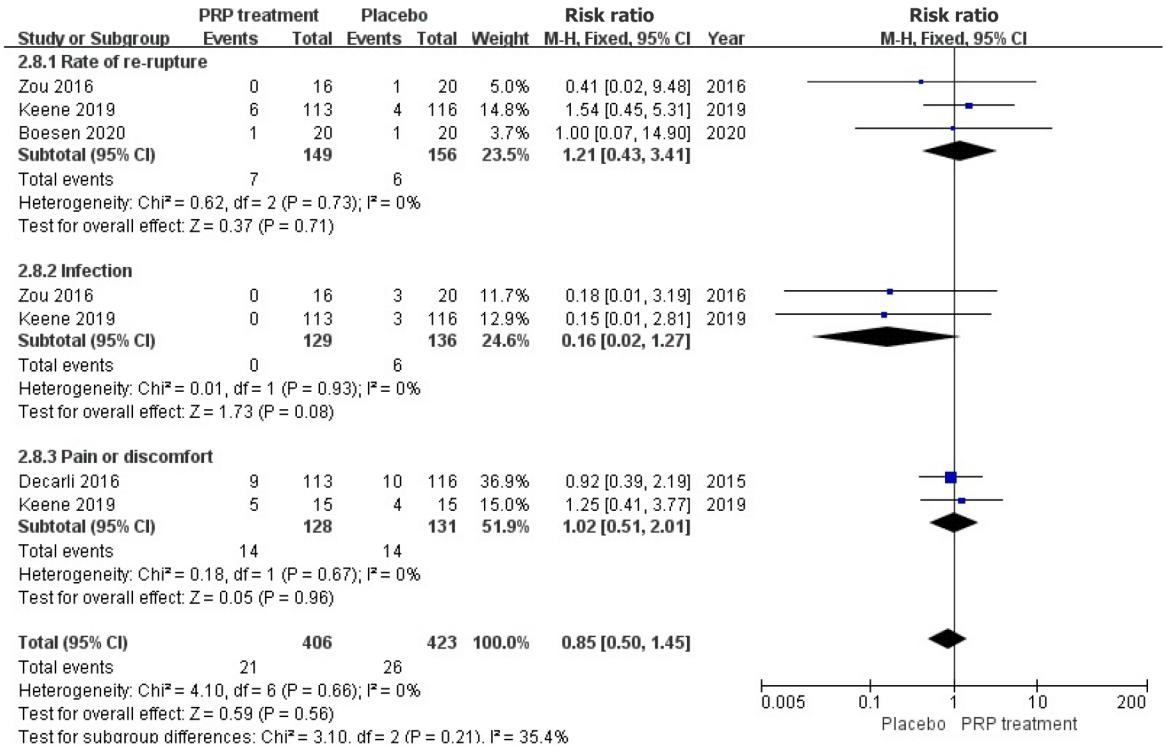

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Figure 14 Forest plot of the incidence of adverse events in patients with Achilles tendon rupture. PRP: Platelet-Rich Plasma.

group. This difference may be because Boesen *et al*[21] considered tendon healing a slow process, so they repeated PRP injections to achieve a prolonged effect of the growth factor on the tendon. Another possibility is that there were differences in the rehabilitation protocols of these studies; for example, Boesen *et al*[21] prescribed running to start 10 d after PRP injection, while other studies ranged from 4 d (Krogh) to 28 d (deVos)[22,42]. Thirdly, there were differences in the effects of PRP on vascular tendon distribution and tendon thickness, with Boesen *et al*[21] concluding that PRP administration reduced vascular distribution and tendon thickness within the tendon. de Jonge *et al*[41] reported an improvement in tendon structure in the PRP and placebo groups, but no significant difference was found between the two groups. These results did not confirm an association between PRP and changes in tendon structure. The results did not confirm an association between PRP and changes in the tendon structure. Finally, it is possible that the location of PRP injections was not uniform, with Krogh *et al*[22] injecting at the very back of the tendon and de Vos *et al*[42] injecting at the most severely affected site.

The Achilles tendon is a relatively blood-deprived tissue, with the blood supply to the Achilles tendon coming mainly from the posterior tibial artery return branch[43]. The surface skin blood supply system is fragile. As a result, healing after an injury is slower than in other tissues. Some studies have shown that growth factors can promote tendon repair[44]. Some studies have shown that growth factors can promote tendon repair. Some *in vitro* experiments have demonstrated that instantaneous injection of plasma-rich protein for tendon injury enhances tendon recovery in rats[45]. Zhang *et al*[46] found that the premature injection of plasma-rich protein into a tendon injury may have provided sufficient growth factors to promote angiogenesis, which ultimately shortened tendon healing time. However, Zou *et al*[27] found that leukocyte-rich platelets may be detrimental to treating tendon injuries in rabbits. Leukocyte-rich platelets caused catabolic gene expression, increased protein production, and promoted an increase in inflammatory mediators. This inflammatory mediator induces non-tendon cell differentiation[47,48].

PRP injections in the treatment of ATR as a new treatment method with no consistent results on its overall efficacy. Therefore, we performed a meta-analysis to provide evidence-based information on using PRP injections for ATR. The results showed that the PRP-treated group (experimental group) was not statistically significantly different from the control group in terms of VISA-A score, single heel lift height, return to motion rate, Achilles tendon re-rupture rate, infection, and incidence of pain and discomfort. There was no significant improvement in ankle mobility in the PRP-treated group at 6 mo, and after 12 mo, the results showed that PRP injection improved ankle mobility. Overall, our findings do not support using PRP for ATR; however, this meta-analysis has some limitations, and the findings need to be considered cautiously. This is because differences in PRP preparation methods can lead to differences in the biological characteristics of the final product. The frequency and dosage of PRP injections in the experimental groups varied in many studies, which may lead to uncertainty in clinical

outcomes. A study by Keene *et al*[33] described each component of PRP injections, as well as several representative growth factors; two studies by Schepull *et al*[28] and Zou *et al*[27] reported only the platelet concentrations of their PRP injections. Zou's study showed that PRP positively affected ankle function in short to medium term[27]. However, in a study by De Carli *et al*[49], there was no difference between the PRP and control groups after acute Achilles tendon rupture surgery as measured by the VISA-A score and the Foot and Ankle Outcome Score. Similar inconsistent results may be due to the inconsistencies in PRP concentrations, preparation protocols and injection sites described above.

Hence, additional research is required to determine the optimal concentration, injection duration, and injection location for PRP for ART and AT. The study results indicate a lack of statistical significance in the impact of PRP on ankle plantarflexion angle, ankle plantar flexion strength, and pain.

Limitations

Although clear inclusion and exclusion criteria have been established for this study, the small total sample size and a limited number of trials limit the strength of the evidence. Moreover, there remains a high degree of heterogeneity in the quantitative analysis of these randomized controlled trial studies. Heterogeneity may stem from the degree of tendinopathy, the method used to produce PRP, the cellular composition of PRP, the conditions in which PRP was stored, the method of injection, the dose and frequency of injection and the setting of the control group. The scoring criteria and methods used in the included studies also differed.

This study was unable to analyze PRP in different subgroups due to the heterogeneous nature of PRP production and application techniques and the absence of an standardized classification system. Consequently, a comprehensive investigation into the effectiveness and safety of a specific form of PRP therapy in treating tendinopathies was not feasible.

CONCLUSION

This study showed no significant efficacy of PRP injection alone in patients with ATR and AT. Thirteen high-quality RCT articles were reviewed to reach this conclusion. Future studies should focus on completing RCTs with large sample sizes and standardizing the preparation/procedure of PRP injections. As well as exploring the clinical efficacy of PRP injections combined with minimally invasive AT techniques.

ARTICLE HIGHLIGHTS

Research background

Achilles tendon rupture (ATR) and Achilles tendinopathy (AT) are commonly seen in orthopaedic outpatient clinics. These conditions have serious complications and are treated clinically, mainly by conservative treatment. However, this treatment is ineffective and prone to recurrence. Along with the deep investigation of research, it is found that growth factors promoted Achilles tendon repair. The use of Platelet-Rich Plasma (PRP) was indicated to treat Achilles tendon diseases.

Research motivation

But the effectiveness of PRP in the treatment of patients with ATR and AT has been controversial.

Research objectives

To determine whether PRP injection is viable for patients with AT and to inform the decisions of physicians faced with challenges when making treatment choices.

Research methods

This study conducted a comprehensive review of relevant literature was conducted utilizing multiple databases such as Cochrane Library, PubMed, Web of Science, Chinese Science and Technology Journal, EMBASE, and China Biomedical CD-ROM. The present investigation integrated randomized controlled trials that assessed the effectiveness of platelet-rich plasma injections in managing individuals with ATR and AT. The eligibility criteria for the trials encompassed publications that were published within the timeframe of January 1, 1966 to December 2022. The statistical analysis was performed utilizing the Review Manager 5.4.1. The Victorian Institute Ankle Function Scale (VISA-A), Visual Analogue Scale (VAS) and Achilles tendon thickness were used to assess outcomes.

Research results

This meta-analysis included 13 randomized controlled trials, 8 of which were randomized controlled trials of PRP for AT and 5 of which were randomized controlled trials of PRP for ATR. PRP for AT at 6

wk, at 3 mo, and 6 mo after which there was no significant difference in VISA-A scores between the PRP and control groups. There was no significant difference in VAS scores between the PRP group and the control group after 6 wk and 6 mo of treatment, and at mid-treatment at 3 mo after mid-treatment, the PRP group demonstrated better outcomes than the control group. Post-treatment patient satisfaction, Achilles tendon thickness and return to sport were not significantly different between the PRP and control groups. There was no significant difference between the PRP and control groups for VISA-A score improvement at 3 mo, 6 mo, and 12 mo for ATR patients. Additionally, no significant difference was observed between the PRP and the control groups in improving heel lift height respectively at 6 mo and 12 mo for ATR patients. There was no significant difference in calf circumference between the PRP group and the control group after 6 mo and 12 mo of treatment. There was no significant difference in ankle mobility between the PRP and control groups at 6 mo of treatment and after 12 mo of treatment there was a significant improvement in ankle mobility between the PRP and control groups. There was no significant difference in the rate of return to exercise after treatment and the rate of adverse events between the PRP group and the control group.

Research conclusions

This study showed no significant efficacy of PRP injection alone in patients with ATR and AT. Thirteen high-quality RCT articles were reviewed to reach this conclusion. Future studies should focus on completing randomized controlled trials with large sample sizes and standardizing the preparation/procedure of PRP injections. As well as exploring the clinical efficacy of PRP injections combined with minimally invasive AT techniques.

Research perspectives

This meta-analysis reviewed 13 high-quality randomized controlled trials articles and the result suggested that there is no significant efficacy of PRP injection alone in patients with ATR and AT.

FOOTNOTES

Author contributions: Huang D, Arthur Vithran DT and Gong HL contribute equally to this study, they share co-first author; Wen J conceived and coordinated the study, designed; Xiao S performed and analyzed the experiments; Tang ZW wrote the paper; Zeng M, Arthur Vithran DT and Gong HL did the data analysis and carried out the data collection; Zeng M revised the paper; and all authors approved the final version of the manuscript.

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CORRECTION

Erratum: Rates of readmission and reoperation after operative management of midshaft clavicle fractures in adolescents

Laura A Carrillo, Hao Hua Wu, Matt Callahan, Aman Chopra, Toshali Katyal, Ishaan Swarup

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Abstract

This is an erratum to an already published paper. We found an error in the results section and Table 1. Specifically, we have revised results with $n \leq 10$ to be reflected as such, which is consistent with the reporting instructions by the Agency for Healthcare Research and Quality. Please note, these changes do not affect our results, and we had previously listed this requirement in the results section. We apologize for our unintentional mistake.

Key Words: Adolescent; Clavicle fracture; Reoperation; Readmission; Correction

Core Tip: This is an erratum to an already published paper. We found an error in the results section and Table 1. Specifically, we have revised results with $n \leq 10$ to be reflected as such, which is consistent with the reporting instructions by the Agency for Healthcare Research and Quality. Please note, these changes do not affect our results, and we had previously listed this requirement in the results section. We apologize for our unintentional mistake.

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TO THE EDITOR

This is an erratum to an already published paper[1]. We found an error in the results section and Table 1. Specifically, we have revised results with $n \leq 10$ to be reflected as such, which is consistent with the reporting instructions by the Agency for Healthcare Research and Quality. Please note, these changes do not affect our results, and we had previously listed this requirement in the results section. We apologize for our unintentional mistake.

Table 1 Adolescent fracture demographics: Reoperation *vs* no reoperation

Predictor variables		Cohort proportion, %	Cohort total, *n*	Cohort proportion, %	Cohort total, *n*	*P* value
Sex	Male	0.68	36	0.83	229	0.01
	Female	0.32	17	0.17	47	
Race	White	0.79	42	0.78	209	0.86
	Hispanic	-	≤ 10[1]	0.12	31	
	Black	-	≤ 10[1]	0.05	14	
	Other	-	≤ 10[1]	0.05	13	
Payer type	Commercial	0.74	39	0.62	175	0.47
	Medicaid	-	≤ 10[1]	0.24	67	
	Self-pay	-	≤ 10[1]	0.06	17	
	Other	-	≤ 10[1]	0.08	22	
State	CA	-	≤ 10[1]	0.20	55	< 0.01
	FL	0.98	52	0.80	226	
Median income quartile	0-25th %	-	≤ 10[1]	0.20	42	0.64
	26th-50th %	0.34	16	0.34	70	
	51st-75th %	0.28	13	0.29	61	
	76th-100th %	0.23	11	0.16	34	
Hospital type	Academic	-	≤ 10[1]	0.07	19	0.07
	Children's	-	≤ 10[1]	-	≤ 10[1]	
	Community	0.75	40	0.77	215	
	County	-	≤ 10[1]	0.14	38	
	Outpatient	-	≤ 10[1]	-	≤ 10[1]	
Age	Mean	15.87 ± 1.8	53	16.08 ± 1.7	281	0.41

[1]Please note that data with ≤ 10 patients is not reported due to database reporting restrictions.
CA: California; FL: Florida.

FOOTNOTES

Author contributions: Carrillo LA, Wu HH, Callahan M, Chopra A, Katyal T, Swarup I wrote this correction manuscript.

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