FRACTURES AROUND THE SHOULDER GIRDLE

Unsolved fractures?

HERMAN FRIMA

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COLOPHON

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Fractures around the shoulder girdle

Unsolved fractures?

Frakturen rond de schouder gordel
Onopgeloste frakturen?

(met een samenvatting in het Nederlands)

P R O E F S C H R I F T

ter verkrijging van de graad van doctor aan de
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te Geldrop

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Dr. M. van Heijl

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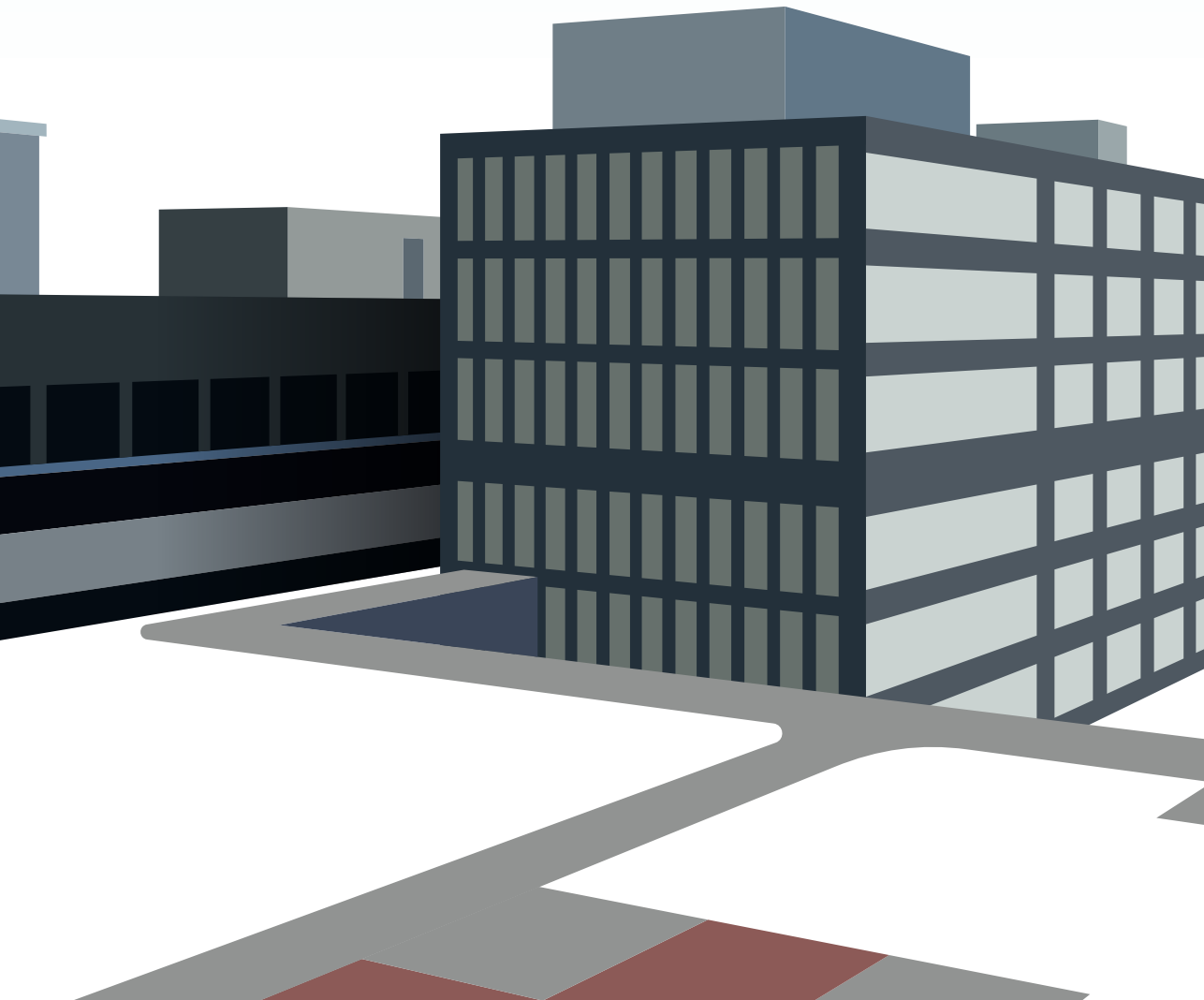
HOW IT STARTED

Five years ago, after completing a two year trauma fellowship in Utrecht, the Netherlands, my family and I moved to the Swiss Alps where I obtained a position as a trauma surgeon in the Kantonsspital Graubünden in Chur. Not only is Graubünden a very beautiful mountainous area, it is also a playground for outdoor activities like skiing and mountain biking. (Un)fortunately, injuries resulting from these sports are often fractures around the shoulder girdle. An interesting aspect of moving to Switzerland was the 'cultural' difference in the treatment of clavicle and shoulder fractures; The Netherlands is a more non-operative minded country and Switzerland is more operative minded. Furthermore, I found that there were some differences in operative techniques. Obviously this raised 'research' questions.

In Utrecht, I had already been involved in the POP trial where I included patients in the trial and operated on many of them. In this study, patients with a displaced midshaft clavicle fracture were randomized between operative treatment with plate osteosynthesis or intramedullary nailing. Furthermore, we started a pilot with the application of an end cap on the medial end of the intramedullary nail to prevent implant-related irritation and migration. However, several problems with these end caps occurred and this technique was not incorporated. When I arrived in Switzerland, I discovered that it was standard protocol to apply an end cap with intramedullary nailing. This resulted in our first international research project where we studied the application of an end cap for intramedullary nailing of displaced midshaft clavicle fractures. After matching two cohorts, we compared patients who were treated with end caps from Chur, Switzerland, with patients who were treated without end caps from Utrecht, the Netherlands.

Other research projects and fellowships in a collaboration between the two countries developed. Marijn Houwert came from Utrecht to Chur for a trauma fellowship and Reinier Beks spent time in the mountains as a research fellow. As a result, several research projects on clavicle- and proximal humeral fractures were initiated resulting in this thesis.



CHAPTER 1

Introduction

PART 1. CLAVICLE FRACTURES

Clavicle fractures are very common fractures with an incidence of 30 per 100,000[1] and represent 2.6% - 4% of all fractures.[1-3] Fractures of the clavicle shaft have the highest incidence and account for 69% of all clavicle fractures. Lateral clavicle fractures and medial clavicle fractures have a lower incidence and account for 28% and 3% respectively.[1] The classical injury mechanisms are a simple fall on the shoulder (31%), followed by road traffic accidents (27%) and then sports (23%).[1] Medial clavicle fractures occur more often as part of a high energy trauma or trauma with multiple injuries.[4]

For decades, displaced midshaft clavicle fractures were treated conservatively.[5, 6] However, non-union rates after conservative treatment appear higher than previously reported, in addition to a presumed better functional outcome following surgical treatment.[2, 7-10] This has led to a paradigm shift during the last 15-20 years towards an increase in operative treatment. Ongoing interest in the literature regarding the optimal treatment for these fracture types seems to have led to an increase in scientific data favoring operative treatment.[3, 8-13]

Medial clavicle fractures, as mentioned above, are rare and scientific data are scarce. The largest available study showed that non-displaced medial clavicle fractures can be treated conservatively.[14] Displaced medial clavicle fractures, however, are even more rare. Although very little evidence exists, non-unions seem to occur in up to 20% of instances.[14] For the operative treatment of medial clavicle fractures no special implants exist. A possible solution is the use of a distal humerus plate in treating these fractures. A first study using this technique is presented in this thesis.

For displaced midshaft clavicle fractures there is a lot of evidence available on both operative and conservative treatment.[3, 9, 10, 15] Operative treatment has the benefit of lower non-union rates and patients seem to have a quicker recovery.[10] The most recently published randomized controlled trial confirmed a faster recovery and higher union rate after the operative treatment.[16] However, after 6 and 12 months the functional results are equal. Therefore the benefit of operative treatment is accelerated functional recovery in the first few months after the operation. These benefits have to be discussed with patients to come to a shared decision as to what is the best treatment for a certain patient.[17]

Operative treatment can be done with plate osteosynthesis or intramedullary nailing.[15, 18] Plate osteosynthesis has the benefit of a faster early recovery compared to intramedullary nailing.[18, 19] Intramedullary nailing has the advantage of a minimally invasive approach,

shorter operation time and non-operative complications.[20] Furthermore, in non-comminuted displaced midshaft clavicle fractures there are fewer major re-interventions and re-fractures after implant removal.[15] One of the disadvantages of intramedullary nailing is the implant-related irritation.[21, 22] In this thesis two studies are described which aimed to reduce implant related irritation. The first study is about the suitability of displaced midshaft clavicle fractures for intramedullary nailing and the second about the influence of end caps on implant-related irritation.

Lateral clavicle fractures can be divided into stable and non-stable based on their location and fracture pattern using the Neer-classification.[23, 24] Stable fractures (Neer I and III) as well as fractures at or medially from the cc-ligaments that are non-displaced can be treated conservatively. Operative treatment is warranted for displaced unstable fractures (Neer IIa, IIb and V) as conservative treatment results in up to 33% non-unions.[25, 26] Many techniques have been described; however there are only a few studies that compare different treatment modalities.[27] Therefore we initiated a retrospective study comparing the clavicle hook plate and the superior clavicle plate with lateral extension for unstable Neer type II and type V lateral clavicle fractures.

Evaluating the available literature shows that there seems to be growing evidence for operative treatment of displaced medial, shaft and lateral clavicle fractures. However, there is still an ongoing debate about what technique should be used. Studies in this thesis provide additional evidence to assist in clinical decision-making.

PART 2. PROXIMAL HUMERAL FRACTURES

The proximal humerus fracture is the third most common fracture seen in the elderly with an incidence of 82 per 100,000 per year with an annual increasing rate of 13.7% per year over the last 33 years.[28] The typical patient is a female aged 65 or over.[29] Nearly 75% of the patients are treated nonoperatively, and one out of five will undergo surgery depending on fracture type and displacement.[30]

Treatment of proximal humeral fractures has also undergone the same shift towards more operative treatment regimens.[31-34] It is the question however, if this trend is justified according to literature. Therefore a systematic review and meta-analysis of randomized controlled trials and observational studies were performed.

Up to now, although many patients with a proximal humeral fracture are operated on, no clear evidence for this operative treatment has been published. The most important question remains which patients will benefit most from surgery. On proximal

humeral fractures there is a cultural difference in treatment between Switzerland and the Netherlands.[35, 36] In Chur (Switzerland), most patients with a proximal humeral fracture are operated on. An important difference between the patients in Chur and the patients from the meta-analysis is that most fractures occurred during outdoor sporting events. These fit and active people might have higher demands of shoulder function and possibly benefit from operative treatment. As long-term functional results after operative treatment are lacking in current literature, we performed a follow-up study of the Swiss population operated on in Chur.

Proximal humeral fracture-dislocations are a special entity. These types of fractures are special in the way that the humeral head is dislocated. In literature there is a consensus that these fractures are treated operatively.[37-40] However there is little evidence available on how to do it. In Chur, these fractures are currently treated using a minimally invasive technique through the anterolateral deltoid split approach. As this technique has not been published before, we described this technique and conducted a study regarding the functional outcome after operative treatment of these proximal humeral fracture-dislocations.

OUTLINE

This thesis consists of two parts, the first about clavicle fracture treatment and the second about proximal humeral fracture treatment (Table 1). In **chapter 2** the treatment of displaced medial clavicle fractures is discussed. We present a new technique for treating intra-articular medial clavicle fractures or extra-articular fractures with a small medial fragment. Furthermore we present the functional results after the operative treatment of displaced medial clavicle fractures. **Chapter 3** is about the suitability of displaced midshaft clavicle fracture for treatment with intramedullary nailing. A retrospective analysis is performed to assess risk factors for implant-related irritation after this procedure. The aim is to provide a recommendation which fractures can be treated using intramedullary nailing. **Chapter 4** also addresses implant-related irritation after intramedullary nailing of displaced midshaft clavicle fractures. In this study we analyse the influence of the application of an end cap on the end of the intramedullary (titanium) nail.

Lateral clavicle fractures are addressed in **chapter 5** where two different fixation methods for operative treatment of unstable Neer type II and type V lateral clavicle fractures (LCF) are compared. This is done by comparing the patient-reported functional outcome after open reduction and internal fixation with the clavicle hook plate and

the superior clavicle plate with lateral extension. In **chapter 6** the available literature together with our own studies are combined in a current concepts paper about clavicle fracture treatment. Medial, midshaft and lateral clavicle fracture treatment is discussed and for all three anatomical locations a treatment algorithm is proposed.

The second part of this thesis addresses proximal humeral fractures. In **chapter** 7 the results of a systematic review and meta-analysis comparing the operative and nonoperative treatment of displaced proximal humeral fractures are presented. In this study both randomized controlled trials and observational studies were included. One of the developments in proximal humeral fracture treatment of the last two decades, the minimally invasive plate osteosynthesis, is studied in **chapter 8.** We analysed the long-term functional results and implant-related irritation after minimally invasive plate osteosynthesis for proximal humeral fractures. Proximal humeral fracture-dislocations are a special entity in proximal humeral fracture treatment and are discussed in **chapter 9**. In these fractures, besides the fracture of the proximal humerus, the head of the humerus is dislocated either anteriorly or posteriorly. In this study we present our technique and functional results of minimally invasive plate osteosynthesis of these special fractures through an anterolateral deltoid-split approach. Finally, putting together the available evidence, the current concepts of proximal humeral fracture treatment are discussed in **chapter 10.**

TABLE 1. Summary of research questions addressed in this thesis.

Chapter	
2	What are the functional results of the operative treatment of displaced medial clavicle fractures?
3	Which displaced midshaft clavicle fractures can be operated with intramedullary nailing?
4	What is the influence of an end cap on implant-related irritation with intramedullary nailing of displaced midshaft clavicle fractures?
5	Which implant, the hook plate or the superior clavicle plate with lateral extension, results in a better functional outcome in displaced lateral clavicle fractures?
6	What are the current concepts in clavicle fracture treatment?
7	Is there a difference in functional outcome between the operative and nonoperative treatment of proximal humeral fractures when analyzing randomized controlled trials together with observational studies?
8	What are the long-term functional results after the operative treatment of proximal humeral fractures with minimally invasive Philos plating?
9	What are the functional results of the operative treatment of proximal humeral fracture-dislocations?
10	What are the current concepts in proximal humeral fracture treatment?

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PART 1

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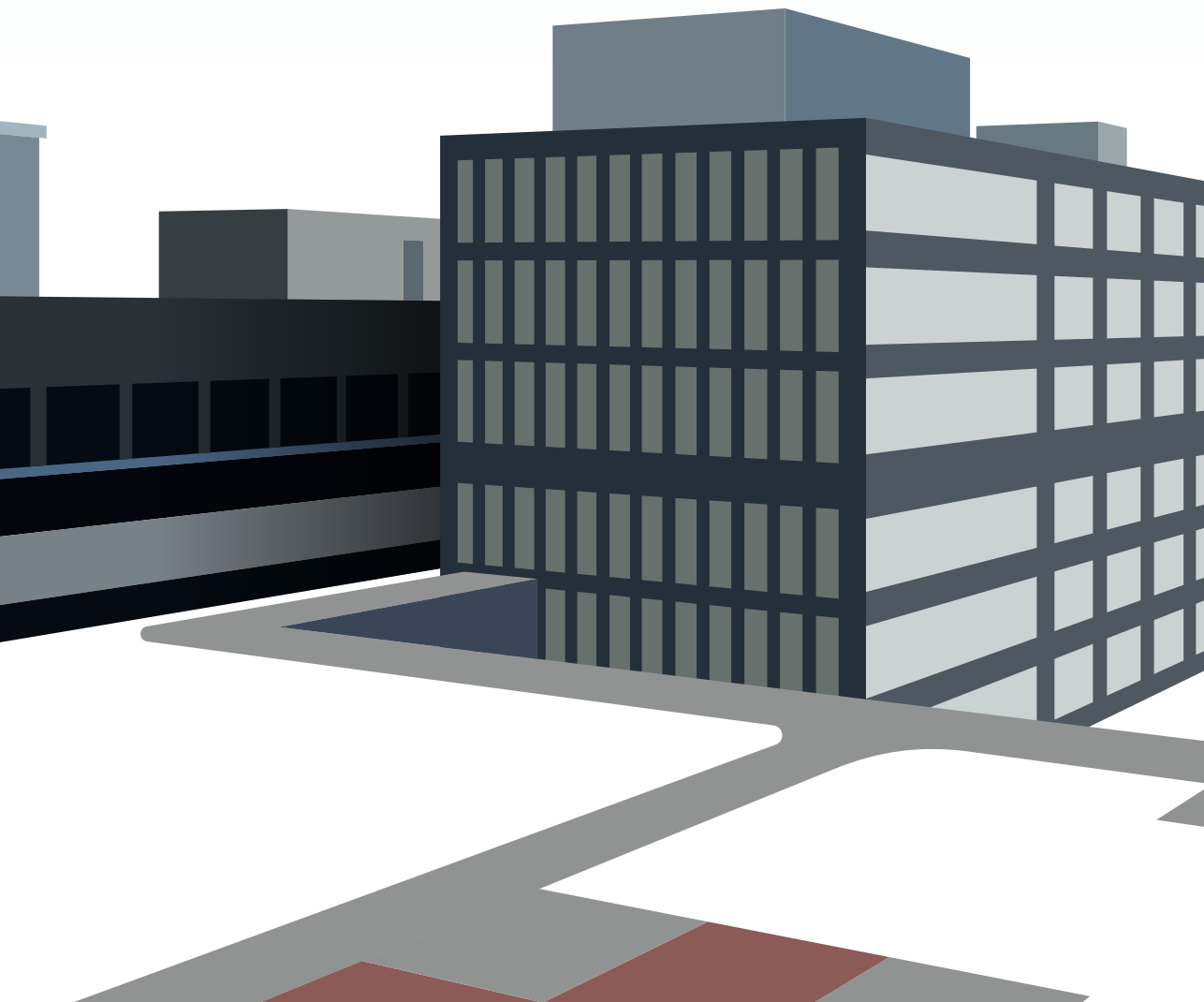

CHAPTER 2

Displaced medial clavicle fractures; operative treatment with locking compression plate fixation

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ABSTRACT

Objectives: Medial clavicle fractures are rare injuries and historically treated non-operatively. Displaced medial clavicle fractures, however, have a higher incidence of delayed- or non-union compared to non-displaced medial clavicle fractures and might benefit from operative treatment. We describe below a new technique for treating intra-articular fractures or extra-articular fractures with a small medial fragment by using special locking plates and present the results of our operatively treated patients.

Methods: First we describe our technique for treating very medial fractures with the radial (VA)-LCP™ Distal Humerus Plate (DePuy Synthes, Switzerland). Second, a retrospective cohort study was performed. All patients operated on for a displaced medial clavicle fracture between 2010 and 2017 were included. Primary outcome was the QuickDASH score and the Subjective Shoulder Value (SSV). Secondary outcomes were operative complications including mal- or non-union and implant removal.

Results: All 15 patients were available for follow-up. Fourteen patients were included in our analysis. One patient was excluded due to severe concomitant injuries. Six patients were treated with the radial (VA)-LCP™ Distal Humerus Plate, eight patients with the LCP™ Superior Anterior Clavicle Plate with lateral extension (DePuy Synthes, Switzerland) and one with a LCP 3.5 plate. The mean follow up was 39 months (range 9-79). The mean QuickDASH score was 0,81 (range 0-4.50, SD +/- 1.44) and the mean SSV was 96 (range 80-100, SD +/- 6.53). One patient had an early revision operation and developed an infection after 1,5 years. No mal- or non-unions occurred. Eight patients had their implants removed.

Conclusions: Operative treatment of displaced medial clavicle fractures with well-fitting 'small fragment' locking plates provides an excellent long-term functional outcome. Intra-articular fractures or extra-articular fractures with a small medial fragment can be treated with the radial (VA)-LCP™ Distal Humerus Plate.

INTRODUCTION

Clavicle fractures account for 2-5% of all fractures in adults [1]. Of all clavicle fractures, midshaft clavicle fractures have the highest incidence at approximately 70-80% [2,3]. The proportion of medial clavicle fractures ranges from 2,8 to 9,3 % [2-5]. They are often a cause of high-energy trauma or as part of a multiple injured patient [3,4,6-8].

In literature, non-operative treatment has been advocated as the golden standard for medial clavicle fractures for a long time [1,5]. Other studies, however, have shown a considerable risk of delayed- and non-union for displaced medial clavicle fractures. In literature, up to 14 % non-unions for displaced medial clavicle fractures compared to 7% for non-displaced medial clavicle fractures are reported [3]. Therefore, a shift towards operative treatment for displaced medial clavicle fractures has been suggested in recent literature [1,4,9-11].

Several operative techniques have been described: fixation with inverted LCP™ Superior Anterior Clavicle Plate with lateral extension [10], distal radial plate [10], a small T-plate with tension band suturing [12], standard T-locking plate [4], a pilon plate crossing the sternoclavicular joint [4], cerclage [9] or transosseous sutures [10]. However, most studies are case reports and the fixation of comminuted and intra-articular displaced medial clavicle fractures remains a challenge, as no specific implant is available for these fractures. In our hospital, these fractures are treated with the radial (VA)-LCP™ Distal Humerus Plate (DePuy Synthes, Switzerland).

The aim of this study is to describe our treatment algorithm, surgical technique and results of the operative treatment of displaced medial clavicle fractures.

METHODS

Study design

A retrospective cohort study was performed at a level 1 trauma centre. All patients who were operated on for a medial clavicle fracture between 2010 and 2017 were eligible for inclusion. Patients under 18 years of age and patients with a physeal fracture were excluded from this analysis. Follow up was done during regular outpatient department visits and by telephone for assessment of long-term functional outcomes. This assessment was done by one of the treating trauma surgeons. Informed consent was obtained from all individual participants included in the study. This study was approved by the Cantonal Ethic Committee Zürich (KEK-ZH-Nr. 2017-00192).

Operative indications

Patients who were clinically suspected of having a medial clavicle fracture were analysed with plain X-ray and/or CT scan (Figure 1). Indications for operative treatment in our hospital include 1) displacement >1 shaft width, 2) open fractures, 3) intra-articular displaced fractures and 4) symptomatic mal- or non-union (referred patients). Fractures were classified using the AO Classification and the Robinson Classification [2,13].

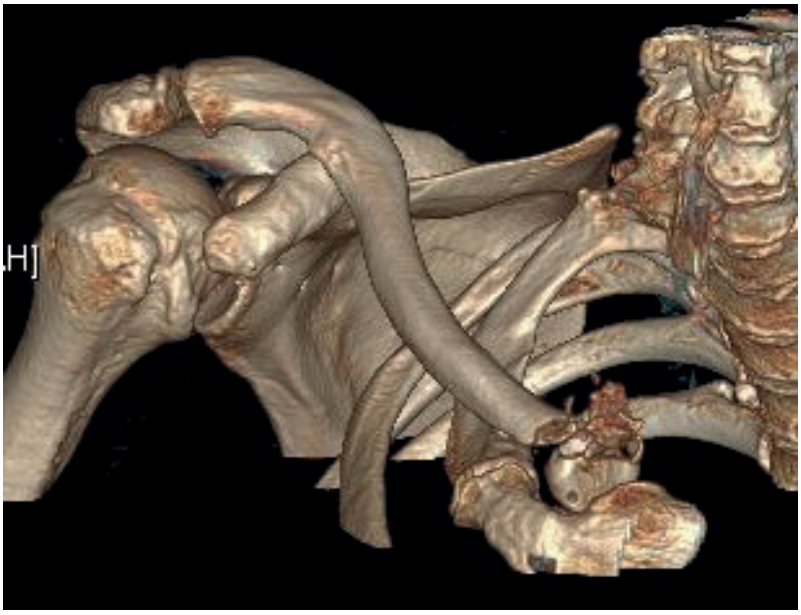

Figure 1. Pre-operative CT scan of a very medial and displaced intra-articular clavicle fracture

Operative procedure

Two different plate types were preferred for fracture fixation depending on the fracture type. If the fracture was extra-articular and if there was enough bone stock to achieve a stable fixation medially, we used the inverted LCP™ Superior Anterior Clavicle Plate with lateral extension (DePuy Synthes, Switzerland). This fixation method has been described before [10,11]. For intra-articular fractures or fractures where this aforementioned plate would not provide enough stability, we used the radial (VA)-LCP™ Distal Humerus Plate (DePuy Synthes, Switzerland). The advantage of this plate is that it is possible to insert angular stable screws in two different planes. With the development of Variable Angle (VA) systems, even more fixation directions are possible.

Patients were placed in a supine position on a radiolucent operation table. An incision was made on the lower edge of the medial clavicle and parallel to it. After dissecting the subcutis, the fracture was exposed. The periost was preserved as much as possible. Direct reduction and temporary fixation was done using reduction forceps and small Kirschner-wires (K-wires). If the LCP™ Superior Anterior Clavicle Plate with lateral extension was used, it was inverted and positioned antero-cranially. If definitive fixation was done with the radial (VA)-LCP™ Distal Humerus Plate, it was positioned with the 'lateral support' of the plate at the caudal side of the clavicle. The length of the plate should allow the insertion of at least three conventional or two angular stable screws in the lateral (diaphyseal) part of the clavicle. The angular stable screws in the medial (comminuted) fragments were inserted bicortically if possible. If necessary, plate-independent (lag)-screws were additionally inserted (Figure 2). Reduction, plate positioning and screw length were intra-operatively verified with x-ray in cranio-caudal and caudo-cranial direction (Figure 3 and 4). After irrigation, the wound was closed in layers.

Postoperative treatment

Patients were treated functionally without weight bearing for six weeks. They were allowed free functional movement of the shoulder with abduction limited to 90 degrees for six weeks supported by physiotherapy. Standard postoperative follow up including x-rays was done at 6, 12 and 24 weeks in the outpatient department. If patients had persistent complaints or fractures had not healed clinically or radiologically, follow up was extended with visits at one year. Implant removal was not routinely performed. It was carried out on clear indication, for instance with implant related irritation.

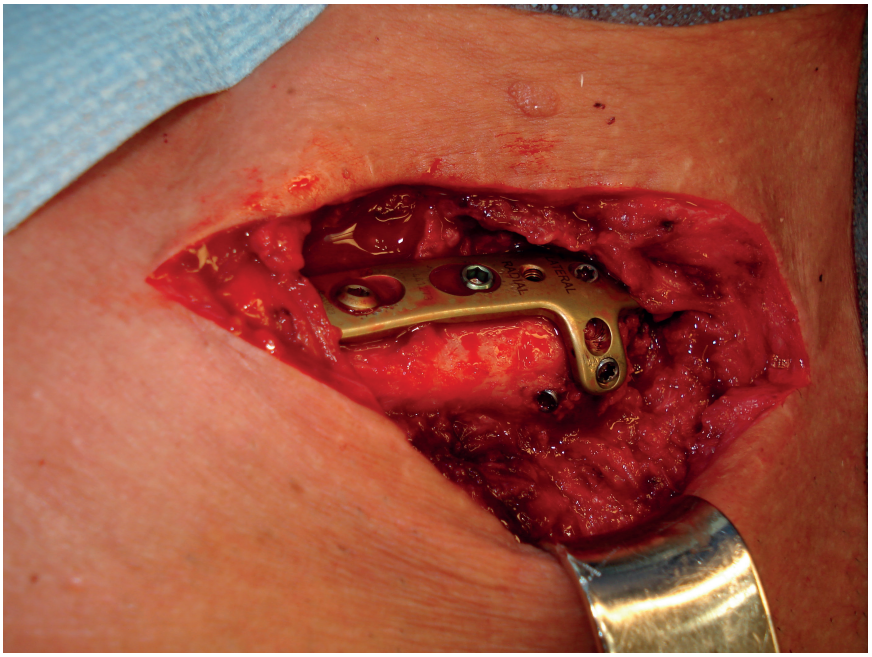

Figure 2. Intra-operative image of radial LCP™ Distal Humerus Plate

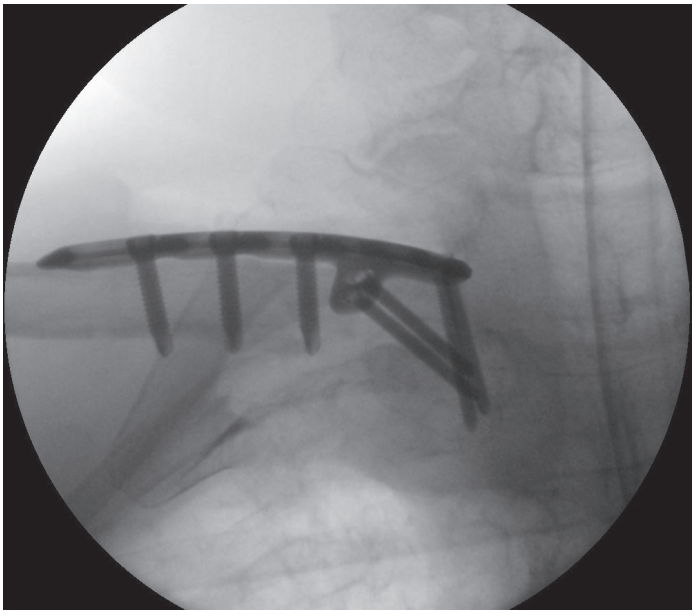

Figure 3. Intra-operative X-ray caudo-cranial

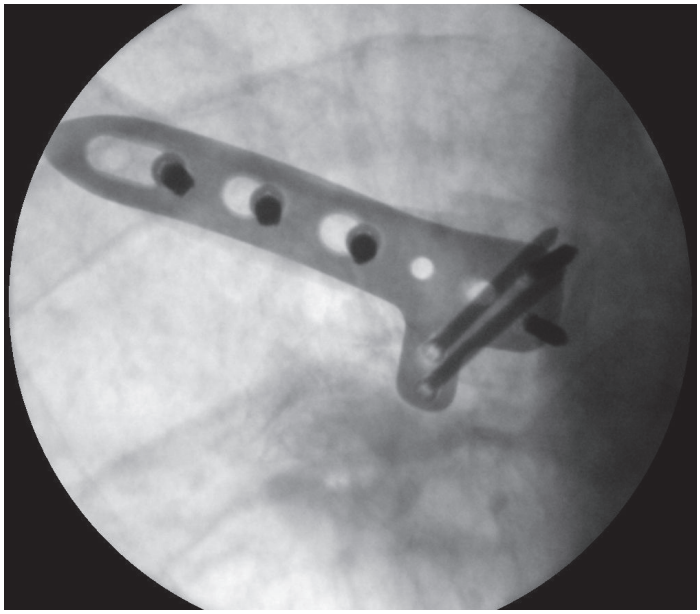

Figure 4. Intra-operative X-ray cranio-caudal

Primary outcome

Primary outcome was the shoulder function measured using the QuickDASH score and the Subjective Shoulder Value (SSV)[14-17]. The QuickDASH provides a summative score on a 100-point scale, with 100 indicating the most disability. A QuickDASH score of less than 10 is considered an excellent result, a score of >40 indicates a poor shoulder function. The SSV is a single measure score from 0-100 developed by Jost et al. with 100 indicating the best function [16]. The SSV has shown a reliable agreement with the Constant Score [15].

Secondary outcome

Secondary outcome parameters were complications, including implant failure, infection (superficial or deep), non-union, mal-union, revision surgery, refracture after implant removal and implant related irritation.

The definition of implant failure was implant loosening, bending or breakage not bridging the fracture anymore resulting in a revision operation. Superficial infection was defined as redness, swelling and/or purulent discharge from the wound that could be treated with antibiotics. If surgical drainage was required, it was considered a deep infection. A lack of radiographic evidence of healing combined with clinical evidence

of pain and motion at the fracture site six months after surgery was considered a non-union. Fracture union in a shortened, angulated, or displaced position on radiographs was considered a mal-union. Interventions needed to treat these complications were also noted. Re-interventions performed before routine implant removal was indicated, were considered complications of treatment.

Implant removal was analysed using the algorithm Hulsmans et al. developed to investigate the presence of implant related irritation [18].

Statistical analysis

Data were presented as mean ± standard deviation (SD) for continuous variables or as absolute numbers (percentage) for categorical variables. The analyses were performed with SPSS, version 22.0 (IBM Corp., Armonk, NY) for Windows.

RESULTS

Between 2010 and 2017, 15 patients were treated with an open reduction and internal fixation (ORIF) for a medial clavicle fracture. Baseline characteristics are presented in Table 1. Fourteen patients were operated for a primary displaced medial clavicle fracture. Eleven fractures were extra-articular and three intra-articular fractures. One patient with a Robinson 1A1 fracture was referred to our hospital with a non-union eight months after is accident. He was initially operated in another hospital with a bridging sternoclavicular plate. After one month the plate was removed due to an infection. The soft tissues recovered uneventfully but a symptomatic non-union developed. One patient was treated with a standard 3.5 LCP™ Plate, 8 patients with an inverted LCP™ Superior Anterior Clavicle Plate with lateral extension and 6 patients with a radial (VA)-LCP™ Distal Humerus Plate. The mean age at time of injury was 52 years old (range 19-79). All patients were male. Twelve patients suffered a single injury, 3 patients were polytrauma patients. The most common mechanism of injury was (winter)sports related (10/15) with traffic accident as the second most common mechanism (3/15).

All patients were available for follow up. The mean follow up was 39 months (range 9-79). Twelve patients had at least one follow-up visit in our hospital resulting in a mean radiological follow-up of 35 weeks (range 5-105). The mean QuickDASH score was 0,81 (range 0-4.50, SD +/- 1.44) and the mean SSV was 96 (range 80-100, SD +/- 6.53), both indicating a very good functional outcome. These results are presented in Table 2.

One 75 year old patient suffered a polytrauma with an Injury Severity Score of 29. He was discharged to a rehabilitation clinic with an incomplete tetraplegia. He had a Robinson 1B1 medial clavicle fracture treated with a radial (VA)-LCP™ Distal Humerus Plate. Currently, 3.5 years post injury, he is in a nursing home. He has no complaints of his left clavicle. The plate is not causing any irritation. His overall condition with a lack of strength, however, results in a QuickDASH of 65 and a SSV of 40. As this is clearly the result of his concomitant injuries and not of his medial clavicle fracture, this patient is not included in our functional analysis.

We did not register any non- or mal-union. We had one patient with an implant failure. This patient with an AO 15-A3.3 and Robinson 1B2 fracture (Figure 5) was treated with a radial (VA)-LCP™ Distal Humerus Plate. After two days there was a cut-out of the medial screws, clearly caused by a non-optimal initial plate position (too medially) with insufficient primary stability (Figure 6). He underwent revision surgery with another radial (VA)-LCP™ Distal Humerus Plate in a better position (Figure 7). The fracture consolidated. Unfortunately after 1.5 years, a skin perforation with subsequent infection occurred due to a broken and displaced screw. The plate was removed and the infection was treated with antibiotics in his regional hospital. In the end he had a good recovery resulting in a QuickDASH of 2.3 and a SSV of 100. Two other patients had one or more broken angular stable 2.7mm screws discovered at 7 weeks and 11 months follow-up without any clinical consequences.

Eight patients (8/14) experienced implant related irritation. In 7 patients this resulted in implant removal. One patient is still considering implant removal. In total, eight patients had their implant removed after a mean of 16 months (range 8-44, SD+/- 11,8).

Figure 5. Pre-operative CT of intra-articular displaced medial clavicle fracture of patient with implant failure and early revision

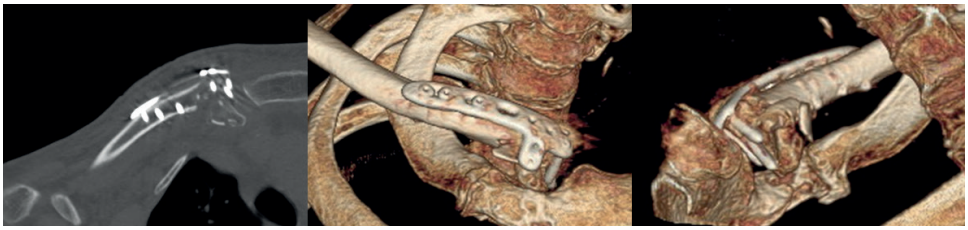

Figure 6. Post-operative CT with implant failure. Plate positioning was too medially with screws being intra-articular

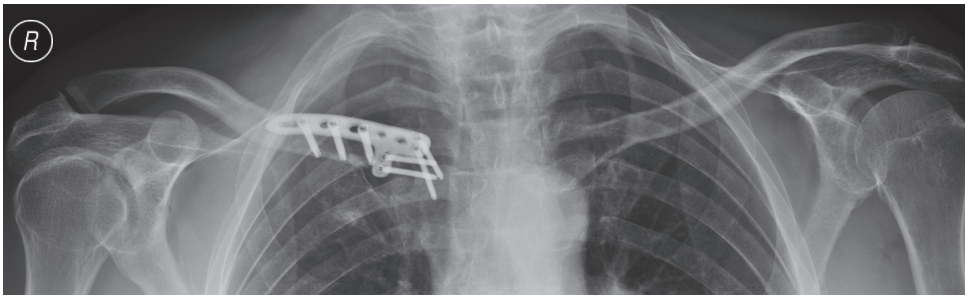

Figure 7. Follow up x-ray 6 weeks post-operative

Table 1. Baseline characteristics

	Patients n=15
Age (years), mean (range)	52 (19-79)
Sex	
Male	15
Female	0
Side	
Right	7
Left	8
Polytrauma (ISS>16)	
Yes	3
No	12
Trauma mechanism	
Traffic	3
Sports	
Ski	4
Snowboard	1
Cross-country skiing	1
Bike	4
Fall from stairs	1
Other	1
Preoperative imaging	
X-ray	10
CT	10
Both	5
Classification	
AO	
15.1-A	12
15.1-B	0
15.1-C	3
Robinson	
1A1	1
1A2	0
1B1	11
1B2	3
Follow Up (months), mean (range)	39 (9-79)
Size of medial fragment (mm), mean (range)	17,8 (0-4,5)
Implant	
LCP™ 3.5 plate	1
LCP™ Superior Anterior Clavicle Plate with lateral extension (2.7/3.5)	8
Radial (VA)-LCP™ Distal Humerus Plate (2.7/3.5)	6

TABLE 2. Results

	n=14
QuickDASH, mean (range, +/-SD)	0,81 (0 - 4.50, +/-1.44)
SSV, mean (range, +/-SD)	96 (80 - 100, +/-6.53)
Implant irritation	
implant not removed, no irritation	5 (36%)
implant not removed, irritation but implant removal not necessary	0
implant not removed, irritation, no request for removal due to fear of surgery	0
implant not removed, irritation, considering removal	1 (7%)
implant removed routinely or on patients request without irritation	2 (14%)
implant removed due to implant irritation	6 (43%)
Complications:	
nonunion	0
malunion	0
implant failure	1 (7%)
superficial infection	0
deep infection	1 (7%)
revision surgery	1 (7%)
refracture after implant removal	0

DISCUSSION

Successful operative treatment of displaced medial clavicle fractures provides excellent long-term functional results. Locking plates are generally ideal implants to stabilise juxta-articular fractures in any location. Both ends of the clavicle, a small bone with small diameter, are predisposed for small, pre-contoured locking plates. For the more common lateral fractures, such plates exist and are extremely helpful to achieve a stable fixation. As the medial end of the clavicle has a rather similar surface and angulation as the lateral one, the inverted LCP™ Superior Anterior Clavicle Plate with lateral extension is an almost ideal implant for fracture fixation, if the medial bone stock is long enough (>2cm). For intra-articular fractures or extra-articular fractures with a small medial fragment, the aforementioned implant is not suitable. We found, that for these rare and very special situations, the radial (VA)-LCP™ Distal Humerus Plate can be successfully used for stable fixation. Due to its design for the distal humerus with extra 'lateral support', it is possible to position this 'lateral support' as 'caudal support' for medial clavicle fractures. This gives the surgeon the possibility to insert the medial locking screws at an almost perpendicular angle to each other resulting in a more

stable fixation. The 'Variable Angle' version of the plate facilitates an even greater range of screw positioning. Sidhu et al. suggested the development of an anatomical medial clavicle plate, but to our knowledge, no such plate has been designed yet [10].

The natural course of medial clavicle fractures has been described in three studies. Non-union rates of 6,7% for non-displaced and 14,3% for displaced medial clavicle fractures have been reported [3]. Salipas et al. found a delayed-union rate of 10% for medial clavicle fractures in general. When distinguishing between displaced and non-displaced medial clavicle fractures, the delayed-union rate was 20% for displaced medial clavicle fractures [7]. The overall functional outcome of non-operative treatment for displaced and non-displaced fractures was good with a reported SSV of 77. Unfortunately no differentiation between displaced and non-displaced fractures was made. Throckmorton et al. reported moderate to severe pain in up to 28% of the patients after non-operative treatment [5]. Taking these results into account, operative treatment of displaced medial clavicle fractures should be considered and discussed with any patient who has this injury.

The following treatment algorithm for medial clavicle fractures is determined by our hospital: non-operative treatment for non-displaced fractures with bony contact of the fragments. Our indications for operative treatment are 1) displacement >1 shaft width, 2) open fractures, 3) displaced intra-articular fractures and 4) symptomatic mal- or non-union. In literature, displacement of >10mm is considered severe [2,5,7]. As the shaft medially is at least 10mm thick, displacement of more than one shaft width, as used in our hospital, should be considered severe. A preoperative CT scan provides a good understanding of the fracture that can be important for the implant choice in case of operative treatment.

Only two other studies describe a larger series of results of surgical treatment of displaced medial clavicle fractures. Sidhu et al. published results of 20 patients with different implants including the inverted LCP™ Superior Anterior Clavicle Plate (15 cases). They found a DASH score after 12 months of 0,9 that represents an excellent result [10]. Oe et al. presented results of 10 patients operated on with different implants like Pilon locking plate, T-oblique locking plate, reconstruction locking plate, Stryker BOS plate and DCP plate. Four patients showed an excellent DASH score (0-0.9), three a good DASH score (10-16) and 1 patient a very poor DASH score (67). This last patient had a complicated course and ended up with a medial clavicle resection. Two patients were not analysed due to tetraplegia/paraplegia [4].

Implants were not routinely removed in our cohort. Implant related irritation, analysed with the algorithm of Hulsmans et al. [18], showed that after a mean of 16 months eight

patients had their plate removed, 6 due to irritation, and 2 on request. The combination of the lack of soft tissue at the medial side of the clavicle and the bulky implants might result in irritation. Oe at al. recommend plate removal no earlier than 18 months after surgery because of the lack of weight bearing that might result in a prolonged healing process [4]. We only recommend implant removal in case of implant related irritation or on patients' request.

Several limitations need to be addressed. First, the retrospective character of this study has its obvious drawbacks. Second, our cohort with 15 patients is relatively small although the largest other published studies describe 10 and 20 patients respectively [4,10]. Third, most patients were not available for long-term clinical follow up. However, our protocol to obtain information and questionnaires by telephone resulted in a 100% follow up rate; even from patients living further away or with a foreign residency. This is an obvious positive aspect of this study. Another strength of this study is the generalizability of our results as the 15 patients were operated on by 6 different surgeons.

CONCLUSIONS

Operative treatment of displaced medial clavicle fractures provides an excellent long-term functional outcome. Fractures with substantial medial bone stock can successfully be treated with the inverted LCP™ Superior Anterior Clavicle Plate with lateral extension. Intra-articular fractures or extra-articular fractures with a small medial fragment can be treated with the radial (VA)-LCP™ Distal Humerus Plate.

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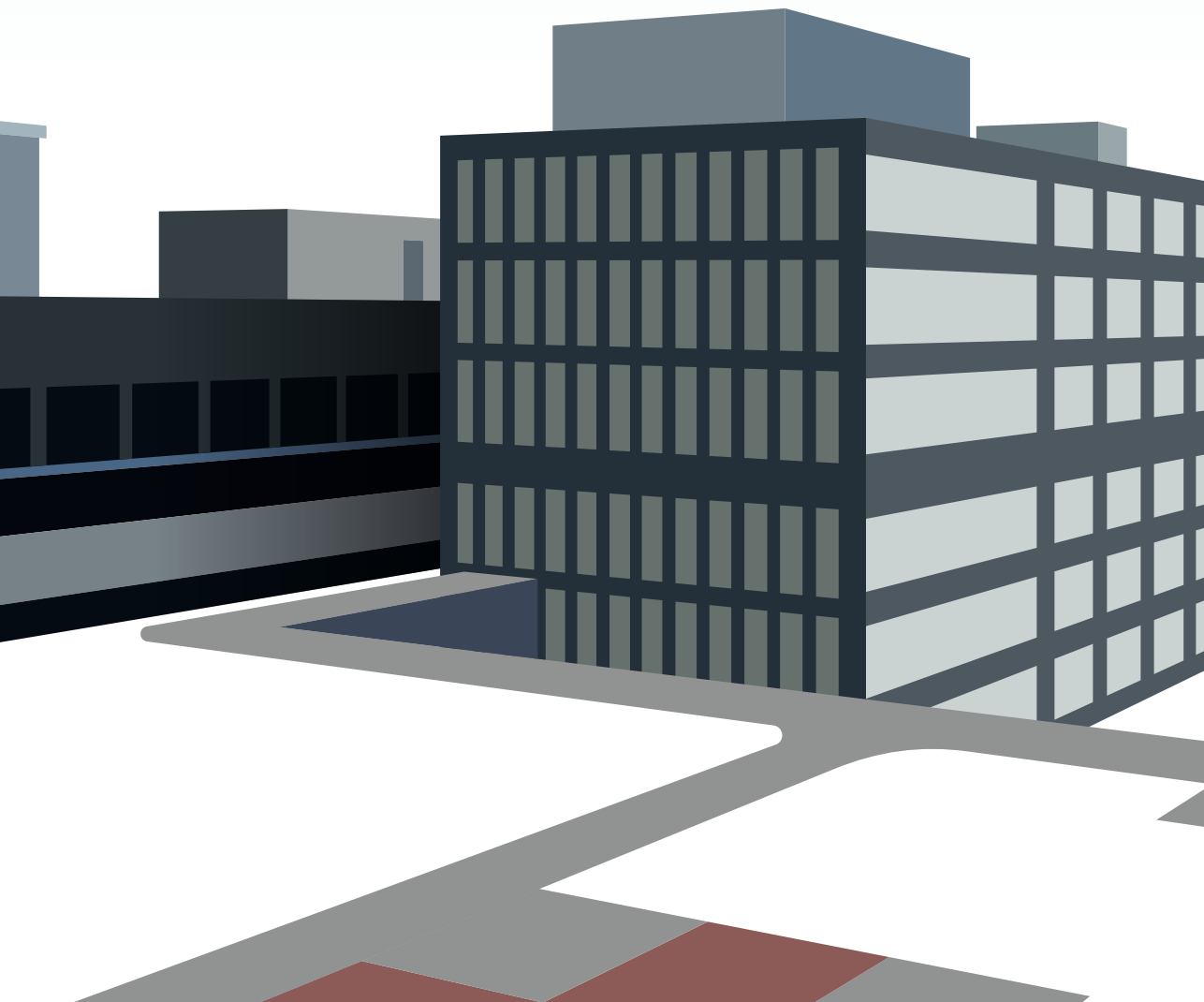

CHAPTER 3

Predicting suitability of intramedullary fixation for displaced midshaft clavicle fractures

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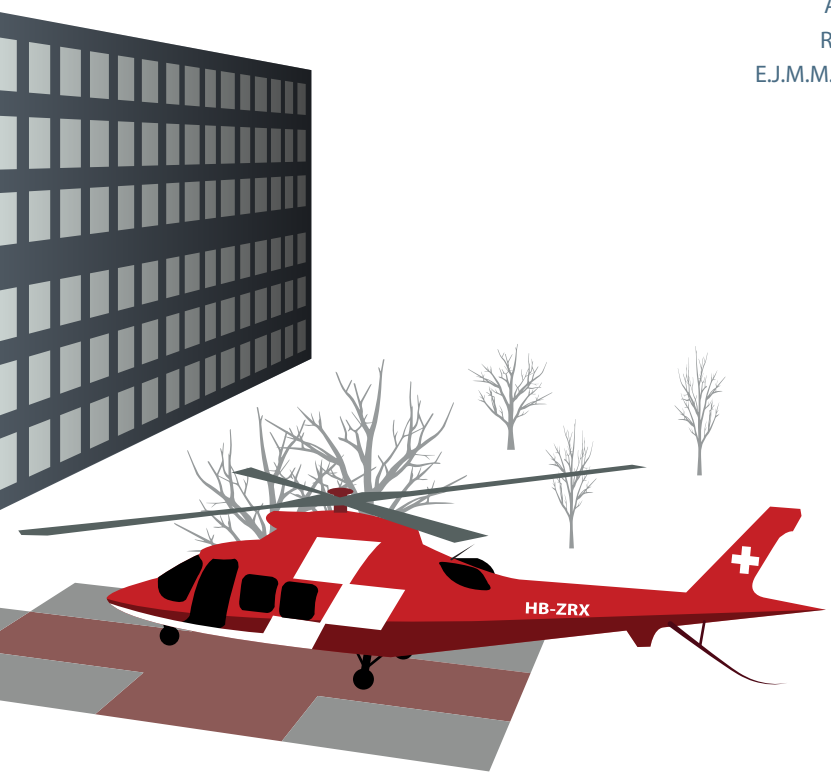

ABSTRACT

Purpose: Implant-related irritation is a technique specific complication seen in a substantial number of patients treated with intramedullary fixation for clavicle fractures. The purpose of this study was to identify predictors for developing implant-related irritation in patients with displaced midshaft clavicle fractures treated with elastic stable intramedullary nailing.

Methods: A retrospective analysis of the surgical database in two level 2 trauma centers was performed. Patients who underwent intramedullary fixation for displaced midshaft clavicle fractures between 2005-2012 in the first hospital were included. Age, gender, fracture comminution and fracture location were assessed as possible predictors for developing irritation using multivariate logistic regression analysis. These predictors were externally validated using data of patients treated in another hospital.

Results: Eighty-one patients were included in initial analysis. In the multivariate analysis, comminuted fractures in comparison to non-comminuted fractures (72%vs.38%, $p = 0.027$) and fracture location ($p < 0.001$) were significantly associated with the development of implant-related irritation. In particular, lateral diaphyseal fractures caused irritation compared to fractures on the medial side of the cut-off point (88% versus 26%).

External validation of these predictors in 48 additional patients treated in another hospital showed a similar predictive value of the model and a good fit.

Conclusion: Comminuted and lateral diaphyseal fractures were found to be statistically significant and independent predictors for developing implant-related irritation. We therefore believe that intramedullary fixation might not be suitable for these types of fractures. Future studies are needed to determine whether alternative surgical techniques or implants would be more suitable for these specific types of fractures.

INTRODUCTION

Intramedullary fixation (IMF) has proven to be a promising alternative to traditional open reduction and internal plate fixation (PF) for completely displaced midshaft clavicle fractures (DMCF).[1] The advantages of using an IM pin include smaller incision, less soft tissue dissection, and load-sharing fixation with relative stability that encourages copious callus formation.[2] In contrast, several studies report technique-specific complications such as medial implant protrusion and implant-related irritation (0% - 54%)[3,4,5,6,7]

Little is known about the predictive value of specific fracture patterns, such as comminution or fracture location, with respect to the occurrence of these implant-related problems after IMF. Preoperative identification of those patients at risk for developing implant-related irritation would help facilitate the selection of the optimal surgical treatment approach.

The main purpose of this study was to identify and evaluate predictors for developing irritation in patients with DMCF treated with IMF. In addition, these potential predictors were validated using an external cohort of patients. The null hypothesis was that fracture classification and fracture location would be predictors for developing implant-related irritation.

MATERIALS AND METHODS

Study design

A retrospective analysis of the surgical databases of two Dutch level 2 trauma centers and regional teaching hospitals was performed. The data from the Diakonessen hospital were used to identify predictors for developing implant-related irritation, and the data from the Catharina hospital were used to externally validate them.

In the Diakonessen hospital, all patients who underwent IMF for an isolated DMCF between January 2005 and December 2010 were eligible for inclusion. Patients who were assigned to IMF as part of a multicenter randomized controlled trial were also included. This previously published study compared PF with IMF in patients with a DMCF and included patients from January 2011 until August 2012.[6] Patients from the Catharina hospital were retrospectively analyzed and underwent IMF for an isolated DMCF between 2006 and 2010.

Study population

Given similar characteristics among the hospitals, it was assumed that the surgical databases consisted of data on similar trauma populations. A DMCF was defined as at least one shaft width difference in height between the fracture parts. In the retrospectively analyzed patients the choice of the IM procedure was based on either surgeon or patient preference or randomization to IMF in the randomized controlled trial.

The following exclusion criteria were used: (1) patients with pre-existing morbidity of the arm, shoulder or hand, (2) open fractures, (3) pathological fractures, (4) presence of neurovascular injury, and (5) fractures older than one month or non-unions. Patients were followed until the implant was removed or until a year after surgery if the implant was still in place.

Data collection

The collected data were patient age, gender, fracture side, fracture classification, trauma mechanism, fracture location, and complications. Fractures were divided into two groups. *Group I*, simple, non-comminuted fractures, were AO/OTA B1.1 - B1.3 fractures.[8] *Group II*, comminuted fractures, were AO/OTA B2.1 - B3.3 fractures.[8] Complications collected were infection, implant-related problems (soft tissue irritation, failure), nonunion, malunion and refracture after implant removal. Interventions needed to treat these complications were also noted. Our current clinical protocol dictates removal of the pin 3 months postoperatively in all patients treated with IMF for DMCF, or after the fracture has healed adequately when delayed union is suspected. The routine removal of the pin is generally performed under local anesthesia. Re-interventions that were performed before routine removal was indicated were considered and registered as complications of treatment. The primary outcome parameter was implant-related irritation on the medial side of the clavicle as reported by the patient during follow-up. The topic of implant-related irritation was discussed at each outpatient visit.

Determining fracture location

The location of the fracture was defined as a percentage of the total length of the clavicle measured from the medial cortex. To determine the exact anatomic fracture location, the length of the medial fracture part was divided by the combined length of the medial and lateral fracture parts. The medial fracture part was determined by drawing a line from the middle of the medial cortex to the middle of the medial fracture-site. The lateral fracture part was measured by drawing a line from the middle of the lateral end up to the first point in which the clavicle cortex was believed to be circularly intact. (figure 1).

Pre-operative radiographs (anteroposterior and 30° cephalad anteroposterior) were reviewed by 2 highly experienced trauma surgeons (E.J.V, R.M.H.) who arrived at a consensus when classifying the fractures according to the AO/OTA classification system.[8] Findings from this consensus meeting were used for the uni- and multivariate logistic regression analysis.

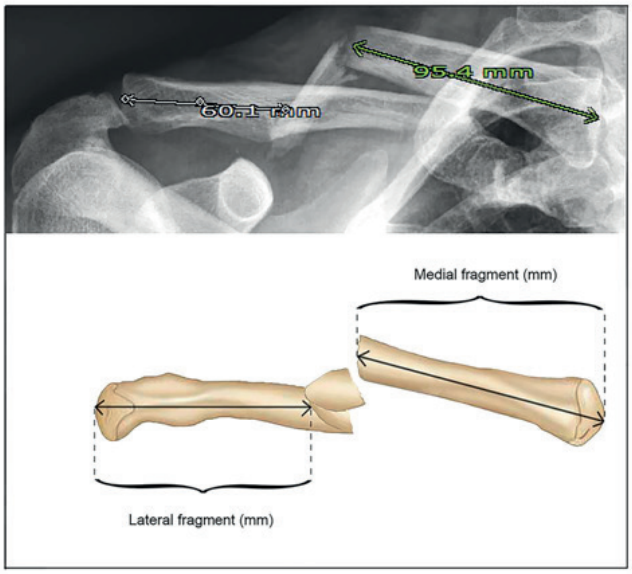

FIGURE 1. Measuring the location of the fracture. The medial fracture part was determined by drawing a line from the middle of the medial cortex to the middle of the medial fracture site. The lateral fracture part was measured by drawing a line from the middle of the lateral end up to the first point in which the clavicle cortex was believed to be circularly intact.

Operative procedure IMF

In both hospitals the same surgical procedure was used for all patients. All patients underwent antegrade IMF with a Titanium Elastic Nail (TEN; DePuy Synthes, or Stryker, Waardenburg, the Netherlands) in the supine position. The operations were performed or supervised by one of the trauma surgeons who had extensive experience (> 20 procedures) with the surgical technique. If possible, a closed fracture reduction using sharp reduction forceps was performed prior to implant placement. A small incision was made just lateral to the sternoclavicular joint, and the anterior cortex was opened using a pointed reamer. A TEN was inserted from the medial side under fluoroscopic control. The diameter of the TEN ranged from 2 to 3.5 mm, depending on the width of the bone.

If closed reduction failed, an additional small incision was made over the fracture site for open reduction. After complete introduction in the lateral fragment and compression, the nail was cut at the introduction point. Fascia and skin were then closed in layers.

Statistical analysis

Data were presented as mean ± standard deviation (SD) for continuous variables or as absolute numbers (percentage) for categorical variables. A Receiver Operating Characteristic (ROC) curve was created to determine the optimal cut-off value for fracture location as a predictor for implant-related irritation.

The predictors for implant-related irritation were assessed using univariate logistic regression analysis. Factors with a P value <0.15 in univariate analysis were considered predictors for the development of irritation and were used in a multivariate logistic regression analysis. These predictors were then externally validated as described below.

The rule of thumb of at least 10 events per predictor was fulfilled to derive and validate the prediction model.[9] The performance of the model was evaluated by the power of explanation of the model (Nagelkerke's R^2), the fit of the model was tested with calibration (Hosmer and Lemeshow goodness of fit test), and the discriminative power of the model was tested with the Area Under the Receiver Operating Characteristic curve (AUC). The analyses were performed with SPSS, version 20.0 (IBM Corp., Armonk, NY) for Windows. Significance of statistical differences was attributed to $p < 0.05$.

RESULTS

Surgical treatment with IMF was performed in 83 patients between 2005 and 2012. Thirty-eight (46%) of these patients participated in the randomized trial. Two patients were excluded because of poor pre-operative radiograph quality. A total of 81 patients were included in this study of which the baseline characteristics are shown in Table I.

A total of 53 complications were seen in 51 patients (Table II). One patient was treated for infection with antibiotics whose implant was removed under general anesthesia after the medial side of the pin perforated the skin 2 months postoperatively. In 13 patients, the protruding end of the pin was cut off under local anesthesia, and in 1 of these patients, the pin was subsequently removed under general anesthesia due to persistent irritation 4 weeks after the minor revision. In 2 patients, the IM pin migrated medially out of the lateral fragment and was not bridging the fracture anymore, so the pin was removed and PF was performed.

Out of 81 patients, 58% complained about implant-related irritation on the medial side during the follow-up period as follows: 19 patients 2 weeks post-op, 11 patients 6 weeks post-op, 8 patients 3 months post-op, 7 patients 6 months post-op, and 2 patients 1 year post-op. Thirty-eight percent of the patients suffered from implant-related irritation in group I and 72% in group II (Table III). No significant difference in complication rates was observed between patients who underwent IMF for an isolated DMCF between January 2005 and December 2010 and patients who were assigned to IMF as part of a multicenter randomized controlled trial.

Using ROC analysis, a fracture location of 58% measured from the medial cortex was determined to be the optimal cut off value for the prediction of implant-related irritation. (figure 2). Irritation was seen in 88% of fractures lateral to this cut-off point versus 26% of fractures medial to it.

Univariate logistic regression of potential predictors including patient age, gender, fracture location, and comminuted fracture are displayed in Table III. Comminuted fracture ($p = 0.003$) and fracture location ($p < 0.001$) were significantly associated with the development of implant-related irritation. Multivariate logistic regression analysis showed these factors to be statically significant and independent predictors for development of implant-related irritation (comminuted fracture $p = 0.027$ and fracture location $p < 0.001$). The R^2 of this model was 0.527, which means that 52.7% of the development of implant-related irritation could be explained by the two predictors in the model. The fit of the model was good ($p = 0.425$). The AUC was 0.869 (95% CI 0.790-0.949), which meant the model was capable of discriminating between patients with and without irritation of the implant.

Univariate logistic regression analysis showed that comminuted fractures and fracture location were no predictors for the development of other complications like infection, implant failure, non- or malunion and refracture after implant removal.

Forty-eight patients were included for validation (Table IV). Among these 48 patients, 52% complained about implant-related irritation during the total period of follow-up. Thirty-two percent of the patients with a simple fracture and 80% of the patients with a comminuted fracture suffered from implant-related irritation. Irritation was also seen in 77% of the fractures located lateral to the 58% cut-off point versus 11% medial to it. The external validation of these predictors showed a similar predictive value of the model. The R^2 was 0.523, the fit was good ($p = 0.639$), and the AUC was 0.851 (95% CI 0.736-0.966).

TABLE I. Baseline characteristics.

Variables	Intramedullary fixation (N=81)
Age, years (mean, range)	36 (14-71)
Gender, n %	
Male	62 (77%)
Female	19 (23%)
Fracture side, n %	
Right	36 (44%)
Left	45 (56%)
Fracture classification[a]	
"Simple" (AO/OTA type B1)	34 (42%)
"Wedge" (AO/OTA type B2)	30 (37%)
"Complex" (AO/OTA type B3)	17 (21%)
Trauma mechanism, n %	
Traffic accident	28 (35%)
Sports	30 (37%)
Fall	18 (22%)
Unknown[b]	5 (6%)

[a] AO classification[8]
[b] was not reported in documentation

TABLE II. Postoperative complications.

Complications	Treatment	Intramedullary fixation (N=81)
Infection		
Superficial	antibiotics	1[a] (1%)
Deep	surgical drainage	0
Irritation due to medial implant protrusion	observation	32 (40%)
	minor revision	13[b] (16%)
	implant removal local anesthesia	0
	implant removal general anesthesia	3 (4%)
Irritation due to lateral implant protrusion	observation	0
	minor revision	1 (1%)
	implant removal local anesthesia	0
	implant removal general anesthesia	1 (1%)
Implant failure	major revision	2[c] (2%)
Nonunion	major revision	0
Malunion	major revision	0
Refracture after implant removal	major revision	0

[a] One patient was treated for infection with antibiotics and removal of the implant under general anesthesia after the skin was at risk at the entry medial side.
[b] Minor revisions included partial removal of the protruding end of the pin under local anesthesia. In 1 of these patients subsequently the pin was removed under general anesthesia due to persistent irritation 4 weeks after the minor revision.
[c] Pin was removed and plate fixation was performed.

TABLE III. Factors associated with implant related irritation in patients with displaced midshaft clavicle fractures

Variables	Irritation (N=47)	No irritation (N=34)	Univariate analysis Odds ratio (95 % CI)	P-value	Multivariate analysis Odds ratio (95 % CI)	P-value
Age						
Mean (SD)	36.91 (13.76)	33.91 (17.12)	1.01 (0.98 - 1.04)	0.380		
Gender						
Male	35 (56%)	27 (44%)	0.76 (0.26 - 2.18)	0.605		
Female	12 (63%)	7 (37%)				
Fracture classification[a]						
Group I (AO type B1)	13 (38%)	21 (62%)	4.23 (1.65 – 10.84)	0.003*	3.91 (1.17 - 13.08)	0.027*
Group II (AO type B2-B3)	34 (72%)	13 (28%)				
Fracture location						
Lateral midshaft; >58%[b]	37 (88%)	5 (12%)	21.46 (6.60-69.73)	<0.001*	20.62 (6.00-70.91)	<0.001*
Non lateral; < 58%	10 (26%)	29 (74%)				

Univariate and multivariate analysis were performed by logistic regression
CI confidence interval. OR odds ratio
[a] AO classification[8]
[b] a fracture location of 58% measured from the medial cortex was determined as the optimal cut off value for prediction of implant related irritation
* P value < 0.05. The factors with P value < 0.15 at univariate analysis were selected into multivariate analysis

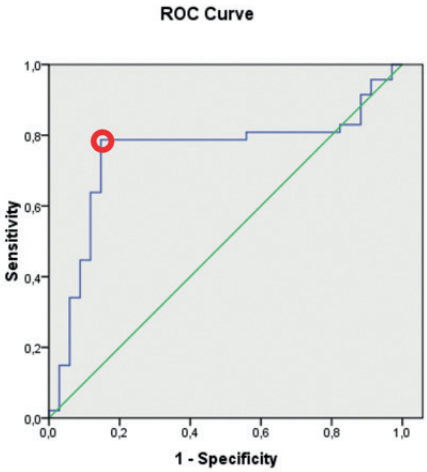

FIGURE 2. Receiver Operating Characteristic (ROC) curve to determine a fracture location in percentage measured from the medial cortex as the optimal cut off value for prediction of implant related irritation. A fracture location of 58% measured from the medial cortex was determined to be the optimal cut off value for prediction of implant related irritation.

TABLE IV. Baseline characteristics Catharina hospital.

Variables	Intramedullary fixation (N=48)
Age, years (mean, range)	34 (16-72)
Gender, n %	
Male	34 (71%)
Female	14 (29%)
Fracture side, n %	
Right	17 (35%)
Left	31 (65%)
Fracture classification[a]	
"Simple" (AO/OTA type B1)	28 (58%)
"Wedge" (AO/OTA type B2)	13 (27%)
"Complex" (AO/OTA type B3)	7 (15%)
Trauma mechanism, n %	
Traffic accident	20 (42%)
Sports	23 (48%)
Fall	5 (10%)

[a] AO classification[8]

DISCUSSION

High rates of implant-related irritation (up to 54%) have been reported in patients treated for DMCF with IMF.[4,5,6,7,10,11,12] It may be hypothesized that specific types of fractures or patient characteristics carry higher risk for implant-related irritation. The results of this study demonstrated that presence of fracture comminution and a more lateral diaphyseal location of the fracture (>58% measured from the medial end) are independent predictors for development of implant-related irritation on the medial side, and external validation of these predictors confirmed these results. This study also illustrates that implant-related irritation is by far the most common complication after IMF of DMCF.

Implant-related irritation could have several causes, one of which is technical. While antegrade nailing allows for easy implant removal under local anesthesia, it also may cause nuisance when the TEN is left to long. Most of the time, however, implant-related irritation is from protrusion of the implant after medial migration.[1,6,7,12,13,14] The origin of this migration may have different explanations, as well.

The IM pin is not fixed in an absolute fashion and is only kept in place because it is relatively fixed in the IM canal due to the S-shape of the clavicle. Intra- or postoperative shortening of the clavicle may cause the pin to migrate medially, as the lateral cortex is generally intact.[15,16] Migration continues until the lateral main fragment is supported by the medial main fragment.[12]

Using the technique of antegrade nailing, the part of the pin that is introduced into the lateral fragment has to be long enough for adequate bridging of the fracture. If the lateral fragment is too small, the IM pin cannot provide a stable construction and may easily migrate. This might be why there is such a high medial irritation rate in patients with clavicle fractures in the lateral part of the midshaft who undergo IMF.

It was previously stated that comminuted fractures (with moderate post-traumatic shortening of <7% of the uninjured side) are eligible for IMF, as they will heal with moderate shortening and without medial pin protrusion.[12] Our data seem to contradict these findings, as comminuted fractures showed a high rate of irritation ($p=0.027$). It should be noted that we did not measure and report post-traumatic shortening. However, we believe that comminution is a logical factor which allows shortening after IMF.

Although our data confirmed the high overall rate of irritation described in previous studies, it is hard to quantify this complication.[4,6,7,12,13,14] In the current study, 16% of the patients underwent a minor revision under local anesthesia, and 4% of the patients required implant removal under general anesthesia. Any surgical technique is accompanied by a certain rate of re-intervention. This rate might be lower with PF compared to pin fixation, but it is done under general anesthesia using a more invasive surgical approach. When selecting an implant, surgeons should always bear in mind the expected rate of re-intervention associated with a certain implant in addition to more obvious criteria, such as fracture classification and location.

Possible solutions for reducing medial migration (and therefore irritation) might be the use of a medial end cap or a novel elastic and locking IM pin (Sonoma CRx).[14,17] The use of an end cap may also avoid soft tissue irritation from the sharp end of a TEN that has not been cut adequately.

The present study has several limitations. First, the design of the study combined data from a RCT with data from a retrospective cohort. Because no significant difference in complication rates was observed between patients who underwent IMF for an isolated DMCF between January 2005 and December 2010 and patients who were assigned to IMF as part of a multicenter randomized controlled trial, we believe it is reasonable to combine the data. Theoretically , the irritation rate in the retrospectively collected data could have been underreported, resulting in underestimation of the problem . Second, a reliable method to quantify irritation of implants is lacking. Although hard to objectify, we believe patient-based outcome parameters are the most relevant measurements in modern day practice. In addition, the relatively low rate of re-interventions needed to treat the irritation suggests the severity might be low or at least bearable in most patients. Third, only reduction and insertion of the pin were performed under fluoroscopic control. No standard radiographs were taken postoperatively to check the implant position at baseline. Lastly, radiographs were not all taken at the exact same angle. However, our standardized digital method of measuring clavicles on radiographs provided us with a useful and reproducible fracture location presented as a proportion of the whole clavicle as measured from medial end.

CONCLUSION

Implant-related irritation was frequently seen in comminuted and lateral diaphyseal fractures after intramedullary fixation. Multivariate logistic regression analysis showed these two factors to be statistically significant and independent predictors for development of implant related irritation. These findings were validated using a similar external population.

Therefore, we believe that intramedullary fixation might not be suitable for comminuted and/or more laterally dislocated midshaft clavicle fractures. Future studies are needed to determine whether other surgical techniques or implants would be more suitable for these specific types of fractures.

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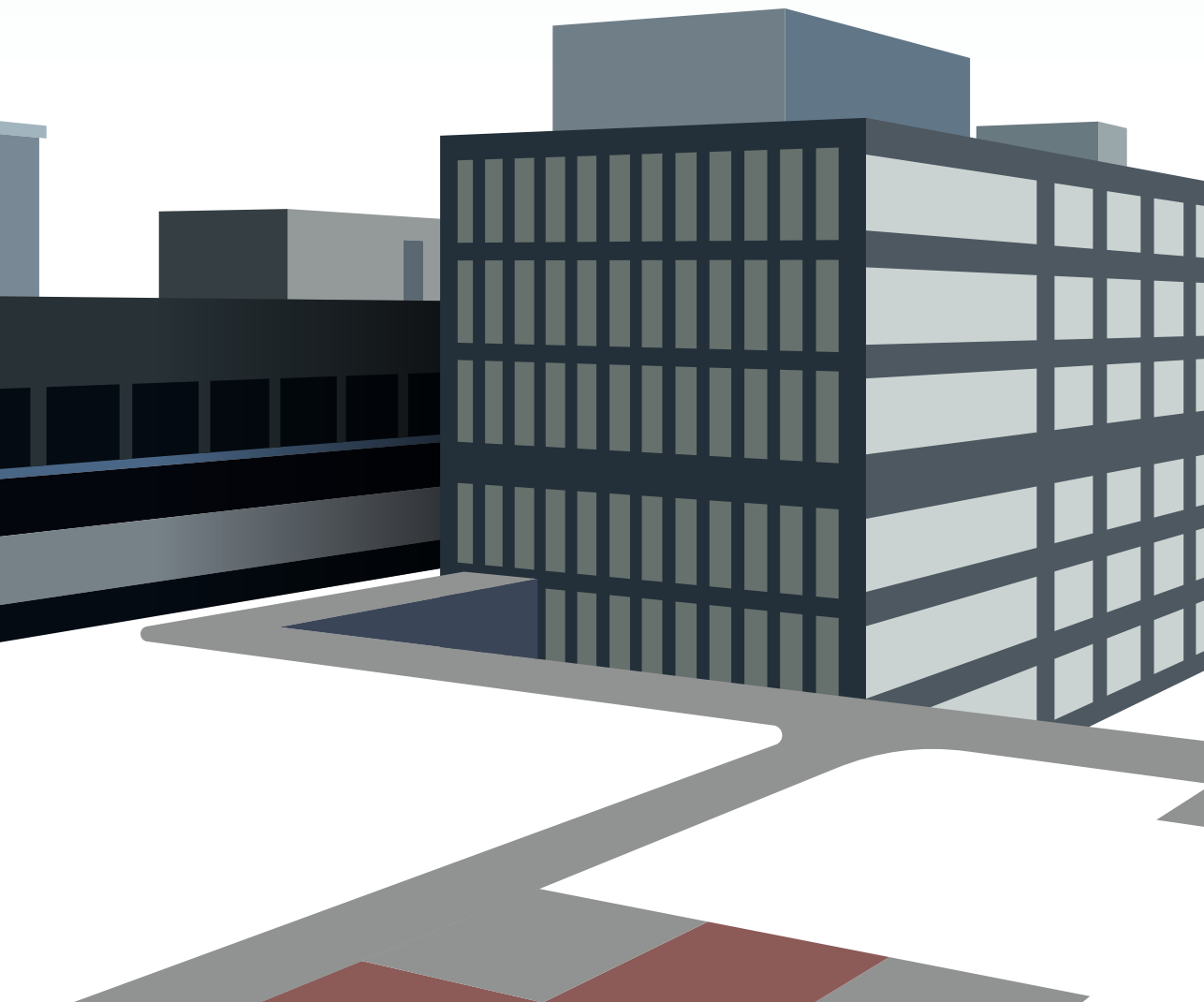

CHAPTER 4

End cap versus no end cap in intramedullary nailing for displaced midshaft clavicle fractures: influence on implant-related irritation

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ABSTRACT

Purpose: Implant-related irritation at the entry site is a known disadvantage of intramedullary nailing for clavicle fractures. The purpose of this study was to compare implant-related irritation rates of intramedullary nailing with or without an end cap for displaced midshaft clavicle fractures.

Methods: Two cohorts of patients treated with intramedullary nailing with or without an end cap were matched and compared. Primary outcome was patient-reported implant-related irritation. Secondary outcome parameters were complications.

Results: A total of 34 patients with an end cap were matched with 68 patients without an end cap. There was no difference in implant-related irritation (41% versus 53%, P=0.26). Significantly more minor revisions were observed in the group without an end cap (15% versus 0%, P = 0.03). For complications requiring major revision surgery, significantly more implant failures were observed in the end cap group (12% versus 2%, P=0.04). Regardless of their treatment, patients with complex fractures (AO/OTA B2 – B3) reported significantly more medial irritation compared to patients with simple fractures (AO/OTA B1)(P=0.02).

Conclusion: The use of an end cap after intramedullary nailing for displaced midshaft clavicle fractures did not result in lower patient-reported irritation rates. Although less minor revisions were observed, more major revisions were reported in the end cap group. Based on the results of this study, no end caps should be used after intramedullary nailing for displaced midshaft clavicle fractures. However, careful selection of simple fractures might be effective in reducing implant-related problems after intramedullary nailing.

INTRODUCTION

Intramedullary (IM) nailing has been widely accepted as a treatment option for displaced midshaft clavicle fractures (DMCF) [1-6]. IM nailing has shown similar results in terms of consolidation and functional outcome after 6 months compared to plate fixation [3,7-10]. Possible advantages of IM nailing over plate fixation are a relatively small incision, less soft tissue dissection and load sharing fixation with relative stability that encourages copious callus formation [11]. One of the previously reported disadvantages is implant-related irritation at the entry site due to the protruding end of the titanium nail [1,3,8,9,11,12]. In the literature, implant-related irritation and medial protrusion has been reported in 5-54% of the cases leading to up to a 20% re-intervention rate in order to shorten the protruding end of the nail [5,8,10,12,13]. A possible solution to this problem might be the application of an end cap over the medial external portion of the titanium nail [1,8,13](Figure 1). The end cap might prevent irritation and medial migration of the nail.

The aim of this study was to compare implant-related irritation rates of IM nailing with or without application of an end cap for DMCF. Our hypothesis was that application of an end cap inserted over the medial end of a titanium nail would reduce development of patient reported implant-related irritation.

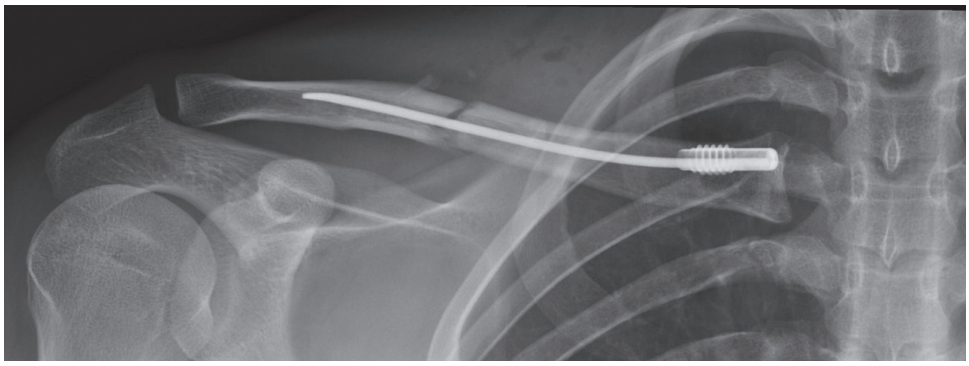

FIGURE 1. Intramedullary nail with end cap covering the medial end of the nail.

METHODS

Study design

A retrospective cohort study of the surgical databases of a level 1 and level 2 trauma center was performed. Data from the database of the Kantonsspital Graubünden (KSGR) Chur, Switzerland, were matched and compared with data from the Diakonessen hospital Utrecht, The Netherlands. Study approval was obtained from the institutional review boards of both hospitals.

All adult patients (≥16 years) with a unilateral DMCF who were treated with IM nailing were included in this study. Displacement was defined as at least one shaft width difference in height between the fracture parts, regardless of fracture shortening. Exclusion criteria were open fracture, pathologic fracture, pre-existing morbidity of the arm, shoulder or hand, previous clavicle fracture nonunion, neurovascular injury, or inability to attend further follow-up.

Patients from the KSGR who underwent IM nailing for an isolated DMCF between 2007 and 2014 were eligible for inclusion. In the Diakonessen hospital, all patients who underwent IM nailing for an isolated DMCF between January 2005 and December 2010 were eligible for inclusion. Patients who were assigned to IM nailing as part of a multicenter randomized controlled trial were also included. This previously published study compared plate fixation with IM nailing in patients with a DMCF and included patients from January 2011 until August 2012 [10]. In both hospitals, treatment of DMCF with IM nailing was based on either surgeon or patient preference. In the trial, the choice for IM nailing was based on randomization. End cap use after IM nailing in the KSGR was standard treatment. In the Diakonessen hospital, no end caps were used.

Data collection

The collected demographic data were patient age, gender, fracture side, fracture classification and trauma mechanism. Fractures were classified according to the AO/OTA classification for clavicular fractures [14]. Fractures were divided into two groups: simple fractures (AO/OTA B1) or complex fractures (AO/OTA B2 – B3) [14]. The trauma mechanism was divided into sports-related injury, traffic accident, fall from stance/height/other and unknown.

Primary outcome

The primary outcome parameter was patient-reported implant-related irritation at the entry site due to a palpable implant during the follow-up period. The topic of implant-related irritation was discussed at each outpatient visit.

Secondary outcomes

Secondary outcome parameters were complications, including implant failure, infection (superficial or deep), nonunion, malunion, minor revision, revision surgery and refracture after implant removal. The definition of implant failure was implant bending or breakage and migration not bridging the fracture anymore. Superficial infection was defined as redness, swelling and/or purulent discharge from the wound that could be treated with antibiotics. If surgical drainage was required, it was considered a deep infection. An unsuccessfully healed clavicle by radiograph 6 months after surgery with clinical evidence of pain was considered a non-union. Malunion was defined as fracture union in an incorrect anatomical position on a radiograph resulting in pain and decreased shoulder function. Interventions needed to treat these complications were also noted. The definition of a minor revision was partial removal of the protruding end of the implant under local anaesthesia. The indication for minor revision was severe patient reported irritation in combination with skin compromise or threatened skin. Revision surgery, in which IM nailing was revised with plate fixation, was considered a major revision. Re-interventions performed before routine implant removal was indicated were considered complications of treatment.

Operative procedure IM nailing

The operations were performed or supervised by trauma surgeons who had extensive experience (> 20 procedures) with the surgical technique. If possible, a closed fracture reduction using sharp reduction forceps was performed prior to implant placement. A small incision at the medial end of the clavicle was made, the anterior cortex was opened with a pointed reamer and the TEN (Titanium Elastic Nail, DePuy Synthes) was inserted. If closed reduction was not successful, a minimal incision at the fracture site was used to perform open reduction. The nail was inserted as far as possible in the lateral part of the clavicle without penetrating the lateral cortex. The diameter of the TEN ranged from 2 to 3.5 mm, depending on the width of the bone. If closed reduction failed, an additional small incision was made over the fracture site for open reduction. Any distraction over the fracture was relieved by lateral manual compression to the shoulder. After satisfactory fluoroscopic control, the nail was cut at the introduction

point approximately 5mm outside of the cortex. If an end cap was used, the 2.5 cm green end cap was inserted over the external portion of the nail and threaded into the cortical bone. Fascia and skin were then closed in layers.

Postoperative rehabilitation

Postoperatively patients were given a sling but encouraged to start immediately with active, pain-dependent mobilization and to discard the sling as soon as pain permitted. Heavy weight-bearing was permitted after fracture-healing was seen on the radiographs.

Implant Removal and Follow-up

The standard clinical protocols of both hospitals dictate removal of the TEN 3 to 6 months postoperatively in all patients treated with IM nailing for DMCF, or after adequate fracture healing in case of a delayed union. Patients were followed until the implant was removed.

Statistical analysis

Data were presented as mean ± standard deviation (SD) for continuous variables or as absolute numbers (percentage) for categorical variables. Continuous variables were compared using the Student t test, and categorical data were compared using Pearson's Chi-square test or Fisher's exact test for increased accuracy in small proportion analysis. A matched design using propensity score matching with nearest neighbour match correcting for age, gender and presence of comminution, was used. The nearest neighbour match algorithm was used to obtain a 1:2 case to control ratio.

Complication rates between the two groups were compared. The analyses were performed with SPSS, version 20.0 (IBM Corp., Armonk, NY) for Windows. Significance of statistical differences was attributed to $P < 0.05$.

RESULTS

Fifty-eight patients were operated on in Chur using a TEN with an End cap. Eighteen patients were excluded due to limited follow-up and one due to pre-operative existence of plexus brachialis neuropraxia. Thirty-nine patients (67%) were eligible for inclusion. Eighty-three patients were operated on in Utrecht using a TEN without an end cap during the inclusion period. Two patients were excluded because of limited follow-up, leaving 81 patients eligible for inclusion. Using the nearest neighbor match algorithm

with a 1:2 case to control ratio, 34 patients with an end cap were matched to 68 patients without an end cap (Table 1). The mean follow-up time was 6.8 months in Chur and 6.5 months in Utrecht (P=0.52).

In 88% of the end cap group and 94% of the no end cap group, the implants were electively removed. One patient without an end cap was asymptomatic and did not want the TEN removed.

No significant difference was seen in implant-related irritation between the end cap and no end cap group (41% versus 53%, P=0.26) (Table 2). Regardless of their treatment, patients with a complex fracture (AO/OTA B2 – B3) reported significantly more medial irritation compared to patients with a simple fracture (AO/OTA B1) (P=0.02).

TABLE 1. Baseline characteristics

	No (%) End cap (N = 34)	**No (%) No end cap (N = 68)**	**P-value**
Age, mean ± SD	27 ± 11	31 ± 13	0.13
Gender, N (%)			0.63
Male	24 (71%)	51 (75%)	
Female	10 (29%)	17 (25%)	
Fracture side, N (%)			0.89
Right	15 (44%)	29 (43%)	
Left	19 (56%)	39 (57%)	
Trauma mechanism, N (%)			0.02
Traffic accident	19 (26%)	22 (32%)	
Sports-related injury	23 (68%)	26 (38%)	
Fall from stance/height/other	2 (6%)	15 (22%)	
Unknown	0	5 (8%)	
Fracture classification‡			0.12
"Simple" (AO/OTA type B1)	22 (65%)	33 (49%)	
"Complex" (AO/OTA type B2-B3)	12 (35%)	35 (51%)	

‡ Fractures classified according to the AO/OTA classification (14).

Although there was no difference between the groups in terms of patient-reported implant-related irritation, the medial irritation in the group without an end cap resulted in significantly more minor interventions. Ten (15%) patients without an end cap underwent a minor revision (P=0.03) (Table 2). For complications requiring major revision surgery, significantly more implant failures were observed in the end cap group

(12% versus 2%, P=0.04) (Table 2). Causes for implant failure are described in Table 3. None of the patients with implant failure in the end cap group suffered a significant second trauma.

TABLE 2. Postoperative complications.

Complication	Treatment	No (%) End cap (N = 34)	No (%) No end cap (N = 68)	P-value
Medial implant-related irritation		14 (41%)	36 (53%)	0.26*
	Conservative	14 (41%)	24 (35%)	0.56*
	Minor revision	0	10 (15%)	0.03°
	Implant removal	0	2 (3%)	0.55°
Lateral implant-related irritation		2 (6%)	1 (2%)	0.26°
	Conservative	2 (6%)	0	0.11°
	Minor revision	0	1 (2%)	1.00°
Implant failure	Major revision	4 (12%)	1 (2%)	0.04°

* Chi square, °Fischer's exact test, P-value of <0.05 was considered statistically significant.

TABLE 3. Implant failure

Patient	Fracture type‡	2nd trauma	Follow-up	Failure cause	Revision
Patient 1§	B1.2	No, abduction	12 weeks	Nail bending during abduction	Plate fixation
Patient 2§	B1.1	No	1 week	Intra-operative lateral perforation. Post-operative lateral migration with dislocation of end cap	Plate fixation
Patient 3§	B1.3	No	12 weeks	Unnoticed broken TEN, discovered during outpatient visit. No union, minimal complaints	Plate fixation with spongiosa transplantation
Patient 4§	B2.1	Bumping into pedestrian	10 weeks	Nail bending after direct impact on the shoulder after collision with a pedestrian	New and thicker TEN
Patient 1†	B1.2	No	4 weeks	Intra-operative inadequate advancement of TEN into lateral fracture fragment	Plate fixation

§ End cap
† No end cap,
‡ Fractures classified according to the AO/OTA classification (14)

One superficial infection in the group without end cap and no deep infections were observed. In all patients, fracture consolidation was achieved; non- or malunions were not reported. There were no refractures after implant removal in either group.

DISCUSSION

Application of an end cap after IM nailing for DMCF did not result in lower patient reported irritation rates in this study. The use of an end cap resulted in lower minor revision rates. More major revisions, however, were reported in the end cap group. No end caps should be used after IM nailing of DMCF based on the results of this study. Reduction in implant-related problems after IM nailing might be achieved by careful selection of simple (AO/OTA B1) fractures.

Our primary hypothesis was that end caps would prevent irritation and therefore irritation was used as primary outcome parameter. If a patient reports irritation, it is a clinically relevant problem in our opinion. Clinical relevant secondary displacement is reflected in the number of small re-interventions due to medial migration and protrusion. These parameters were reported as secondary outcome parameter. Although less objective, patient reported irritation provides an overview of the total scope of the irritation problem whereas secondary displacement only describes a part of it. Despite the similar irritation rates between the two groups, our data showed significantly higher rates of minor interventions in the group without an end cap (P=0.03). As all minor revisions were due to secondary displacement of the TEN, we concluded that secondary displacement was prevented by the end cap. Thus, the benefit of an end cap might be prevention of a second intervention rather than prevention of irritation. In addition, the difference in this minor intervention rate suggests that the severity of irritation might be lower or at least bearable in patients with an end cap.

Implant-related irritation of the titanium elastic nails is a considerable problem [1,12]. Development of implant-related irritation might be caused by two different factors. First, after cutting the nail, the sharp end may irritate the subcutaneous tissue or cutaneous nerves. Second, medial migration and protrusion of the implant may cause irritation [1,7,8,10,12,15]. The application of an end cap could be a solution for both, as it covers the sharp end of the nail and prevents medial migration. We used green end caps in all cases. Green end caps have a longer thread compared to pink end caps providing more optimal fixation in the clavicle. The disadvantage of end caps in general is their bulky size which might lead to higher patient reported irritation rates.

Care should be taken interpreting the aforementioned benefits of an end cap. Like Frigg et al., we also observed other complications in this group [1]. Significantly more implant failures were observed in the end cap group. In fractures with a large fracture gap or comminution, which may shorten post-operatively, the presence of an end cap might prevent the fracture parts from gliding towards each other over the TEN. This might prevent fracture healing, as none of the patients with implant failure in the end cap group suffered a significant second trauma (Table 3). Additionally, fixation of the medial part of the nail could result in lateral protrusion or migration.

Previous studies showed comminuted fractures to be prone to shortening, resulting in (medial) migration of the nail [15,16]. As Smekal et al. reported previously, only simple, non-comminuted fractures should be treated with IM nailing [15]. These findings are similar to our data, as higher rates of patient-reported implant-related irritation in complex fractures (AO/OTA B1-B2) were reported compared to simple fractures (AO/OTA B1). In addition, none of the patients who required a minor revision under local anesthesia had a simple transverse fracture (AO/OTA B1.3). Therefore, careful fracture selection could be effective in reducing implant-related problems.

Several limitations need to be addressed. First, the retrospective character of this study has its obvious drawbacks. The irritation rate could have been underreported, resulting in underestimation of the problem. Second, the severity of irritation was not quantified in most cases. Mild irritation might not have been registered. Irritation of the end cap might have been of a different type compared to irritation caused by the end of a nail. No validated questionnaire was available to quantify the severity of implant-related irritation during the study period. Therefore we asked patients about irritation on each post-operative outpatient department visit. A recent paper of Hulsmans et al. proposed a schematic way to question patients about implant related irritation which would have been useful in this study [17]. However, the approach used in their study is also based on patient reported symptoms as we did in our study. Furthermore, implant failure and revision surgery are well-defined and reproducible endpoints.

Finally, sixteen patients could not have been included because of loss to follow-up in the end cap group. These patients were mostly visiting tourists and follow-up was not possible due to geographical reasons. We tried to overcome this problem by using the nearest neighbour match algorithm.

CONCLUSION

Results of this study indicate that the use of an end cap after intramedullary nailing for displaced midshaft clavicle fractures did not result in lower patient-reported irritation rates. Although the use of an end cap resulted in lower minor revision rates, more major revisions were reported in the end cap group. Based on the results of this study, no end caps should be used after intramedullary nailing for displaced midshaft clavicle fractures. However, careful selection of simple (AO/OTA B1) fractures might be effective in reducing implant-related problems after intramedullary nailing.

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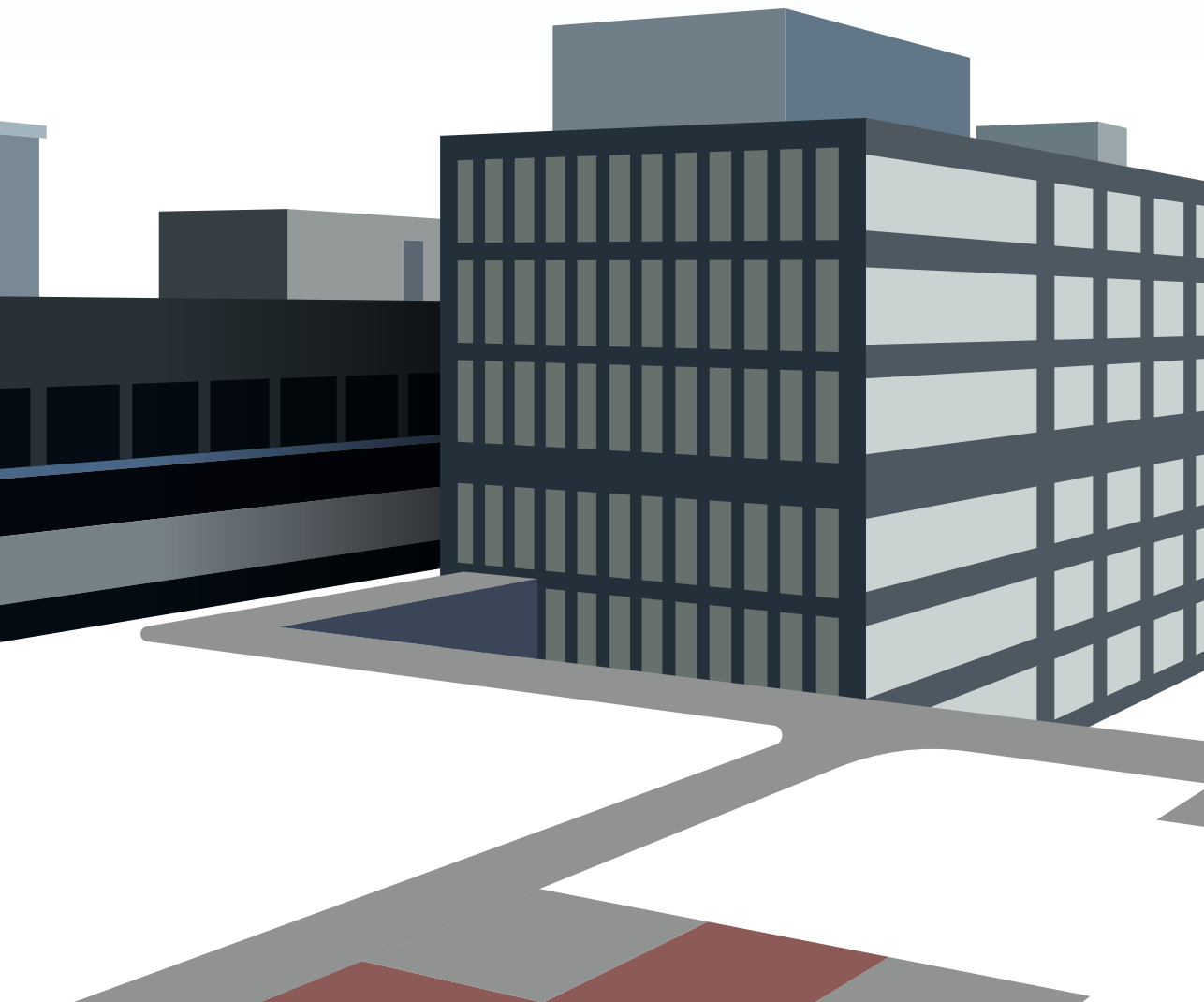

CHAPTER 5

Surgical treatment of Neer type II and type V lateral clavicular fractures: comparison of hook plate versus superior plate with lateral extension: a retrospective cohort study

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ABSTRACT

Purpose: Different fixation methods are used for treatment of unstable lateral clavicle fractures (LCF). Definitive consensus and guidelines for the surgical fixation of LCF have not been established. The aim of this study was to compare patient-reported functional outcome after open reduction and internal fixation (ORIF) with the clavicle hook plate (CHP) and the superior clavicle plate with lateral extension (SCPLE).

Methods: A dual-center retrospective cohort study was performed. All patients operatively treated for unstable Neer type II and type V LCF between 2011 and 2016, with the CHP (n=23) or SCPLE (n=53) were eligible for inclusion. The primary outcome was the QuickDASH score. Secondary outcomes were the Numerical Rating Scale (NRS) pain score, complications, and implant removal.

Results: 67 patients (88%) were available for final follow-up. There was a significant difference in bicortical lateral fragment size, 15 mm (±4, range 6–21) in the CPH group, compared to 20 mm (±8, range 8–43) in the SCPLE group (p= <0.001). There was no significant difference in median QuickDASH score (CHP; 0.00 [IQR 0.0–0.0], SCPLE; 0.00 [IQR 0.0–4.5]; p= 0.073) or other functional outcome scores (NRS at rest; p = 0.373, NRS during activity; p = 0.559). There was no significant difference in median QuickDASH score or other functional outcome scores between Neer type II and type V fractures. There was no significant difference in complication rate, CHP 11% and SCPLE 8% (relative risk, 1.26; [95% CI, 0.25–6.33; p= 0.777]). The implant removal rate was 100% in the CHP group, compared to 42% in the SCPLE group (relative risk, 2.40; [95% CI, 1.72–3.35; p= <0.001]).

Conclusion: Both the CHP and SCPLE are effective fixation methods for the treatment of unstable LCF, resulting in excellent patient-reported functional outcome and similar complication rates. SCPLE fixation is an effective fixation method for the treatment of both Neer type II and type V LCF. The SCPLE has a lower implant removal rate. Therefore, if technically feasible, we recommend SCPLE fixation for the treatment of unstable LCF.

INTRODUCTION

The fracture of the clavicle is frequently encountered in the emergency department, accounting for 2.6%–4% of fractures in the adult population. Furthermore, clavicle fractures represent 35%–44% of fractures in the shoulder region. Although the majority involve the midshaft, lateral fractures account for 10%–30%.[1–6]

Lateral clavicle fractures (LCF) are classified according to Neer based on their relation to the coracoclavicular ligaments.[6, 7] Neer type I, III and IV are considered to be stable fractures and are generally treated conservatively. The unstable Neer type II and V fractures account for approximately 10%–52% of LCF. Surgical management is recommended for these unstable LCF, as non-operative treatment results in a 22%–50% non-union rate.[1–6, 8, 9]

Neer type II fractures are unstable due to the detachment of the coracoclavicular ligaments from the medial fragment. Neer type V fractures have a comminuted character, with only an inferior fragment remaining attached to the coracoclavicular ligament.[4, 6, 7]

Fixation of LCF proves to be a challenge as it can be difficult to get a firm hold on small lateral fragments. In addition, opposing forces contribute to considerable displacement of the fracture ends. Therefore, LCF can usually only be stabilized by rigid fixation methods.[4, 9] Different surgical fixation methods are available for the treatment of unstable LCF. However, at present, no consensus has been reached regarding the optimal fixation method.

The clavicle hook plate (CHP) is fixated with a small hook under the acromion posterior to the acromioclavicular joint. Complications related to the CHP such as acromial osteolysis, acromion fractures, rotator cuff tears and sub-acromial impingement have been reported.[4, 5, 10, 11]

The superior clavicle plate with lateral extension (SCPLE) is a more recently developed locking compression plate. The SCPLE has multiple locking screws on the lateral end, divergently configured to maximize screw purchase on LCF fragments. The SCPLE does not interfere with the acromioclavicular joint and has a relatively low-profile.[12–17] Previous case series have shown the SCPLE to be an effective fixation method for the treatment of unstable Neer type II fractures.[12–17] However, the results after SCPLE fixation of Neer type V fractures have not yet been studied.

Currently, both the CHP and SCPLE are being used for the treatment of LCF. However, definitive consensus and guidelines for the surgical fixation of LCF have not yet been established. The aim of this study was to retrospectively evaluate patients treated with CHP and SCPLE fixation by comparing patient-reported functional outcome, complication-, and implant removal rates. Our hypothesis was that the SCPLE would result in better functional outcome and would lead to a reduction of complication- and implant removal rates.

MATERIALS AND METHODS

Study design

A retrospective cohort study was performed using data from two level II trauma centers. All patients with an unstable LCF who were treated operatively between January 2011 and June 2016 were eligible for inclusion. Inclusion criteria were: (1) acute LCF, (2) age 18 years or older, (3) Neer type II or type V fracture, (4) fixation with CHP or SCPLE, (5) fixation within two weeks of injury, (6) minimum of one-year follow-up. Exclusion criteria were: (1) history of prior shoulder injuries or (2) neurovascular disorders of the affected shoulder. Data collection was performed by reviewing electronic medical records, operative reports, radiology reports and telephone interviews by an independent research fellow. Electronic medical records were reviewed to collect baseline characteristics regarding affected shoulder, age, gender, trauma date, trauma mechanism, time from injury to surgery, fixation method, previous shoulder injuries and lateral fragment size. Lateral fragment size was measured in millimeters (mm) on the anterior–posterior view radiograph. Overall lateral fragment size was defined as the total length of the largest lateral fragment. The largest intact bicortical fragment, which would allow for adequate screw fixation, was considered as the bicortical lateral fragment length. Informed consent was obtained from all subjects and approval was granted by the Institutional Review Board.

Surgical procedure

Patients were treated by means of open reduction and internal fixation (ORIF) using a CHP (3.5 mm LCP; Depuy Synthes GmbH, Oberdorf, Switzerland) or SCPLE (3.5/2.7 mm LCP; Depuy Synthes GmbH, Oberdorf, Switzerland). Implant selection was based on the surgeon's preference. CHP and SCPLE fixation were performed by several surgeons in both trauma centers. Operations were performed under general anesthesia with the patient placed in a beach chair position. An incision was made using a standard superior approach. The fracture site was exposed preserving as much periosteum as possible.

Reduction was performed under direct visualization and fragments were temporarily fixated using K-wires or reduction forceps. Fracture reduction, implant position, and screw placement were checked under fluoroscopic guidance. Coracoclavicular ligament repair was not routinely performed. Finally, the fascia and skin were closed in layers.

Clavicle hook plate

In cases of CHP fixation, a small incision was made in the posterior capsule of the acromioclavicular joint to allow sub-acromial hook placement. Trial plates were used to determine correct length and depth. Definitive CHP fixation was completed with the insertion of 3.5mm angular stable or conventional screws (Fig. 1).

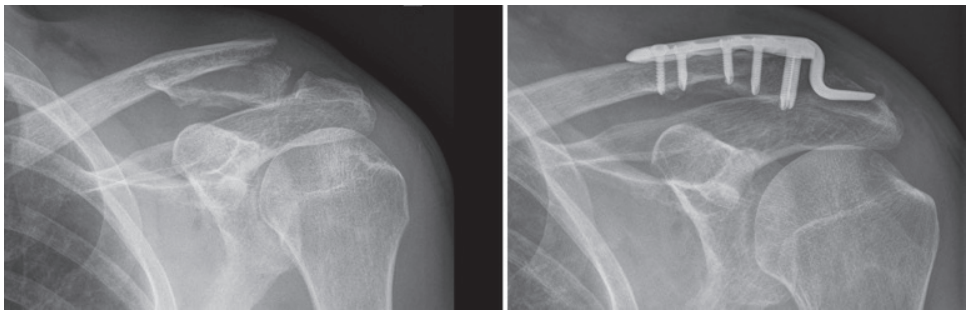

FIGURE 1. Preoperative radiograph of lateral clavicular fracture and postoperative radiograph after clavicle hook plate (CHP) fixation.

Superior clavicle plate with lateral extension

In cases of SCPLE fixation, there was no involvement of the acromioclavicular joint. A plate with an appropriate length was chosen to allow adequate fixation with 3.5mm conventional or angular stable screws in the medial fragment and smaller 2.7mm angular stable screws in the lateral end (Fig. 2).

Postoperative management

Both groups received the same postoperative management. Radiographs were taken one day postoperatively. Patients were temporarily immobilized in a sling until the pain subsided; early mobilization and active range of motion exercises were allowed when tolerated. Weight-bearing activities and resisted exercises were not permitted until approval from the treating surgeon. Follow-up visits were scheduled at two, four and

12 weeks postoperatively. Additional outpatient visits were scheduled depending on fracture consolidation. Removal of the SCPLE was not routinely performed, as opposed to the CHP where removal was recommended to all patients.

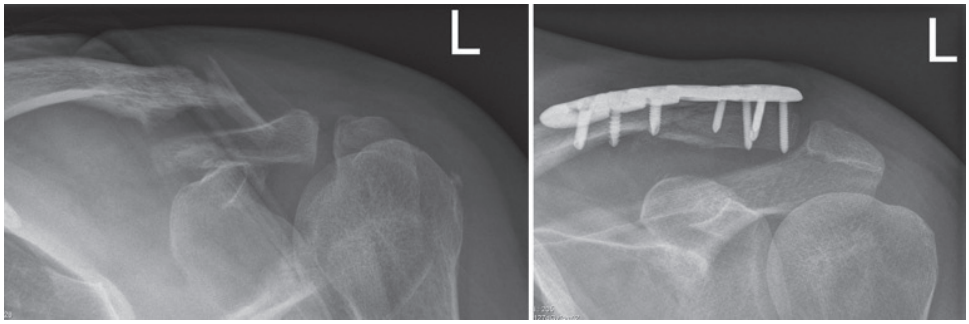

FIGURE 2. Preoperative radiograph of lateral clavicular fracture and postoperative radiograph after superior clavicle plate with lateral extension (SCPLE) fixation.

Primary outcome

Functional outcome was assessed at least 12 months following ORIF, using the Dutch language version of the QuickDASH score. The QuickDASH is a validated and shortened version of the Disabilities of the Arm, Shoulder and Hand questionnaire (DASH). The QuickDASH is a patient-reported outcome instrument developed to measure upper extremity disability and symptoms, resulting in a score ranging from 0 (no disability) to 100 (most severe disability).[18, 19]

Secondary outcome

Secondary outcomes were the Numerical Rating Scale (NRS) pain score at rest and during activity, complications, revision surgery and implant removal. The NRS is a reliable and commonly used 11 point scale to measure pain intensity, ranging from 0 (no pain) to 10 (worst imaginable pain).[20] Complications included infection, non-union, mal-union, implant failure and implant removal-related complications. Infections were subdivided in superficial-skin or deep-wound infection. Superficial infection was defined as redness, swelling or purulent discharge from the wound that was treated with antibiotics alone. If surgical irrigation and debridement was required, it was considered a deep infection. Non-union was defined as absence of fracture consolidation six months after surgery. Mal-union was defined as a symptomatic deformity of the clavicle. Implant failure was defined as implant displacement, implant breakage, or breakage of screws. Revision

surgery was defined as the need for subsequent surgery other than implant removal. Infection and re-fracture following implant removal were considered implant removal-related complications. Implant-related irritation and indication for implant removal were analyzed using a series of questions developed by Hulsmans et al.[21] Responses to these questions allowed categorization of implant removal into (1) routinely or on patient's request without irritation or (2) patient's request due to irritation. Patients with the implant still in situ received a different series of questions, leading to categorization of why implant was not removed; (1) not experiencing irritation, (2) experiencing irritation but removal not necessary, (3) experiencing irritation but no request for removal due to fear of re-operation or (4) experiencing irritation, considering removal.

Statistical analysis

Descriptive results are presented as mean values with standard deviations and range (±SD, range), median values with interquartile range (IQR) or absolute numbers and percentages (%). Continuous variables were evaluated using an independent sample t-test or Mann–Whitney U test. Categorical variables were compared using the Pearson's chi-squared test. The Fisher's Exact test was used in case of small count sizes. Mean differences and relative risks (RR) were calculated with 95% confidence intervals (CI's). The significance level was defined as a p value <0.05. All statistical analyses were performed using IBM SPSS Statistics Version 24 for Windows (IBM Corp, Armonk, NY).

RESULTS

Study population

A flowchart of the patient cohort is shown in Fig. 3. In total, 76 patients met the inclusion criteria. However, eight patients could not be contacted, and one patient refused participation. This resulted in the inclusion of 67 patients (88%) for analysis. The baseline characteristics are shown in Table 1. The CHP group included 19 patients (28%), compared to 48 patients (72%) in the SCPLE group. The most frequent fracture pattern was Neer type II found in 43 patients (64%). The overall lateral fragment size was 39 mm (±12, range 14–83). There was a significant difference in bicortical lateral fragment size, 15 mm (±4, range 6–21) in the CPH group, compared to 20 mm (±8, range 8–43) in the SCPLE group (p= <0.001). The mean time from injury to surgery was 6.9 days (±3.6, range 0–14). The mean follow-up was 37.5 months (±17.9, range 12–76).

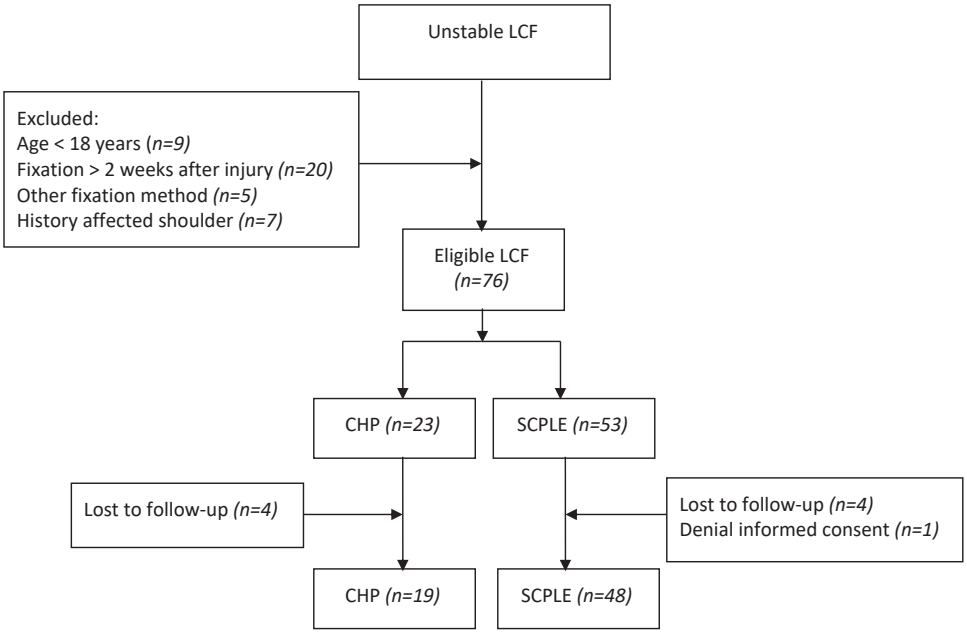

FIGURE 3. Flowchart representing patient selection for analysis of CHP versus SCPLE for unstable LCF.

Functional outcome

There was no significant difference in functional outcome, as shown in Table 2. The median QuickDASH score in the CHP group was 0.00 (IQR;0.0–0.0), as opposed to 0.00 (IQR;0.0–4.5) in the SCPLE group (p= 0.073). There were 15 patients (79%) with a QuickDASH score of 0 in the CHP group (range 0-21), compared to 25 patients (52%) in the SCPLE group (range 0-23). The median NRS pain score at rest was 0.00 (IQR;0.0–0.0) in the CHP group and 0.00 (IQR;0.0–0.0) in the SCPLE group (p= 0.373). There were 16 patients (84%) with a NRS pain score at rest of 0 in the CHP group (range 0-6), compared to 44 patients (94%) in the SCPLE group (range 0-3). In the CHP group the median NRS pain score during activity was 0.00 (IQR;0.0–1.0), compared to 0.00 (IQR;0.0–2.0) in the SCPLE group (p= 0.559). There were 14 patients (74%) with a NRS pain score during activity of 0 in the CHP group (range 0-8), compared to 30 patients (63%) in the SCPLE group (range 0-7).

TABLE 1. Baseline characteristics

	Overall n (%)*	**CHP n (%)***	**SCPLE n (%)***	**95% CI of the difference**	**p-value**
Patients	67	19	48		
Age [mean ± SD]	43 (14)	42 (17)	43 (12)	-8,29-6,54	0,814
Gender					
Male	54 (81)	13 (68)	41 (85)		0,169
Female	13 (19)	6 (32)	7 (15)		
Side injury					
Left	39 (58)	8 (42)	31 (65)		0,108
Right	28 (42)	11 (58)	17 (35)		
Affected side dominant side					
Yes	27 (40)	10 (53)	17 (35)		0,270
No	40 (60)	9 (47)	31 (65)		
Neer classification					
Type II	43 (64)	13 (68)	30 (63)		0,780
Type V	24 (36)	6 (32)	18 (38)		
Overall lateral fragment (mm) [mean ± SD]	39 (12)	37 (12)	40 (12)	-9,39-3,55	0,371
Bicortical lateral fragment (mm) [mean ± SD]	19 (7)	15 (4)	20 (8)	-8,40--2,64	**<0.001**
Time injury to surgery (days) [mean ± SD]	6,9 (3,6)	7,5 (3,5)	6,7 (3,6)	-1,15-2,72	0,419
Follow-up (months) [mean ± SD]	37,5 (17,9)	31,3 (16,3)	40,0 (18,0)	-18,25-0,77	0,071

* Percentages may not add up to 100 due to rounding. Bold values indicate statistically significant results (e.g., $p < 0.05$).

TABLE 2 Functional outcome and implant-related complications

	CHP (n=19) n (%)*	SCPLE (n=48) n (%)*	Relative risk (95% CI)	p-value
QuickDASH median [IQR]	0.00 (0.0-0.0)	0,00 (0.0-4.5)		0,073
QuickDASH distribution [range]	0-21	0-23		
0	15 (79)	25 (52)		
0-10	3 (16)	19 (40)		
10-20	0	3 (6)		
20-25	1 (5)	1 (2)		
NRS pain at rest [median, IQR]	0.00 (0.0-0.0)	0.00 (0.0-0.0)		0.373
NRS pain at rest distribution [range]	0-6	0-3		
0	16 (84)	44 (92)		
0-3	2 (11)	3 (6)		
3-6	1 (5)	1 (2)		
NRS pain during activity [median, IQR]	0.00 (0.0-1.0)	0.00 (0.0-2.0)		0,559
NRS pain during activity distribution [range]	0-8	0-7		
0	14 (74)	30 (63)		
0-3	1 (5)	7 (15)		
3-6	2 (11)	8 (17)		
6-8	2 (11)	3 (6)		
Complications	2 (11)	4 (8)	1.26 (0.25-6.33)	0,777
Complication classification				0,929
Implant failure	1 (5)	3 (6)		
Non-union	1 (5)	1 (2)		
Revision surgery	1 (5)	2 (5)	1.26 (0.12-13.13)	1.000

* Percentages may not add up to 100 due to rounding. QuickDASH score: 0=no disability to 100=most severe disability. NRS pain score: 0=no pain to 10=worst imaginable pain. Bold values indicate statistically significant results (e.g., p <0.05).

Functional outcome according to Neer type

In both treatment groups, there was no significant difference in median QuickDASH score or other functional outcome scores between the Neer type II and type V fractures (Table 3). The median QuickDASH score in the Neer type II group following CHP fixation was 0.00 (IQR;0.0–2.3), as opposed to 0.00 (IQR;0.0–0.6) in the Neer type V group (p= 0.623). In the SCPLE group, the median QuickDASH score in the Neer type II group was 0.00 (IQR;0.0–5.1), as opposed to 2.30 (IQR;0.0–4.5) in the Neer type V group (p= 0.764).

TABLE 3. Functional outcome according to Neer classification

Neer	Type II	Type V	p-value
CHP n (%)*	13 (68)	6 (32)	
QuickDASH median [IQR]	0.00 (0.0-2.3)	0,00 (0.0-0.6)	0.623
NRS pain score at rest [median, IQR]	0.00 (0.0-0.0)	0.00 (0.0-0.0)	1.000
NRS pain score during activity [median, IQR]	0.00 (0.0-2.0)	0.00 (0.0-2.0)	0.734
SCPLE n (%)*	30 (63)	18 (38)	
QuickDASH median [IQR]	0.00 (0.0-5.1)	2,30 (0.0-4.5)	0.764
NRS pain score at rest [median, IQR]	0.00 (0.0-0.0)	0.00 (0.0-0.0)	0.609
NRS pain score during activity [median, IQR]	0.00 (0.0-3.3)	0.00 (0.0-1.0)	0,100

* Percentages may not add up to 100 due to rounding. QuickDASH score: 0=no disability to 100=most severe disability. NRS pain score: 0=no pain to 10=worst imaginable pain. Bold values indicate statistically significant results (e.g., p <0.05).

Implant removal

Implant removal rates and indications are presented in Table 4. CHP fixation was associated with a significant higher removal rate. CHP removal was, according to protocol, performed in all 19 patients (100%), compared to 20 patients (42%) in the SCPLE group (relative risk, 2.40; 95% CI, 1.72–3.35; p= <0.001). The mean time to removal was 4.3 months (±2.2, range 2–10) and 13.6 months (±11.5, range 5–50) in the CHP and SCPLE groups, respectively (mean difference, -9.287; 95% CI, -14.757–3.817; p= 0.002). In the CHP group, 3 patients (16%) reported removal without irritation and 16 patients (84%) reported removal due to irritation. There were no cases of implant removal-related complications. In the SCPLE group, 28 patients (58%) did not have the implant removed and 12 patients (43%) reported not to experience irritation.

Complications

Complications were reported in two patients (11%) in the CHP group, compared to four patients (8%) in the SCPLE group (relative risk, 1.26; 95% CI, 0.25–6.33; p= 0.777) (Table 2). Complications in the CHP group consisted of one case of implant failure due to implant displacement and one case of non-union. Complications in the SCPLE group included three cases of implant failure and one case of non-union. The implant failures in SCPLE group consisted of two implant displacements and one case of screw breakage. No cases of infection or mal-union were observed. In total, there were three patients that needed revision surgery. In the CHP group one patient received a lateral clavicle resection due to non-union. Two revision surgeries were performed in the SCPLE group, one due to severe implant displacement and one case of non-union. The SCPLE implant displacement was treated by repeat SCPLE fixation. The non-union was treated with temporary K-wires fixation for 9.5 months.

TABLE 4. Implant removal rate and indication

	CHP (n=19) n (%)	SCPLE (n=48) n (%)	Mean difference (95% CI)	Relative risk (95% CI)	p-value
Implant removal	19 (100)	20 (42)		2.40 (1.72-3.35)	**<0.001**
Reason implant removed					0.695
Routinely or patient's request, without irritation	3 (16)	5 (25)		0.63 (0.17-2.29)	
Due to irritation	16 (84)	15 (75)		1.23 (0.81-1.55)	
Time to implant removal (months) [mean ± SD]	4.3 (2.2)	13.6 (11.5)	-9.287 (-14.757-3.817)		**0,002**
Status implant not removed					NP
Not experiencing irritation	0	12 (43)			
Irritation, but implant removal not necessary	0	6 (21)			
Irritation, no request removal due to fear re-operation	0	5 (18)			
Irritation, considering removal	0	5 (18)			

Bold values indicate statistically significant results (e.g., p <0.05). NP statistical analyses Not Possible because all CHP implants were removed.

DISCUSSION

There was no significant difference in patient-reported functional outcome or complication rate between CHP and SCPLE fixation. However, the CHP was used more often on fractures with a small lateral bicortical fragment. There was no significant difference in patient-reported functional outcome between Neer type II and type V LCF fractures. Furthermore, there was a significant higher implant removal rate in the CHP group. In the SCPLE group, 57% of patients with the implant still in situ reported varying degrees of implant-related irritation.

Both the SCPLE and CHP result in excellent functional outcome. These findings are in accordance with previous comparative studies. Zhang et al.[22] compared functional outcome of 36 patients with the SCPLE implant to 30 patients with the CHP using the Constant-Murley score and demonstrated no significant difference between groups. Erdle et al.[23] compared the results of 19 patients with CHP and 13 patients with SCPLE fixation, they reported no significant difference between the groups when using the Constant score, the Oxford shoulder score, and the subjective shoulder value.

In the current study, the bicortical lateral fragment size was significantly smaller in the CHP group. Erdle et al.[23] reported no significant difference in lateral fragment size, however, they did not report whether the intact lateral fragment was bicortical. In the current study, the largest intact bicortical lateral fragment size which would allow for adequate screw fixation was measured. Our results indicate implant selection was influenced by the bicortical lateral fragment size. We recommend further research to focus on lateral fragment size, to determine whether lateral fragment size negatively affects functional outcome and complication rates with the use of different implants.

Previous case series have shown the SCPLE to be an effective fixation method for the treatment of unstable Neer type II fractures.[12–17] Zhang et al.[22] treated fractures with a lateral fragment size larger than two cm with the SCPLE, comminuted fractures close to the acromioclavicular joint were treated with the CHP with additional ligament repair. The comparative study by Erdle et al.[23] only included Neer type IIb fractures. To our knowledge this is the first study to evaluate the use of SCPLE fixation for the treatment of Neer type V fractures. In the current study, treatment with SCPLE fixation resulted in good functional outcome in both 30 patients (63%) with Neer type II and 18 patients (38%) with Neer type V fractures. These findings indicate SCPLE fixation is also an acceptable treatment option for acute Neer type V fractures, despite their comminuted character.

There was no significant difference in complication rate between CHP and SCPLE fixation, which is in contrast with previous comparative studies. Zhang et al.[22] found a significantly higher complication rate, 23.3% in the CHP group, compared to 5.6% in the SCPLE group (p=0.04). However, Zhang et al.[22] included symptomatic hardware as a complication, they reported three cases (10%) of symptomatic hardware in the CHP group and none in the SCPLE group. Erdle et al.[23] also reported a significantly higher overall prevalence of complications in the CHP cohort (89%) compared to the SCPLE cohort (38%) (p=0.014). Erdle et al.[23] included radiographical proof of persistent acromial osteolysis and posttraumatic acromioclavicular joint arthrosis as complications.

The previous comparative studies included complications such as acromial osteolysis, posttraumatic acromioclavicular joint arthrosis, and sub-acromial impingement syndrome. These complications could be regarded as CHP implant-specific. The CHP is fixated with a small hook under the acromion, posterior to the acromioclavicular joint which acts as a lever and maintains fracture reduction. However, this mechanism not only limits abduction of the arm, it may also affect the acromion and induce discomfort. The SCPLE does not interfere with the acromioclavicular joint, which results in the absence of acromial and impingement complications. Furthermore, there are several reports that indicated that these CHP implant-specific complications can resolve after removal.[11, 24] Renger et al.[11] evaluated the use of the CHP in 44 patients, 30 patients (68%) reported implant related discomfort. Renger et al.[11] found all implant-related complaints and osteolytic defects to disappear after implant removal.

Implant-related irritation and implant removal were analyzed using the series of questions developed by Hulsmans et al.[21] In the current study all CHP implants were removed after a mean of 4.3 months, in line with previous studies recommending CHP removal after fracture consolidation.[11] The comparative study by Zhang et al.[22] reported all CHP's were removed, compared to 12 SCPLE's (33%). Erdle et al.[23] reported CHP removal was recommended and all CHP implants were removed after a mean period of 4.7 months. In the Erdle et al.[23] study, 77% of SCPLE implants were removed after a mean period of 12.5 months due to local irritation or on patient's explicit request. In the current study, after a minimum of 12 months following ORIF, 42% of SCPLE implants were removed. Moreover, 43% of the patients with the SCPLE still in situ reported not to experience any irritation.

This study has some limitations. First, the study is limited by the retrospective nature. This study did not include prospective collection of functional and radiological measures during different follow-up times, which would increase the understanding of the impact implants have prior to implant removal. Second, fixation method was

based on surgeon's preference, which could cause bias through selection-by-indication. Therefore, different measurements were performed to determine whether lateral fragment size influenced implant selection. Finally, our study is limited by the small number of included patients in the treatment groups. However, these number are in accordance with previous comparative studies. Unfortunately, results after the use of CHP and SCPLE fixation have not yet been widely studied.

To our knowledge this is the first study to evaluate the use of the CHP and SCPLE, focusing solely on implant selection without major differences in surgical technique or ligament repair. Furthermore, this is the first study to present the results of SCPLE fixation for the treatment of both Neer type II and type V fractures. Unfortunately, comparison of literature remains difficult due to small sample sizes, wide variety of functional outcome scores, definitions and surgical techniques. Therefore, a large multicenter study might provide insight into long-term results following different treatment modalities, influence of different LCF fractures types, and different patient populations.

CONCLUSION

Both the CHP and SCPLE are effective fixation methods for the treatment of unstable LCF resulting in excellent patient-reported functional outcome and similar complication rates. SCPLE fixation is an effective surgical fixation method for the treatment of both Neer type II and type V LCF. The SCPLE has a lower implant removal rate compared to the CHP. Therefore, if technically feasible, we recommend SCPLE fixation for the treatment of unstable LCF.

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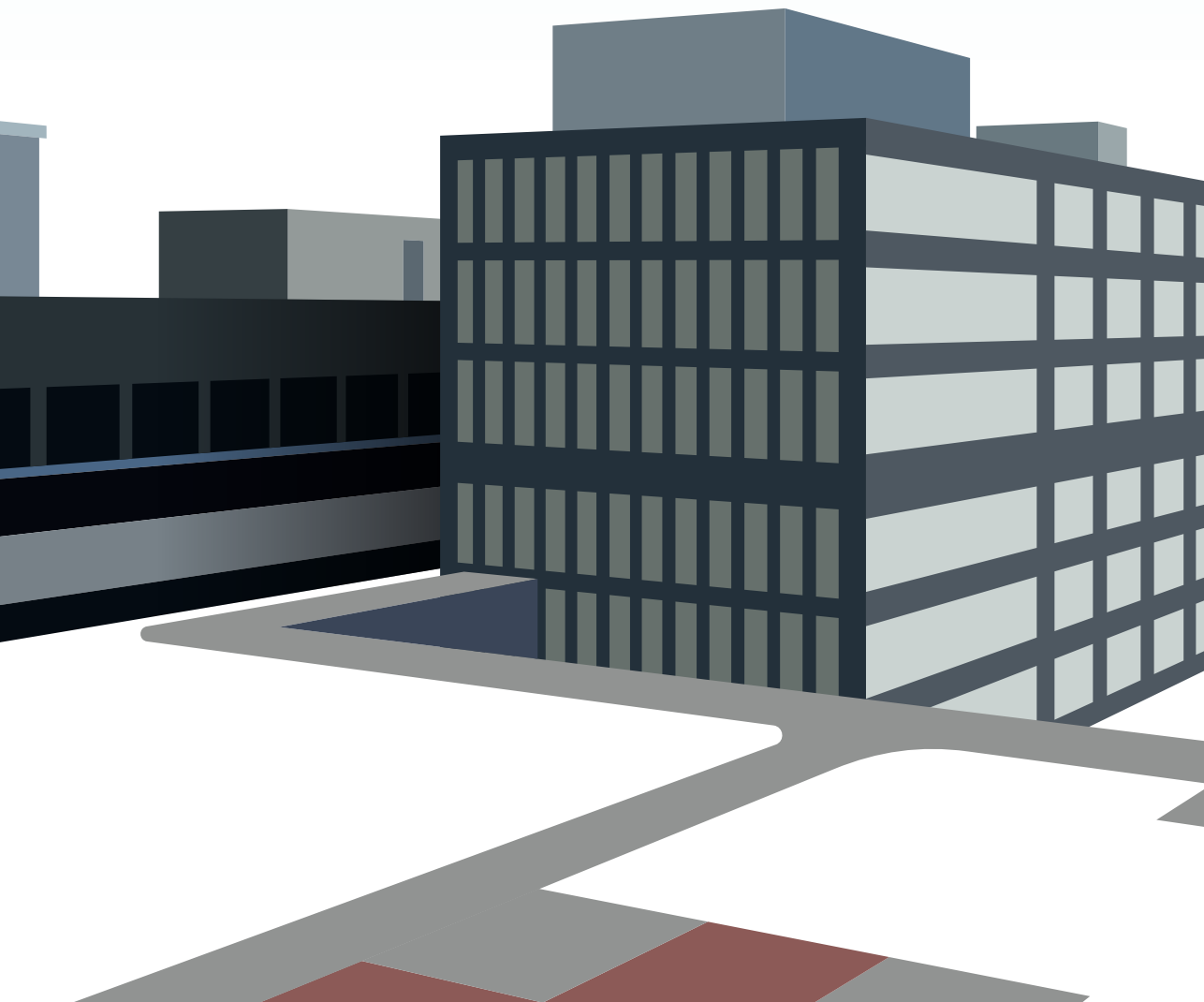

CHAPTER 6

Clavicle fractures in adults; current concepts

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ABSTRACT

Background: For decades, clavicle fractures have been treated conservatively. In the last twenty years, however, non-union rates after conservative treatment appear higher than previously reported and more evidence regarding operative treatment has become available. This has led to a paradigm shift towards an increase in operative treatment. The aim of this review is to present the current concepts and available evidence regarding clavicle fracture treatment.

Methods: Conservative and operative treatment options together with their indications for medial, shaft and lateral clavicle fractures are discussed. For all three anatomical locations, a treatment algorithm is proposed.

Conclusion: In general, non-displaced fractures are treated conservatively. Operative treatment has to be discussed with patients with displaced fractures, especially in the young and active patient.

INTRODUCTION

For decades, displaced midshaft clavicle fractures have been treated conservatively [1, 2]. However, non-union rates after conservative treatment appear higher than previously reported, in addition to a presumed better functional outcome following surgical treatment [3-7]. This has led to a paradigm shift during the last 15-20 years towards an increase in operative treatment. Ongoing interest in the literature regarding the optimal treatment for these fracture types seems to have led to an increase in scientific data favoring operative treatment [5-11].

The aim of this overview is to discuss the currently available evidence on clavicle fracture treatment. We discuss the classification systems, indications and treatment options for displaced and non-displaced medial, shaft and lateral clavicle fractures. In addition, we propose a treatment algorithm based on currently available evidence.

Epidemiology and mechanism of injury

Clavicle fractures are very common fractures with an incidence of 30 per 100,000 [12] and represent 2.6% - 4% of all fractures [3, 10, 12]. Fractures of the clavicle shaft have the highest incidence and account for 69% of all clavicle fractures. Lateral clavicle fractures and medial clavicle fractures have a lower incidence and account for 28% and 3% respectively [12]. The classical injury mechanisms are a simple fall on the shoulder (31%), followed by road traffic accidents (27%) and then sports (23%) [12]. Medial clavicle fractures occur more often as part of a high energy trauma or trauma with multiple injuries [13].

Diagnosis and imaging

The suspected diagnosis of a clavicle fracture is made clinically and confirmed with conventional x-ray in two directions. X-rays are preferably performed using craniocaudal and caudocranial views as described by Hoogervorst et al. [14]. These projections had a significant influence on the decision for conservative or operative treatment. For lateral and shaft fractures conventional imaging is in most cases sufficient. Medial clavicle fractures however are often difficult to diagnose on conventional x-rays. If the clinical suspicion is there and the conventional imaging is not conclusive a CT scan should be performed [15]. This is also a great help in preoperative planning for these fractures.

Classification systems

Several classification systems for clavicle fractures have been developed [12, 16, 17]. Allman divided the clavicle into three groups; a proximal (medial), middle (shaft) and

distal (lateral) part which has been the basis of the development of different classification systems [17]. Robinson defined a medial clavicle fracture as a fracture in the medial fifth of the clavicle, a lateral clavicle fracture if the fracture is in the lateral fifth and a clavicle shaft fracture if the fracture is in the intermediate three-fifth of the clavicle [12]. In case of fractures in more than one group each group should be separately classified. The classification systems of the AO/OTA, Edinburgh and Neer are most often used in clavicle fracture literature [12, 18-20]. All three are anatomical classifications. The Edinburgh classification has shown a relationship with clinical outcome for shaft fractures [21]. The Neer classification addresses the stability of lateral clavicle fractures, which can be used to aid in deciding between conservative and operative treatment.

The AO/OTA classification follows the structure described by Marsh et al. [18]. This classification assigns a general number to a certain bone. For the clavicle, this is the number 15. This bone is then divided into a medial, shaft and lateral part and given the numbers 1, 2 and 3 respectively. Further sub-classification follows the A, B and C system for simple, wedge and comminuted fractures with additional numbers representing different fracture patterns.

The Edinburgh classification, sometimes in literature also referred to as the Robinson classification, is a more simplified clavicle fracture classification system [12]. First, the location of the clavicle fracture determines the first number. A fracture in the medial fifth of the clavicle is classified as Type 1, in the middle three-fifth as Type 2 and in the lateral fifth as Type 3. Second, a letter A or B is added. The letter A is added for non-displaced or less than 100% displaced fractures and the letter B for >100% displaced fractures. Lastly, another number (1 or 2) is added to address the presence of articular involvement for Type 1 medial and Type 3 lateral fractures or the presence of comminution in middle third Type 2 fractures.

The Neer classification is a clavicle fracture classification system only for lateral clavicle fractures [19, 20]. This classification system is based on its relation to the CC-ligament and consists of five different fracture types [19, 20]. Type I fractures occur laterally to the CC-ligament with both parts of the ligament being intact. In type II fractures, a subdivision is made in A, B1 and B2 fractures. Neer type IIA fractures are localized medial to the CC-ligament, with both the conoid and trapezoid part attached to the lateral fragment. Neer type IIB1 fractures are localized between the conoid and trapezoid part and the conoid part of the ligament is ruptured. In Neer type IIB2 fractures, the fracture is lateral to the CC-ligament and both the conoid and trapezoid parts are torn. Type III and IV fractures are respectively intra-articular and physeal fractures with intact CC-

ligaments. Neer type V fractures have a comminuted character with an inferior clavicular fragment remaining attached to the CC-ligament. Neer type I, III and IV are considered to be stable fractures; Neer type II and V fractures are considered unstable.

In our opinion both the AO/OTA and Edinburgh classification are suitable for medial and midshaft clavicle fractures, especially for scientific purposes. The Edinburgh classification has a predictive value regarding functional outcome. For lateral clavicle fractures we prefer the Neer classification as it addresses the stability of the fracture, which can assist in decision-making regarding operative indications.

MEDIAL CLAVICLE FRACTURES

Case1

After a skiing accident a sixty year old woman sustained a displaced intra-articular medial clavicle fracture Robinson 1B2 (Figure 1a and 1b). She was treated operatively with a radial (VA)-LCP™ Distal Humerus Plate (DePuy Synthes, Switzerland) (Figure 1c and 1d). She had an uncomplicated recovery and the fracture consolidated (Figure 1e and 1f).

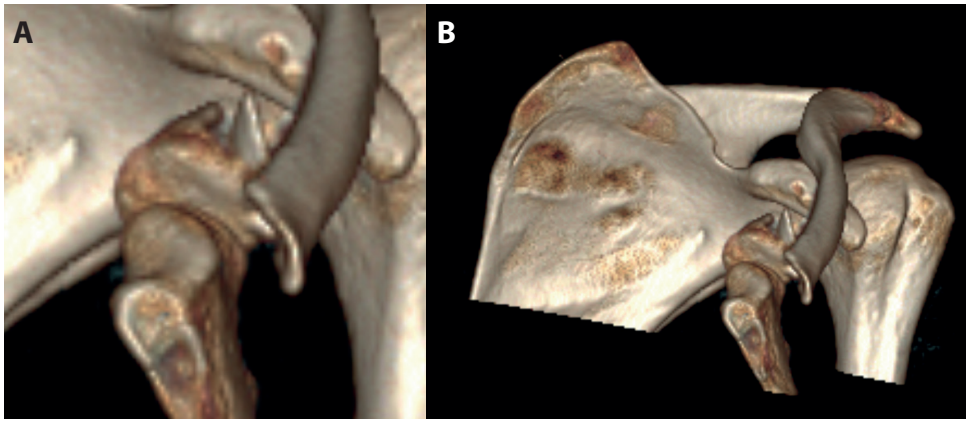

FIGURE 1A AND 1B. 3D reconstruction of a left displaced intra-articular medial clavicle fracture with an anterior and medially displaced clavicle shaft.

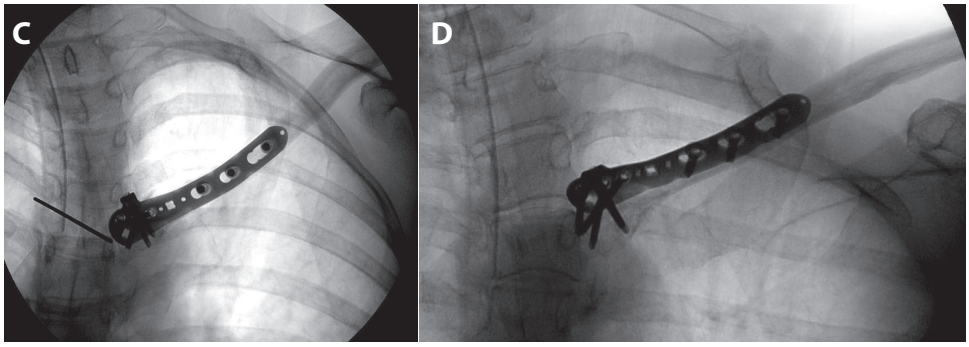

FIGURE 1C AND 1D. Intraoperative x-rays of open reduction and internal fixation with an antero-superiorly placed radial (VA)-LCP™ Distal Humerus Plate (DePuy Synthes, Switzerland) in a bridging technique through a longitudinal approach.

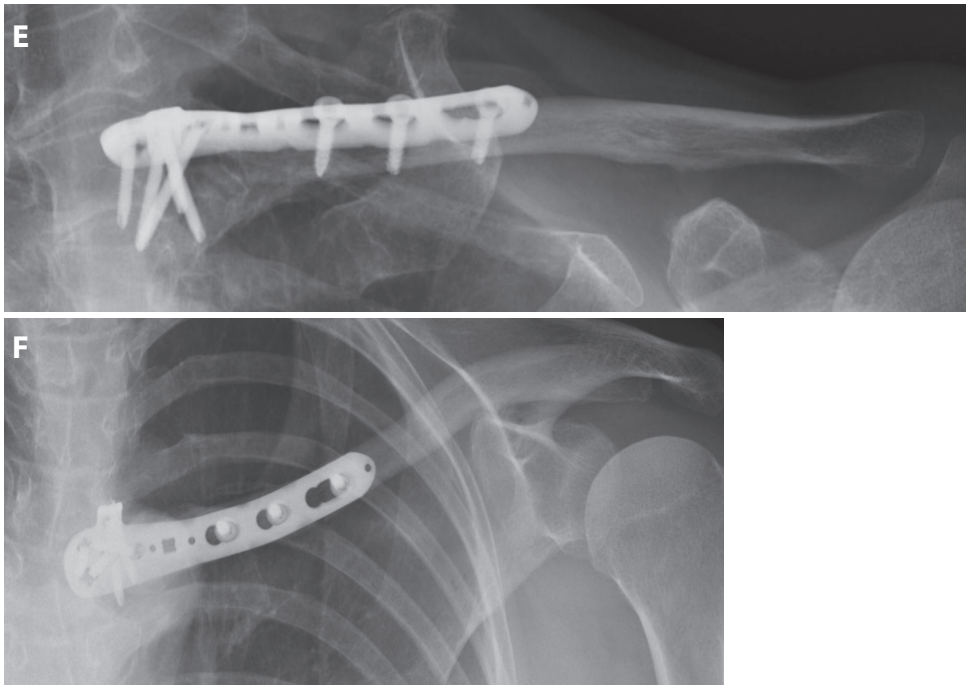

FIGURE 1E AND 1F. Six months follow-up with consolidation of the fracture on caudocranial (1e) and craniocaudal (1f) view [14].

Conservative treatment

Most medial clavicle fractures are non-displaced and can be treated conservatively [8, 22, 23]. There is little variation among conservative treatment protocols, but generally they consist of a shoulder sling (collar and cuff) for 6 weeks, 2-3 weeks fixed- and 3 weeks intermediate use. The main purpose of this sling is patient comfort during the initial phase. As soon as pain subsides, usually after 2-4 weeks, physiotherapy may start with passive ROM followed by active ROM and strengthening exercises preventing abduction more than 90 degrees for 6 weeks [5, 8, 16, 22, 24-26]. After 6 weeks, free movement and progressive strain is allowed. Furthermore, patients are advised to avoid contact sports for 4 months [25]. Radiological follow-up should be performed at 1 to 2 weeks and again at 6 weeks to check for secondary displacement.

The natural course of medial clavicle fractures has been described in three studies with relatively small numbers of patients. Non-union rates of 6,7% for non-displaced and 14,3% for displaced medial clavicle fractures have been reported [8]. Salipas et al. found a delayed-union rate of 10% for medial displaced and non-displaced clavicle fractures in general. After a mean follow-up of 3 years, the overall functional outcome of non-operative treatment for displaced and non-displaced fractures was good: reporting a mean American Shoulder and Elbow Society scoring system (ASES) of 80 and a mean Subjective Shoulder Value (SSV) of 77 [22]. Throckmorton et al. also reported a good functional outcome after non-operative treatment after 15 months. However, 28% of the patients had moderate to severe remaining pain [23].

Operative treatment

Indications for open reduction and internal fixation (ORIF) of medial clavicle fractures have traditionally been 'open fracture, extensive soft tissue damage and neurovascular impairment and symptomatic mal- and non-unions' [15, 28]. ORIF for displaced medial clavicle fractures, where displaced is defined as more than one shaft width displacement, is still under debate [22, 23]. Displaced medial clavicle fractures may lead to up to 14-20% of non-unions compared to 7% for non-displaced medial clavicle fractures [8, 22]. Therefore, operative treatment for displaced medial clavicle fractures can be considered according to recent literature [9, 15, 16, 28, 29]. The epifysiolysis of the medial clavicle is a special entity that belongs to adolescent fractures. As it is outside the scope of this overview, it is not further discussed.

Several operative techniques and implants for ORIF of medial clavicle fractures have been described: fixation with inverted LCP™ Superior Anterior Clavicle Plate with lateral extension [9], distal radial plate [9], a small T-plate with tension band suturing

[30], standard T-locking plate [28], a pilon plate crossing the sternoclavicular joint [28], cerclage [29] and transosseous sutures [9]. More recently the radial (VA)-LCP™ Distal Humerus Plate [15] has been described as a solution for intra-articular fractures or extra-articular fractures with a small medial fragment. As far as we know, no anatomical shaped medial clavicle plate has been developed yet. ORIF is performed though an open anterior approach. Depending on the fracture pattern the plate can be positioned a bit more superiorly or inferiorly to obtain a good position for screw insertion in different fragments resulting in a stable fixation [9, 15, 28].

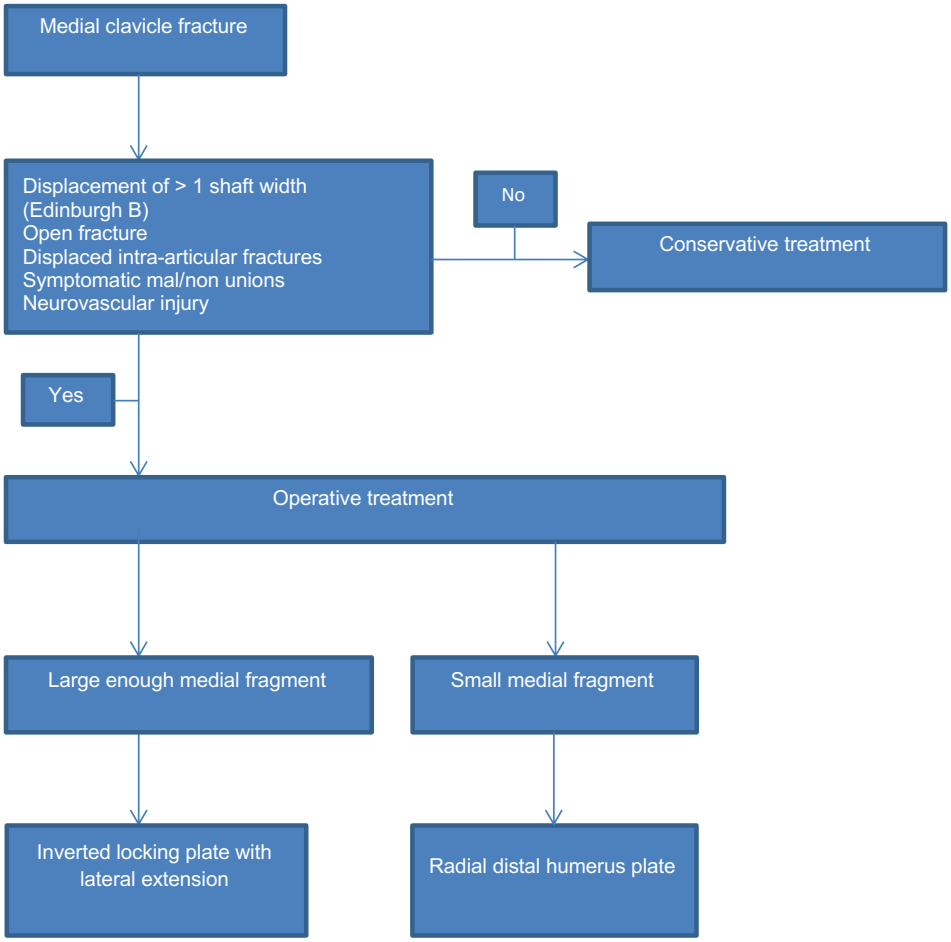

FIGURE 2. Treatment algorithm medial clavicle fractures

Three studies describe a larger series of surgical treatment results of displaced medial clavicle fractures [9, 15, 28]. All three, with in total 45 operated patients, showed good to excellent functional results with mean DASH and QuickDASH scores between 10 and 0 at a follow-up ranging from 6 – 79 months. In these 45 patients one non-union occurred.

Very little is known and published about implant removal. An analysis of 15 patients showed an implant removal rate of 64%; in 14% of the patients this was on patients' request without irritation and in 50% it was because of implant related irritation [15].

Our proposed treatment algorithm

We propose the following treatment algorithm for medial clavicle fractures (Figure 2): non-operative treatment for non-displaced and less than one shaft width displaced fractures. Indications for operative treatment are 1) displacement >1 shaft width (Edinburgh B), 2) open fractures, 3) displaced intra-articular fractures, 4) symptomatic mal- or non-union and 5) fractures with neurovascular compromise. Fractures with substantial medial bone stock can successfully be treated with an inverted locking plate with lateral extension. Intra-articular fractures or extra-articular fractures with a small medial fragment can be treated with the radial (VA)-LCP™ Distal Humerus Plate.

CLAVICLE SHAFT FRACTURES

Case 2

A 53 year old man sustained a skiing accident and fell on his left shoulder. He suffered a displaced midshaft clavicle fracture (AO/OTA 15.2.B3) (Figure 3a and 3b). He was treated operatively with an anterior placed LCP 3.5 plate (Figure 3c and 3d). His fracture consolidated and after eleven months the plate was removed on patients request without having any complaints (Figure 3e and 3f).

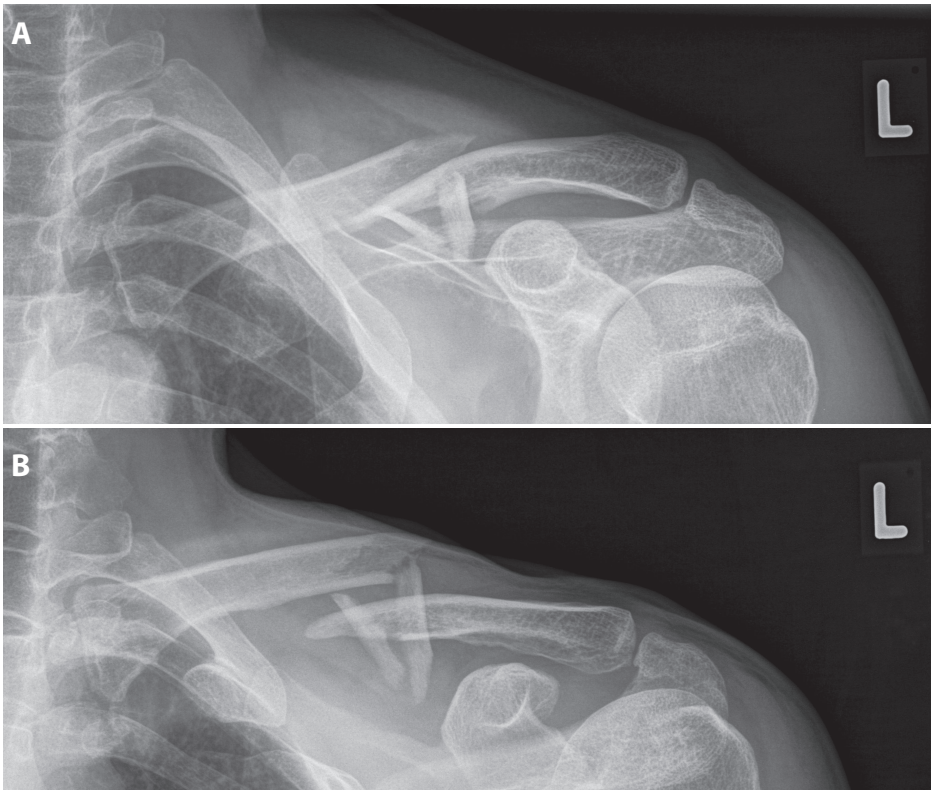

FIGURE 3A AND 3B. Comminuted displaced midshaft clavicle fracture left with anterior-posterior (AP) (3a) and caudocranial view (3b).

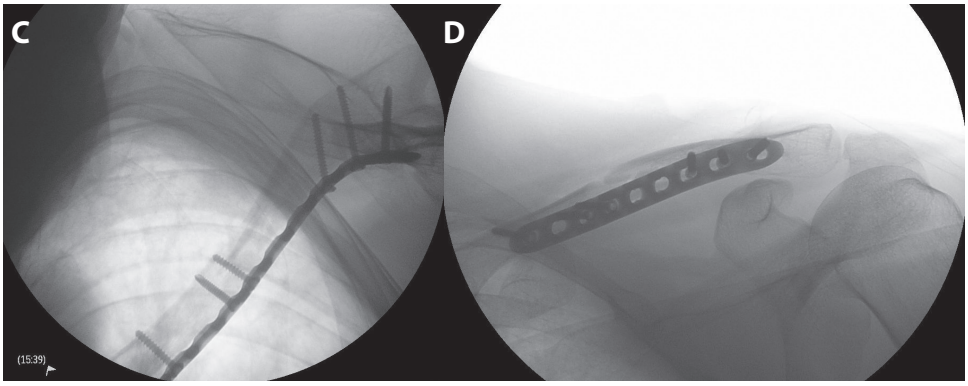

FIGURE 3C AND 3D. Intraoperative x-rays of open reduction and internal fixation with anterior placed 3.5 Locking Compression Plate (DePuy Synthes, Switzerland) in a bridging technique through a longitudinal approach.

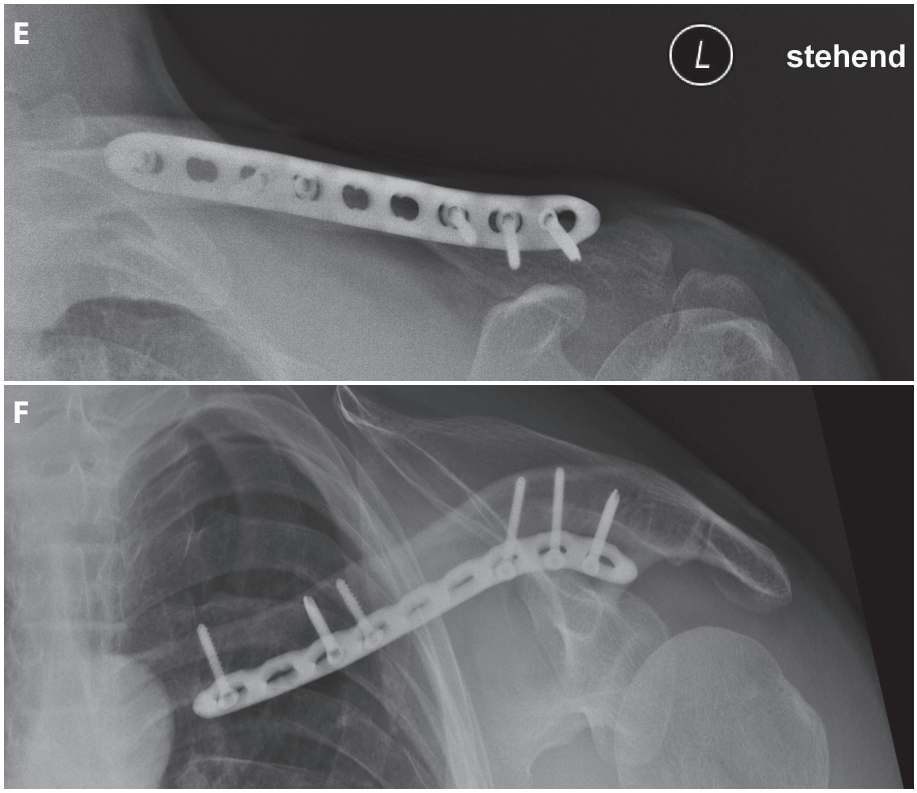

FIGURE 3E AND 3F. Eleven months follow-up with consolidated fracture on caudocranial (3e) and craniocaudal (3f) view.

Conservative treatment

Many midshaft clavicle fractures, and most certainly the non-displaced midshaft clavicle fractures, can be treated conservatively. Conservative treatment follows the same protocol as described above for medial clavicle fractures. A different possibility for conservative treatment of shaft fractures is a figure of eight bandage with free movement. However, a comparative study by Ersen, et al. did not show a difference in functional results, and patients with a sling had significantly more comfort during the first three days compared to those with the figure of eight bandage [31]. Complications of conservative treatment are mostly non- and mal-union, neurologic and may result in secondary operations [4, 6]. Non-unions after displaced midshaft clavicle fractures are reported in 10 – 23% of the conservatively-treated patients [3-8, 24, 26]. Comminution, displacement and smoking are significantly associated with higher risk of non-union [5,

8]. Secondary operative treatment of non-unions with or without bone graft also results in good functional outcomes and a non-union rate of 7,5%. However, these patients have a longer recovery time and 27% of these patients are still not satisfied [7, 32].

Operative treatment

Open fractures, fractures with concomitant neurovascular injuries, pathological fractures, fractures with near skin perforation, polytrauma patients and patients with a floating shoulder are almost always excluded in clavicle studies as these are accepted indications for operative treatment [16]. Operative treatment for displaced midshaft clavicle fractures is still under debate. Benefits of operative treatment include: less chance of non-union (1-2%) [3-6, 10, 11, 26, 33-35], faster return to work in an active population [3, 4, 10, 26] and a better short-term functional outcome [4, 24]. Functional outcomes after one year are equally good in both groups [4, 6, 7, 11, 24]. Some other studies [3, 6, 10] found slightly better functional outcome scores at all times although clinical relevance can be debated. Traditionally, clavicle shortening is often mentioned as a possible indication for operative treatment. However, a recent study of Goudie, et al. on this subject could not support this statement [25]. A recent systematic review also did not find an influence of clavicle shortening on the functional outcome [36]. Interestingly, although this might be due to cultural influences, patient satisfaction appears to be better after operative treatment [3, 7].

Operative treatment may consist of (percutaneous) intramedullary fixation (IMF), either antegrade or retrograde, or plate fixation (PF). Several studies regarding this topic have recently been published [33-35, 37]. Both treatment modalities result in equally good functional outcomes after one year with DASH mean scores of 0.5 – 3 [33-35]. Some studies show a faster recovery and better short-term functional outcome at three to six months after plate fixation [33, 35]. Both fixation methods achieve equal union rates with non-unions in 1-2% [3-6, 10, 11, 26, 33-35]. Benefits of IMF compared to PF include, besides the obvious smaller scar, shorter operation time and fewer infections [33, 37]. In a review analyzing RCTs and observational studies on mostly non-comminuted fractures, Houwert et al. also found fewer major re-interventions and a lower re-fracture risk after implant removal with IMF. They did not find a difference in union rate, functional outcome, and, contrary to previously mentioned studies, infection rate [38]. Open reduction also seems to be a predictor of poorer functional outcome after IMF according to Fuglesang, et al. [33]. Van der Meijden, et al. however did not see such an effect [35]. Open reduction is relatively frequently necessary, occurring in 52-74% of the

cases in literature. The need for open reduction seems to be correlated with the elapsed time between injury and fixation [33]. One can conclude that to prevent open reduction to a certain extent, IMF should be performed early after the injury.

Several plates, like reconstruction plates and pre-contoured locking plates, can be used and have been described. Reconstruction plates however tend to have a higher incidence of implant failure than locking plates and are therefore considered less suitable [39]. Plate fixation can be performed after open reduction or minimally invasive plate osteosynthesis (MIPO). Open reduction and internal fixation can be done through a longitudinal or oblique approach. The first provides a wider exposure of the clavicle but has a cosmetic disadvantage for women and has a high risk of supraclavicular nerve damage. The aim is to have at least 3 conventional or 2 locking screws at each side of the fracture. In good cortical bone conventional screws are mostly sufficient. Osteoporotic bone requires a more stable construct with locking screws. Simple fractures, however often treated with IMF, can be anatomically reduced and stabilized using absolute stability. Comminuted fractures are most often stabilized with a bridging plate. The larger the comminuted zone the more rigid the plate should be to achieve adequate stabilization. Larger fragments can be fixated using smaller leg-screws or suture cerclage. Plate positioning can be either superior or anterior/inferior [40]. A recent meta-analysis did not find a difference in functional outcome, infection rate, non-union or complications between these plate positions [40]. Sohn, et al. also published a study comparing superior and anterior/inferior plating in a MIPO technique, both resulting in satisfactory clinical outcomes [41]. They found no clear clinical difference. This is in accordance with another study of Hulsmans er al. who found no difference in implant-related irritation or implant removal between the superior and anterior/inferior plate position [42]. Fractures in the more lateral half of the clavicle shaft can be more challenging if addressed from anterior. As the clavicle is more flat at the lateral side screw insertion, and especially the locking screw insertion, can be difficult. In this case the long precontoured superior plate for lateral clavicle fractures can be of assistance as it offers the possibility for angular stable screw insertion from superior. However no clear evidence is available in literature regarding this topic.

Postoperative treatment itself has, to the best of our knowledge, not been studied. Study protocols differ from one another; immobilizing the patients postoperatively in a sling for 1-4 weeks [3, 5, 7, 26] with passive ROM exercises after 2-3 weeks.

Complications

One of the disadvantages and complications of operative treatment in general is implant related irritation, encountered in both treatment modalities in up to 70% [33, 43]. As

soon as the swelling has subsided, clavicle plates become prominent and often irritate. Implant related irritation after IMF could be caused by telescoping of the nail at the entry side [35, 44]. Application of an end cap with the aim to prevent this telescoping did not result in less implant related irritation as the end cap is in itself bulky [44]. The degree of fracture comminution seems to be a strong predictor of slower recovery, poorer functional outcome and more implant related irritation [33, 45]. This effect has not been seen after plate fixation. Taking these influences into account, several studies advocate IF for non-comminuted displaced midshaft clavicle fractures only [33, 38, 45].

Other known and feared complications are wound infections. Different trials reported deep infection rates between 0 and 4% [5, 7, 33].

Implant removal

Possible implant removal is a clear disadvantage of operative treatment resulting in secondary operations. Wide ranges of implant removal rates are reported. Implant removal after one year was 17% and 35% according to Woltz and Smeeing [7, 10]. Two other studies however showed much higher rates of plate and nail removal [33, 43]. They also found a significant difference between plate and nail removal. Plates were removed in 38-50% and nails were removed in 73-82%. An advantage of IMF is that implant removal may be performed under local anesthesia [43].

Our proposed treatment algorithm

We propose the following treatment algorithm for midshaft clavicle fractures (Figure 4): Non-operative treatment using a sling for 3-6 weeks for all non-displaced and slightly displaced fractures with bony contact. Operative treatment for 1) open fractures, 2) fractures with concomitant neurovascular injuries, 3) fractures with near skin perforation, 4) polytrauma patients who need early functional rehabilitation and 5) patients with a floating shoulder. Operative treatment should be discussed with and offered to patients with 6) a displaced midshaft clavicle fracture presenting the above-mentioned advantages and disadvantages resulting in shared decision making. Especially young and high demanding active people who prefer a low non-union risk and early functional movement will benefit from this operative treatment. Simple fractures can be treated with IMF. Comminuted fractures should be treated with PF. Based on currently available literature, neither superior plating nor anterior/inferior plating is clearly better than the other.

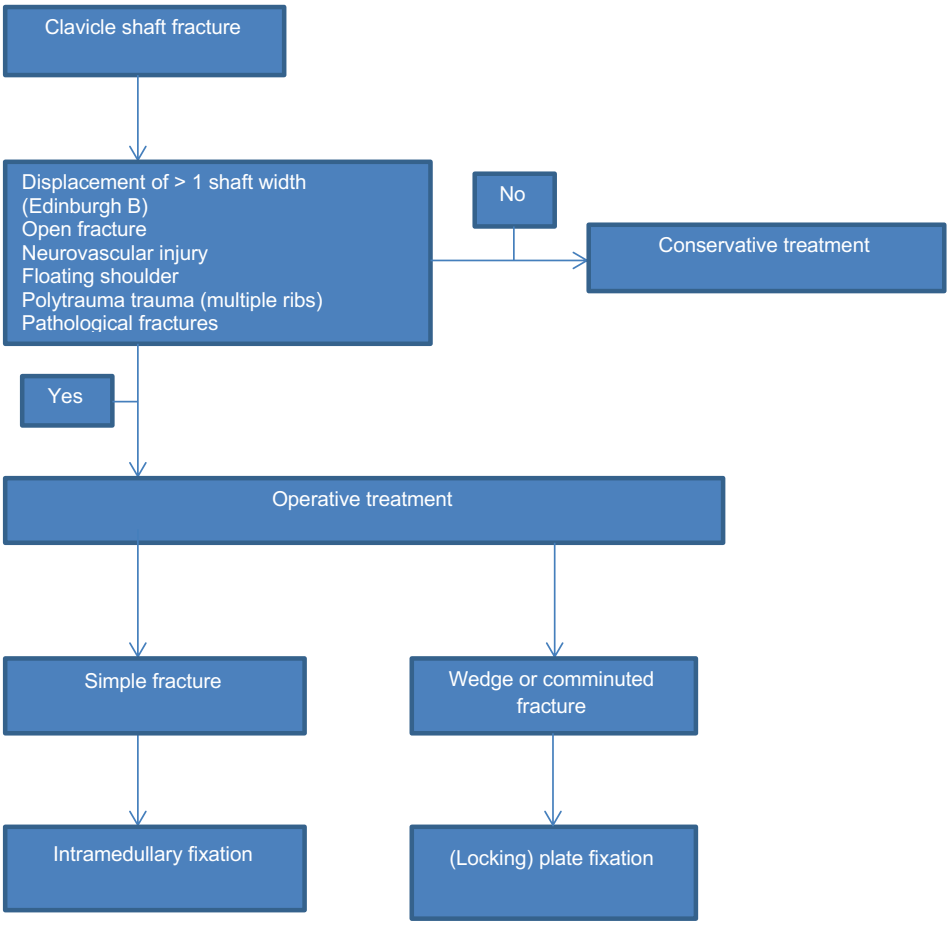

FIGURE 4. Treatment algorithm clavicle shaft fractures

LATERAL CLAVICLE FRACTURES

Case 3

A 63 year old man fell down with is bike and sustained an unstable displaced lateral clavicle fracture (Figure 5a and 5b). After 2 days he was treated with an open reduction and internal fixation with a 3.5 LCP hook plate as a bridging plate (Figure 5c and 5d). The fracture consolidated (Figure 5e and 5f) and after 5 months the plate was removed following our protocol.

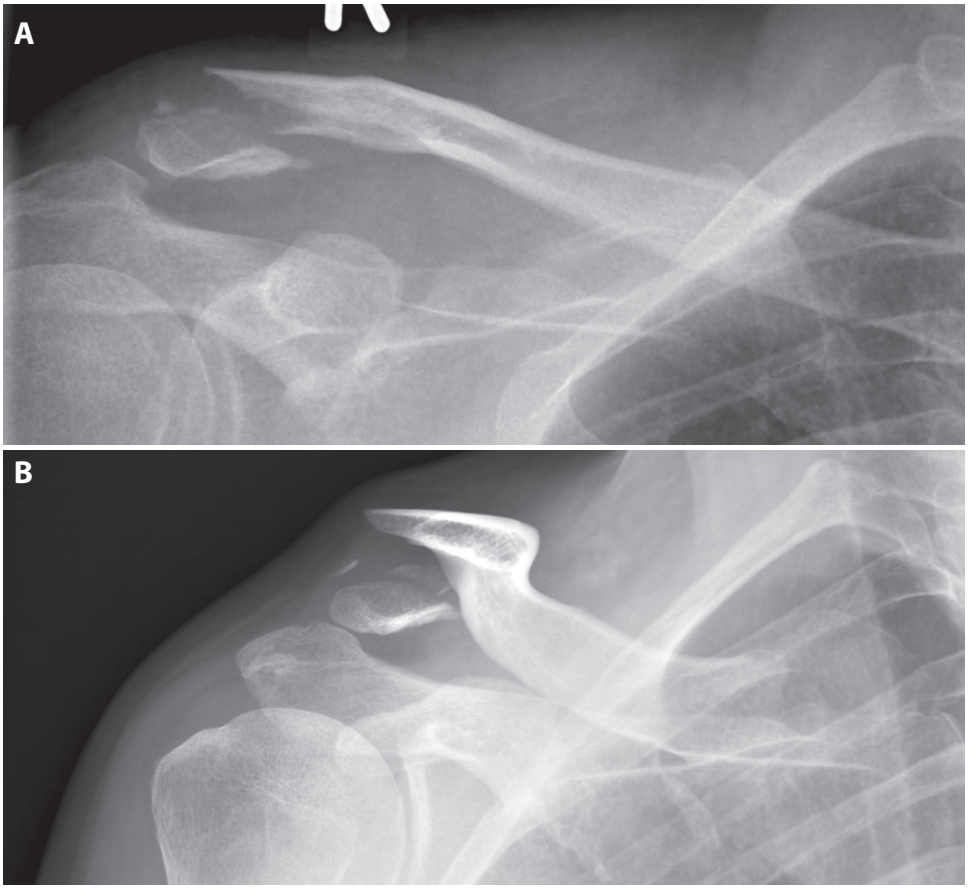

FIGURE 5A AND 5B. Right instable displaced lateral clavicle fracture with AP (5a) and caudocranial (5b) view.

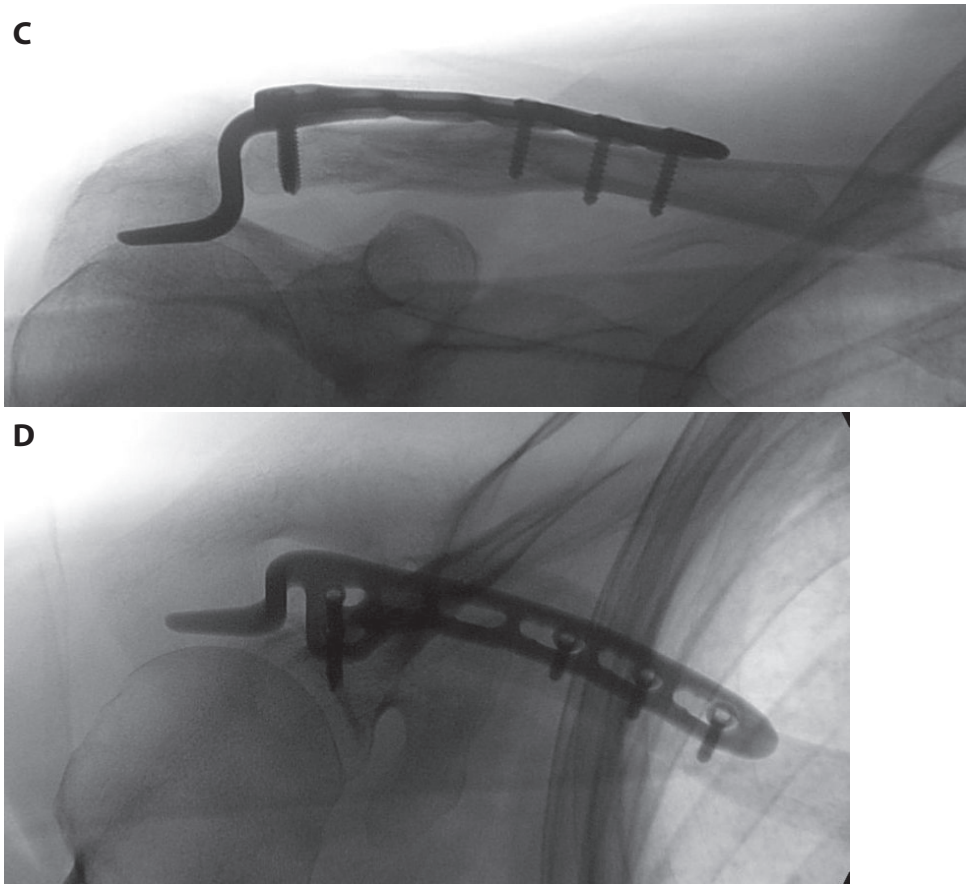

FIGURE 5C AND 5D. Intraoperative x-rays of open reduction and internal fixation with 3.5 LCP hook plate (DePuy Synthes, Switzerland) in a bridging technique through a longitudinal approach.

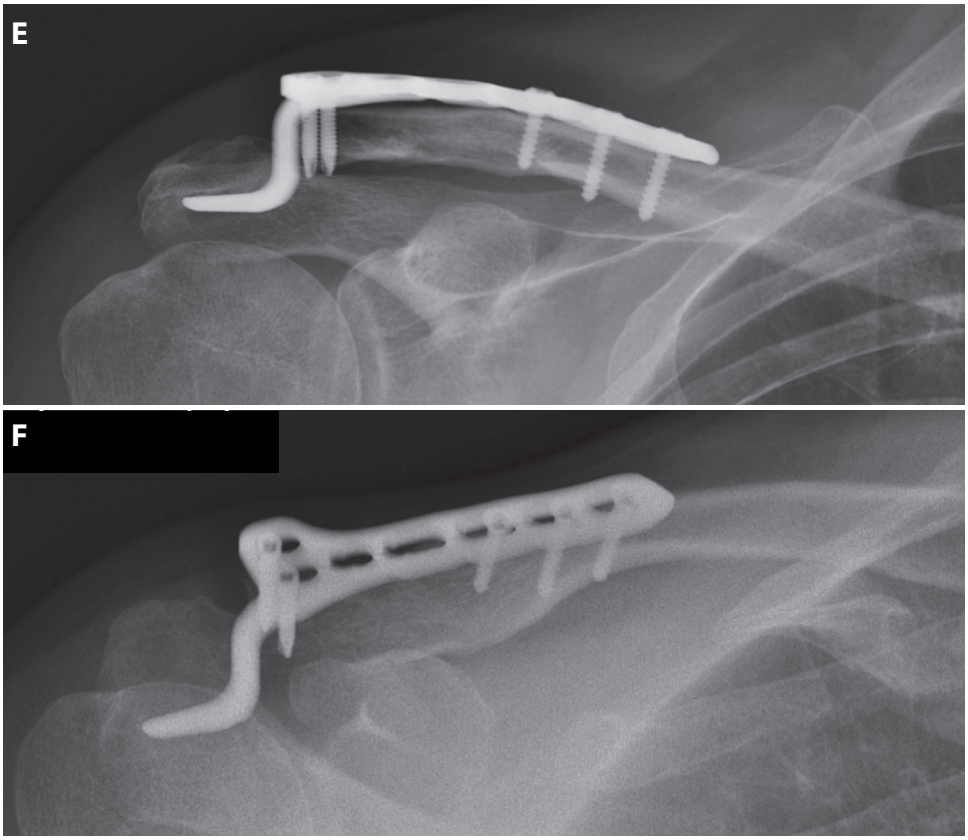

FIGURE 5E AND 5F. Five months follow-up with consolidated fracture on AP (5e) and caudocranial (5f) view.

Conservative treatment

Stable fractures (Neer I and III) as well as fractures at or medially from the CC-ligament that are non-displaced (less then one shaft-width) can be treated conservatively and follow the protocol as described above for medial clavicle fractures. Especially potentially instable fractures need to be evaluated by x-ray after one, two and six weeks for secondary displacement [27].

Operative treatment

Operative treatment is warranted for more than one shaft width displaced unstable fractures (Neer IIa, IIb and V) as conservative treatment result in up to 33% non-unions [27, 46]. Until now many different treatment options like K-wire fixation, locking plate

fixation, hook plate fixation, coracoid-clavicle screw fixation and (arthroscopical) button fixation have been proposed. However, in current literature, none of them have proved to be the golden standard to date [46-48]. No RCTs are available and most studies have been reporting about small series. The largest amount of available evidence comes from a few studies that are comparing hook plate fixation and locking plate fixation [47-49]. Hook plate fixation and locking plate fixation both result in high union rates (93-100%) and excellent functional outcomes [47-49]. The hook plate however clearly has a higher complication rate and is always removed as soon as possible, depending on the consolidation of the fracture. Subacromial impingement, rotator cuff lesions, acromial fractures, implant failure and mainly implant related irritation are reported in up to 40-70% [27, 48, 49].

K-Wire fixation was used for a long time but because of complications like K-wire migration, implant failure, pseudoarthrosis and infection, it lost its popularity [27]. Coracoclavicular screw fixation also lost its popularity because of complications [27].

More recently coracoclavicular button fixation, either open, minimally invasive or arthroscopically, have been described [50-52]. Ranaletta, et al. presented a case series in athletes with lateral clavicle fractures treated with minimally invasive double-button fixation with 95% union and excellent functional results [52]. Loriaut also published excellent functional results after arthroscopically double button fixation in 21 patients with a Neer IIB fracture [51]. In another case series, Teoh, et al. published a technique using a PDS sling fixation with excellent functional results and only one non-union in 23 patients [53]. Cho, et al. also presented a small case series with 18 patients with good functional outcome and 95% union rate using the TightRope system in Neer IIB fractures [50]. One of the advantages of these procedures is that there is no implant related irritation and no necessity for implant removal. A disadvantage is that these techniques can only be used in Neer IIB fractures, not in Neer IIA or V fractures. Another study analyzing the arthroscopic-assisted endobutton procedure showed good functional results however with a high number of delayed unions. A risk analysis however showed that early mechanical stress, a lateral clavicular fragment larger than 3cm and a time delay to surgery were risk factors for non-unions [54]. Other reported complications are fracture of the coracoid process, transient capsulitis, symptomatic joint osteoarthritis and migration of the button through the clavicle [50, 51]. These newer techniques seem promising but future comparative studies are necessary to determine their clinical value.

Our proposed treatment algorithm

We propose the following treatment algorithm for lateral clavicle fractures (Figure 6): conservative treatment for stable Neer I and III fractures as well as non-displaced

instable Neer IIA, IIB and V fractures. These non-displaced instable fractures need close observation for secondary dislocation. Operative treatment is recommended for 1) displaced Neer IIA, IIB and V fractures, 2) open fractures and 3) fractures with concomitant neurovascular injuries. Our first choice is ORIF with pre-shaped locking plate fixation whenever sufficient stable fixation in the lateral fragment is possible. For fractures with a small lateral fragment, where stable fixation is not possible, a hook plate can be used. Hook plate removal is mandatory as soon as possible after consolidation to prevent the above-mentioned complications.

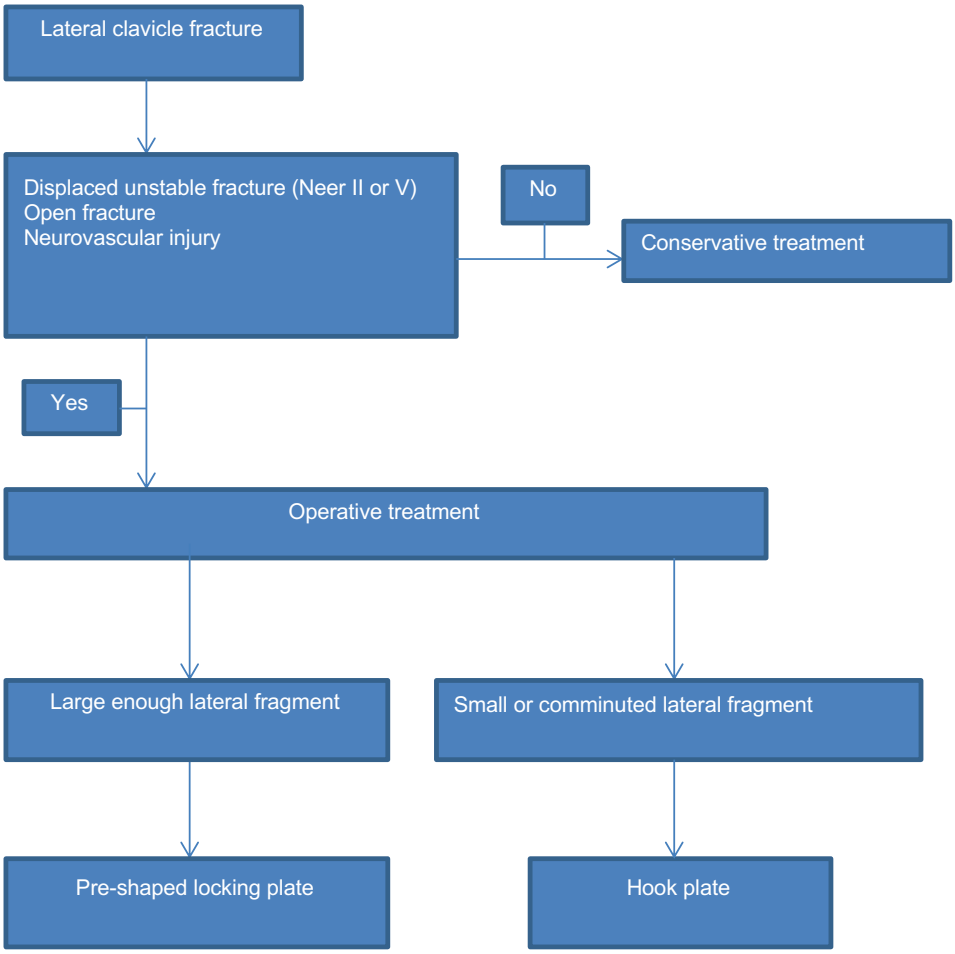

FIGURE 6. Treatment algorithm lateral clavicle fractures

CONCLUSION

Clavicle fracture treatment has evolved during the last few decades from conservative treatment towards more often an operative treatment. In general, non-displaced fractures are treated conservatively. Operative treatment has to be discussed with patients with displaced fractures, especially in the young and active patient. Different operative techniques are available for different types of clavicle fractures. Benefits of the operative treatment are a low non-union rate, early return to work and sports and a higher patient satisfaction. Clear disadvantages are the need for operation with the general surgical complications and particularly the high rates of implant related irritation and subsequently the high implant removal rates requiring a second operation. Both the pros and cons have to be discussed with patients resulting in shared decision making.

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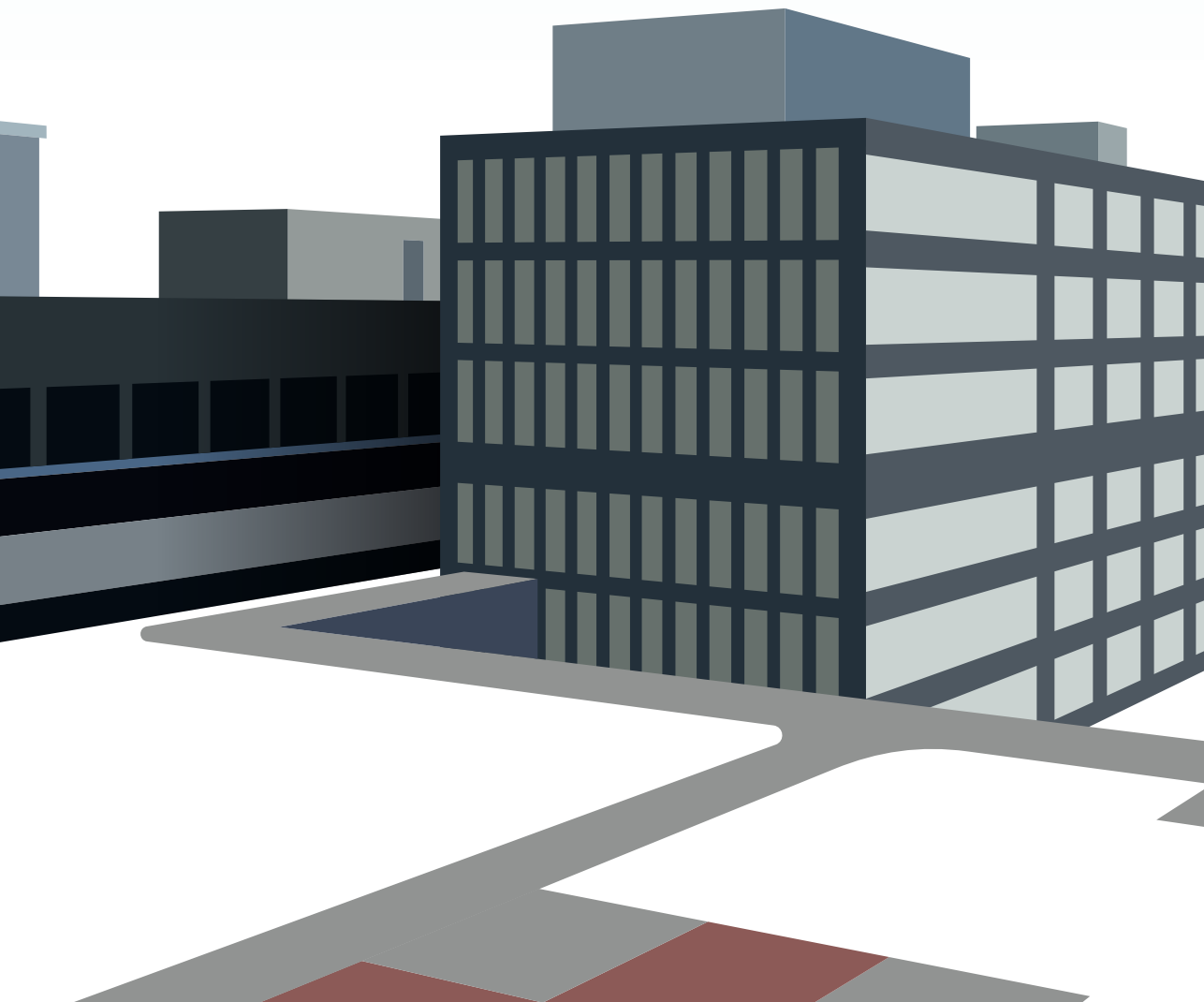

CHAPTER 7

Operative versus nonoperative treatment of proximal humerus fractures. A systematic review, meta-analysis and comparison of observational studies and randomized controlled trials

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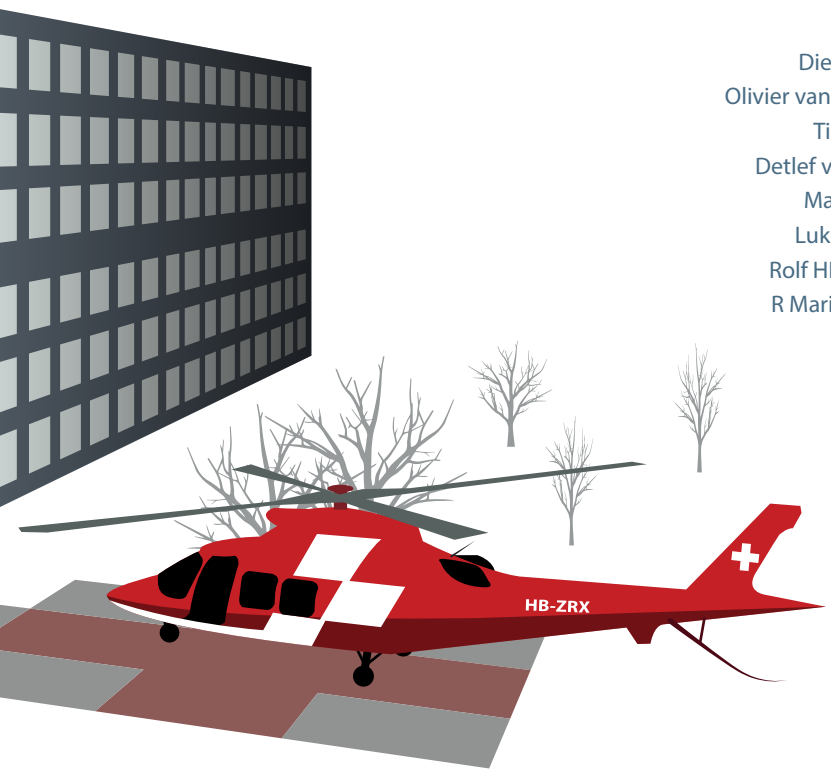

ABSTRACT

Background: There is no consensus on the choice of treatment for displaced proximal humerus fractures in older (> 65 years) patients. The aim of this systematic review and meta-analysis was (1) to compare operative with nonoperative management of displaced proximal humeral fractures and (2) to compare effect estimates obtained from randomized controlled trials (RCT) and observational studies.

Methods: The databases of MEDLINE, Embase, CENTRAL, and CINAHL were searched on September 5th 2017 for studies comparing operative versus nonoperative treatment of proximal humerus fractures; both RCTs and observational studies were included. The MINORS criteria, a validated instrument for methodological quality assessment, were used to assess study quality. The primary outcome measure was physical function as measured by the absolute Constant-Murley score after operative or nonoperative treatment. Secondary outcome measures were major reinterventions, nonunion, and avascular necrosis.

Results: Twenty-two studies were included; seven RCTs and 15 observational studies, resulting in 1743 patients total: 910 treated operatively and 833 nonoperatively. The average age was 68.3 years, and 75% were female. There was no difference in functional outcome between operative and nonoperative treatment with a mean difference of -0.87 (CI, -5.13 – 3.38; P=0.69; I^2=69%). Major reinterventions occurred more often in the operative group. Pooled effects of RCTs were similar compared to pooled effects of observational studies for all outcome measures.

Conclusions: We recommend nonoperative treatment for the average elderly (aged >65 years) patient with a displaced proximal humerus fracture. Pooled effects of observational studies were similar to those of RCTs and including observational studies led to more generalizable conclusions.

INTRODUCTION

The proximal humerus fracture is the third most common fracture seen in the elderly with an incidence of 82 per 100,000 person years with an annual increasing rate of 13.7% per year over the last 33 years.[25,33,37] The typical patient is a female aged 65 or over.[9] Nearly 75% of patients are treated nonoperatively, and one out of five will undergo surgery depending on fracture type and displacement.[22]

Depending on related factors such as patient age, activity and fracture pattern, operative treatment options include minimally invasive reduction and intramedullary fixation, open reduction and internal plate fixation (ORIF) or arthroplasty of the glenohumeral joint. Nonoperative treatment usually starts with immobilization followed by passive and active rehabilitation.[22] Despite the fact that the available literature is inconclusive regarding the superiority of either treatment option, it is common practice to attempt joint saving operative procedures in younger patients.[16,22] Additionally, there is no consensus whether surgery is beneficial for the older patient with a displaced proximal humerus fracture.

There is increasing scientific evidence which demonstrates that meta-analyses of both high quality observational studies and RCT's can be similar in value to meta-analyses of RCTs alone in the field of orthopedic trauma surgery.[1,2,19,42] Observational studies may give better insight into infrequent outcome measures, rare complications, and small effects of operative treatment, while also increasing generalizability of the results due to an increase in patient numbers available for (meta-) analysis.

The aim of this systematic review and meta-analysis is (1) to compare operative versus nonoperative treatment of displaced proximal humeral fractures and (2) to compare effect estimates obtained from RCTs and observational studies. We hypothesized that (1) operative treatment for proximal humerus fractures does not improve functional outcome as compared to nonoperative treatment and (2) including observational studies in this meta-analysis will lead to more robust conclusions without decreasing quality of the results.

METHODS

This systematic review and meta-analysis followed guidelines published by PRISMA and MOOSE.[26,44] These checklists aim to improve the reporting of systematic reviews and meta-analyses for RCTs and observational studies, respectively.

Search Strategy and Eligibility Criteria

Two reviewers (RBB, YO) independently searched MEDLINE, Embase, CENTRAL, and CINAHL databases on September 5th, 2017, for studies comparing operative and nonoperative treatment of proximal humerus fractures. The search syntax is provided in Appendix 1. Both RCTs and observational studies were included. After screening title and abstract of identified records, studies were independently assessed based on full-text. Eligibility criteria were proximal humerus fracture; operative versus nonoperative treatment; reporting of functional outcomes, and complications. Exclusion criteria were language other than English, Dutch, or German; no availability of full-text; inclusion of patients younger than 18 years old; letters, meeting proceedings, and case reports; external osteosynthesis as operative treatment. Disagreement over eligibility was resolved by discussion with a third reviewer (RMH). References of included studies were screened for eligibility, and citation tracking was performed by using Web of Science to identify articles not found in the original search. Authors were approached via ResearchGate when no full-text version of the paper was available.

Data Extraction

Data extraction was done independently by two reviewers (RBB, YO) with a data extraction file. The following data were extracted: first author, journal, year of publication, study period, study design, country/countries in which the study was/were performed, fracture displacement, fracture classification system (Neer classification), follow-up, treatment groups, operative treatment, nonoperative treatment, number of patients, loss to follow-up, implant removal, and outcome measures. Definitions of fracture characteristics, such as displacement, were applied according to the description in the original study. Major reintervention was defined as an additional, initially unplanned, surgery for implant failure, deep infection, symptomatic nonunion, subacromial impingement, or avascular necrosis. Planned implant removal was not considered a major reintervention. Fjalestad et al. reported additional follow up of previously published date which were merged with the original article for this meta-analysis.[10,11]

Quality Assessment

Two reviewers (RBB, HF) independently assessed the methodological quality of all included studies with the Methodological Index for Non-Randomized Studies (MINORS).[39] The MINORS is a validated instrument for methodological quality assessment and clear reporting of observational studies of surgical interventions.[39] Other quality assessment tools focus on a specific study design, while the MINORS is externally validated on RCTs by comparison with the CONSORT statement, making it a suitable instrument for meta-analyses of different study designs. The MINORS score ranges from 0 – 24; a higher score represents better methodological quality. Further details on the MINORS criteria and scoring system are provided in Appendix 2. Disagreements were resolved by involving a third reviewer (RMH).

Outcome Measures

The primary outcome measure was physical function as measured by the absolute Constant-Murley[8] score at least one year after initialization of either treatment. Normalized (sex and age adjusted) Constant-Murley scores were converted to absolute Constant-Murley scores using normal population-based values.[7] Secondary outcome measures were major reinterventions, nonunion, and avascular necrosis. If available, other functional outcome measures, such as the American Shoulder and Elbow Surgeons Shoulder Score[27] or the Neer score[28], were extracted as well.

Statistical Analysis

Statistical analyses were performed using Review Manager (RevMan, Version 5.3.5. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). All continuous variables were converted to means and standard deviations (SD) when sufficient information was available using methods described in the Cochrane Handbook for Systematic Reviews of Interventions.[18]

All analyses were performed stratified by study design (i.e., RCTs and observational studies separately) as well as including both designs. Outcomes reported by two or more studies were pooled in a meta-analysis. Pooled effects of operative versus nonoperative treatment of dichotomous outcome measures were presented as risk ratios with confidence intervals (CI) using the Mantel-Haenszel method.[18] Pooled effects of continuous outcome measures were presented as mean differences with CI using the inverse variance weighting method.[18] Heterogeneity between studies was assessed by visual inspection of the forest plots and by estimating statistical measures for heterogeneity, i.e., the I^2 statistic and the Chi-square test. The main quantitative assessment of heterogeneity was the I^2 statistic where the following interpretation

was used: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; and 75% to 100% considerable heterogeneity.[18] When heterogeneity was present a random-effects models was used instead of a fixed-effects model. Inspection of a funnel plot of the primary outcome measure against its standard error was done to detect potential publication bias.

Sensitivity Analyses

Several sensitivity analyses were performed for study quality, year of publication, osteosynthesis by (locking) plate fixation and arthroplasty, and Neer classification. For the analysis of study quality only studies with an arbitrarily chosen MINORS score of 16 or higher were included, similar to previously published meta-analyses in orthopaedic trauma surgery studying both study designs.[19,40] To assess the influence of the period in time in which the study was performed (and consequently, development of different operative techniques), only studies published after 2005 were included in a separate analysis. Since the locking plate is the most commonly used type of osteosynthesis, another sensitivity analysis was conducted with studies where at least 80% of patients was treated with a locking plate. Furthermore, a sensitivity analysis was done for all studies in which arthroplasty was the operative intervention. Finally, to explore the impact of fracture type on the functional outcome, a sensitivity analysis was performed including only Neer 3-part and 4-part fractures.

Different methods of meta-analysis may be differentially sensitive to studies with zero events on one or both study arms. Therefore, a sensitivity analysis to the choice of method of analysis was performed by means of the DerSimonian Laird method with correction and the inverse variance with and without correction for zero event data.[5]

RESULTS

Figure 1 shows a flowchart of the literature search. In the end, 22 studies were included.[3,4,9–12,15,17,20,21,23,24,29–32,35,36,38,43,45,46,49] There were seven RCTs and 15 observational studies, of which nine were retrospective, four prospective, and two a combination of retrospective and prospective design.

Quality Assessment

The MINORS score for all included studies ranged from 12 to 22 with a median of 17.5 (IQR 14-21). The MINORS score ranged from 16 to 22 with a median of 21 (IQR 21-22) for RCTs and from 12 to 21 with a median of 16 (IQR 14-18) for observational studies. Study-

specific MINORS scores are provided in Appendix 3. The MINORS criteria for unbiased assessment of study end-points and prospective calculation of study size were rarely met.

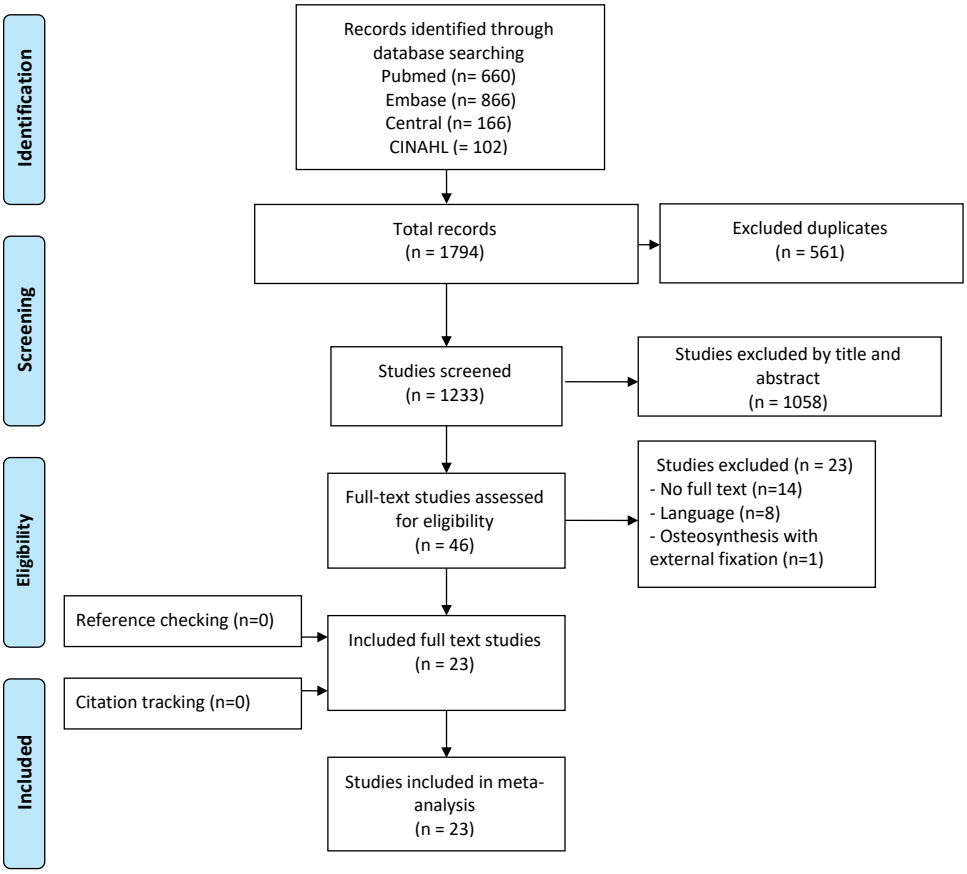

FIGURE 1. PRISMA flow diagram representing the search and screen process of studies comparing surgical to conservative treatment of proximal humerus fractures.

Baseline characteristics of study participants

Details of the included studies and patients are provided in Table 1. The 22 studies included a total of 1743 patients for meta-analysis: 910 treated operatively and 833 nonoperatively. The weighted average age was 68.3 years, and 75% were female. Follow-up ranged from 12 to 86 months.

TABLE 1. Baseline characteristics of studies included in a meta-analysis of proximal humerus fractures comparing operative to nonoperative treatment

Study	Study design	Country	Fracture classification	Treatment groups	Number of patients	Follow-up (months)	Age (years, range or ± SD)	Female/ Male
Boons 2012[4]	RCT	Netherlands	Neer 4-part	Operative: arthroplasty Nonoperative: Sling	25 25	12 12	76,4 (5,6) 79,9 (7,7)	24/1 23/2
Fjalestad 2012-14*[10,11]	RCT	Norway	AO type B2-C2	Operative: LP Nonoperative: Sling + closed reduction	25 25	24 24	72,2 (60-86) 73,1 (60-88)	20/5 24/1
Olerud 2011[31]	RCT	Sweden	Neer 4-part	Operative: hemiarthroplasty Nonoperative: Sling	27 28	24 24	75,8 (58-90) 77,5 (60-92)	23/4 24/4
Olerud 2011b[32]	RCT	Sweden	Neer 3-part	Operative: LP Nonoperative: Sling	30 29	24 24	72,9 (56-92) 74,9 (58-88)	24/6 24/5
Rangan 2015[35]	RCT	England	Neer 2,3,4-part	Operative: PHN(n=4), LP(n=90), TB(n=1), arthroplasty(n=10), screw(n=2), other(n=2) Nonoperative: Sling or hanging cast	125 125	24 24	66,6 (11,8) 65,43 (12,09)	97/28 95/30
Stableforth 1984[43]	RCT	England	Neer 4-part	Operative: arthroplasty Nonoperative: Sling	16 16	Overall (range): 18-144	65,6 (52-88) 70,1 (60-85)	12/4 13/3
Zyto 1997[49]	RCT	Sweden	Neer 3,4-part	Operative: Tension band Nonoperative: Sling	20 20	50 50	73 (7,5) 75 (6,7)	18/2 17/3
Court-Brown 2001[9]	PC	Scotland	Neer 2-part	Operative: PHN + tension band fixation Nonoperative: Sling	18 31	12 12	73 78	NR
Hauschild 2013[17]	PC	Germany	AO type A2, A3	Operative: PHN, LP Nonoperative: Sling	133 31	12 12	62,9 (17,2) 65,6 (13,3)	97/36 22/9
Innocenti 2013[21]	PC	Italy	Neer 2,3,4-part	Operative: K-wire Nonoperative: Sling	23 19	Overall: 86	73,92 (6,01) 77,47 (6,95)	Total: 38/13
Noureai 2014[29]	PC	Iran	Neer 2,3,4-part	Operative: LP, Tension band, K-wire Nonoperative: Sling	57 57	12 12	Total: 52,9 (15,0)	Total: 70/44

TABLE 1. Continued

Study	Study design	Country	Fracture classification	Treatment groups	Number of patients	Follow-up (months)	Age (years, range or ± SD)	Female/ Male
Fjalestad 2005[12]	RC+PC	Norway	AO type A,B,C	Operative: K-wire(n=4), LP(n=5), Screws(n=4), Screws + cerclage(n=2)	15	12	Total: 70 (25-95)	Total: 50/20
				Nonoperative: Sling	55	12		
Ilchman 1998[20]	RC+PC	Sweden / Swiss	Neer 3,4-part	Operative: Tension band	18	63	61 (23-80)	13/5
				Nonoperative: Sling (n=10), Closed reduction(n=4), Open reduction(n=2)	16	70	70 (23-91)	13/3
Blonna 2009[3]	RC	Italy	AO type A2,2	Operative: K-wire	42	32	73 (7,83)	20/12
				Nonoperative: Sling	37	35	75,1 (8,0)	26/9
vd Broek 2007[46]	RC	Netherlands	Neer 4,5,6 fracture	Operative: PHN	27	16	64,6 (27-87)	NR
				Nonoperative: Sling	17	69	69,4 (35-84)	
Hageman 2016[15]	RC	Netherlands	Neer 2,3,4-part	Operative: PHN (n=3); LP (n=23); K-wire (n=2), Screws (n=5)	33	37	59,0 (12,5)	22/11
				Nonoperative: Sling	33	70	60,1 (15,3)	24/9
Kollig 2003[23]	RC	Germany	Neer 4,5,6 fracture	Operative: LP(n=2), Screws + cerclage(n=7), K-wire(n=4)	13	82	52,5 (14,7)	NR
				Nonoperative: Sling	9	76	52,7 (11,5)	
Lange 2016[24]	RC	Germany	Neer 2,3,4-part	Operative: PHN	41	Overall: 55	69,1 (37-88)	35/6
				Nonoperative: hanging cast or dessault dressing	41		68,9 (42-93)	35/6
Okike 2015[30]	RC	US	Neer 2,3,4-part	Operative: LP	61	Overall: 40	total: 76,9	109/37
				Nonoperative: Sling	146			46/15
Roberson 2017[36]	RC	US	Neer 3,4-part	Operative: reversed arthroplasty	20	53	Overall: 71	19/1
				Nonoperative: Sling	19	29	(Range 52-88)	15/4
Sanders 2011[38]	RC	Australia	Neer 2,3,4-part	Operative: LP	17	37	58 (14)	9/8
				Nonoperative: Sling	18	42	64 (15)	12/6
Tamimi 2015[45]	RC	Canada	Neer 2,3,4-part	Operative: PHN(n=19),LP(n=44),K-wire(n=25)	88	26	Total: 65,3	Total:
				Nonoperative: Sling	25	28	(15,2)	57/31

*Fjalestad 2012[11] and 2014[10] were analyzed as one study as both described the same patient cohort
RC retrospective cohort study; RCT randomized controlled trial; PC prospective cohort study; NR not reported
TB tension band; PHN proximal humerus nail; LP locking plate

All studies but one included displaced proximal humerus fractures in their study. The majority of the included studies excluded patients with pathological fractures, open fractures, fractures of the skeletally immature, and other sustained injury to the affected side. Most studies (n=18, 82%) used the Neer classification and included patients with a Neer 2,3 or 4-part proximal humerus fracture. In seven studies at least 80% of patients were treated with a locking plate.[10,11,15,17,30,32,35,38] Four studies investigated arthroplasty; three hemiarthroplasty and one reverse shoulder arthroplasty[4,31,36,43], three studies assessed proximal humeral nails[9,24,46], and eight studied fixation by means of Kirschner wires, screws, tension band, or a combination of techniques.

Functional Outcome

Fourteen studies (64%, n=817) reported the Constant-Murley score after at least one year of follow-up (Appendix 4).[3,4,10,11,15,17,21,23,24,30–32,45,46] In patients with a proximal humerus fracture, the functional outcome as measured by the Constant-Murley score showed no difference in operative versus nonoperative treatment with a mean difference of -0.87 (CI, -5.13 – 3.38; P=0.69; I^2=69%)(Figure 2). Pooled effects of RCTs were similar to those of observational studies for all outcome measures (Figure 1 and Table 2). Figure 3 shows a funnel plot of the mean difference and standard error of the included studies using the Constant-Murley score; there was no important asymmetry observed.

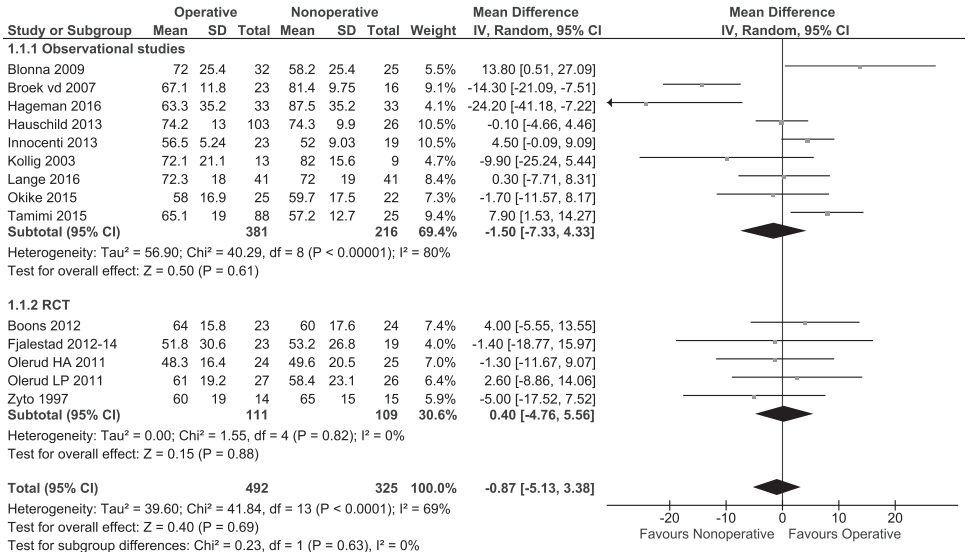

FIGURE 2. Functional outcome as measured with the Constant-Murley score in a systematic review of proximal humerus fractures comparing operative to nonoperative treatment

TABLE 2. Subgroup & sensitivity analyses of studies included in a meta-analysis of proximal humerus fractures comparing operative to nonoperative treatment

	Constant score				Major reintervention				Nonunion				Avascular necrosis			
Analysis description	**n**	**MD (95% CI)**		**P value**	**n**	**RR (95% CI)**		**P value**	**n**	**RR (95% CI)**		**P value**	**n**	**RR (95% CI)**		**P value**
All studies	14	-0.87	(-5.13, 3.38)	0.69	15	2.72	(1.71 - 4.34)	**< 0.0001**	13	0.45	(0.23 - 0.89)	**0.02**	13	1.24	(0.87 - 1.77)	0.24
Subgroup analysis																
RCT	5	0.40	(-4.76, 5.56)	0.88	6	1.45	(0.78 - 2.70)	0.25	6	0.48	(0.19 - 1.20)	0.12	6	0.88	(0.55 - 1.41)	0.59
Observational studies	9	-1.50	(-7.33, 4.33)	0.61	7	5.43	(2.51 - 11.74)	**< 0.0001**	7	0.41	(0.15 - 1.16)	0.09	7	1.93	(1.11 - 3.37)	**0.02**
Sensitivity analysis																
High-quality studies	11	0.55	(-2.93, 4.03)	0.76	11	2.52	(1.55 - 4.11)	**0.0002**	11	0.44	(0.21 - 0.93)	**0.03**	10	1.14	(0.74 - 1.74)	0.55
Studies after 2005	12	-0.14	(-4.65, 4.38)	0.95	14	2.58	(1.59 - 4.20)	**0.0001**	12	0.41	(0.18 - 0.89)	**0.03**	10	1.10	(0.72 - 1.69)	0.65
Locking plate	5	-0.15	(-0.43, 0.13)	0.30	7	1.81	(1.04 - 3.16)	**0.04**	6	0.37	(0.12 - 1.17)	0.09	6	1.35	(0.86 - 2.11)	0.19
Arthroplasty	2	1.50	(-5.24, 8.23)	0.66	4	2.66	(0.72 - 9.77)	0.14	3	0.52	(0.13 - 1.99)	0.34	2	0.17	(0.02 - 1.37)	0.10

Bold: significant pooled effect ($p < 0.05$); RCT randomized controlled trial; RR risk ratio; MD mean difference; CI confidence interval
Sensitivity analysis of locking plate includes studies comparing locking plate to nonoperative treatment
Sensitivity analysis of arthroplasty includes studies comparing hemiarthroplasty and reversed arthroplasty to nonoperative treatment

For studies that did not use the Constant-Murley score, we performed additional analysis with the standardized mean difference of different functional outcome measures which yielded the same result as the primary analysis (SMD -0.06; CI, -0.25 – 0.12; P=0.52; I^2=53%)(Appendix 5). Seven studies (n=327) reported functional outcome of patients treated with a Neer 3-part or 4-part fracture.[4,10,24,31,32,36,49] Forty-three percent of patients with Neer 4-part fractures were initially treated with arthroplasty (Table 1). A subgroup analysis of these studies showed no difference in standardized mean difference of functional outcome measures between operative and nonoperative treatment with a mean difference of 0.02 (CI, -0.20 – 0.24; P=0.86; I^2=0%)(Appendix 6).

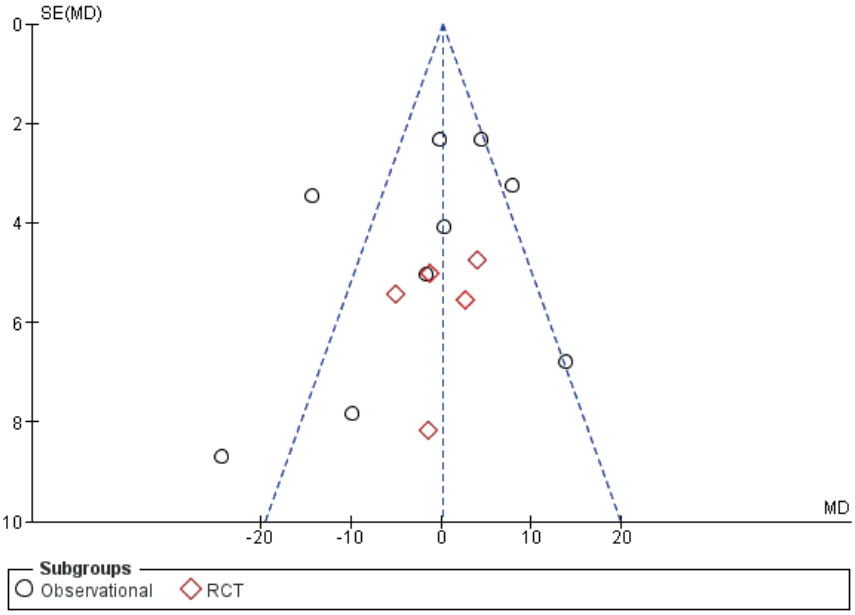

FIGURE 3. Funnel plot of studies included in a meta-analysis reporting Constant-Murley scores after operative or nonoperative treatment of proximal humerus fractures. (MD mean difference; SE standard error)

Major reinterventions

Fifteen studies (68%, n=938) reported on major reinterventions (Appendix 4).[3,4,10,11,15,20,21,24,30–32,35,36,38,43,46] Two studies had no major reintervention in either treatment arm at follow-up. Major reinterventions occurred more often in the operative group than the nonoperative group with a risk ratio (RR) of 2.72 (CI, 1.71 – 4.34; P < 0.0001; I^2=0%)(Appendix 7). Utilizing different methods of incorporating studies in the meta-

analysis with zero event data in one or both arms yielded similar results (Appendix 8). Implant removal was reported in 10 studies (45%). The mean percentage of implant removal across studies was 21% (range 0 – 100%). When stratified by study design, observational studies showed a greater risk for major reinterventions in the operative treatment group compared to the nonoperative group (RR 5.43; CI 2.51 – 11.74; P < 0.0001; I^2=0%)(Table 2). Five studies specified their reinterventions for nonoperatively treated patients: four patients received arthroplasty for displacement and malunion, two patients received ORIF for displacement, and two patients received acromioplasty for impingement complaints.

Nonunion

Thirteen studies (59%) reported on nonunion (Appendix 4). Operative treatment of proximal humerus fractures resulted in fewer nonunions compared to nonoperative treatment with a RR of 0.45 (CI, 0.23 – 0.89; P=0.02; I^2=0%)(Appendix 9). When stratified by study design, both subgroups showed a similar, non-significant, pooled effect (Table 2).

Avascular necrosis

Thirteen studies (59%) reported on avascular necrosis (Appendix 4). There was no difference in the rate of avascular necrosis between operative and nonoperative treatment for proximal humerus fractures with a RR of 1.24 (CI, 0.87 – 1.77; P=0.24; I^2=24%)(Appendix 10). When stratified by study design, observational studies showed a higher risk of avascular necrosis for the operative group compared to the nonoperative group (RR 1.93; CI 1.11 – 3.37; P=0.02; I^2=9%)(Table 2).

Sensitivity Analysis

Sensitivity analysis did not significantly alter the primary and secondary outcome measures (Table 2).

DISCUSSION

In this systematic review and meta-analysis of patients with displaced proximal humerus fractures, there was no difference in physical function as measured with the Constant-Murley score after operative or nonoperative treatment. Subgroup analysis for Neer 3-part or 4-part fractures neither showed differences in functional outcome. Results of the primary and secondary outcome measures were similar from the pooled effects of RCTs and observational studies. There was a higher risk for major reinterventions and a

lower risk of nonunion after operative treatment compared to nonoperative treatment. This the largest meta-analysis in the current literature by including both RCTs and observational studies.

Compared to nonoperative treatment, there is no improved functional outcome after operative treatment for displaced proximal humerus fractures, which confirms findings from previous meta-analyses.[16,48] A recent systematic review of displaced proximal humerus fractures is based on only 7 RCTs with just over 500 patients.[16] With a total of 250 patients, the PROFHER trial represents the most substantial evidence currently available.[35] Demographic patient characteristics of the PROFHER trial are comparable to the included studies in this meta-analysis (Table 1). However, only 4.4% of patients in the PROFHER trial suffered a Neer 4-part fracture compared to 21% of patients in this meta-analysis. Therefore, compared to previous, smaller magnitude meta-analyses, this review contributes substantially to the current evidence and enables recommendations for a broader patient population. Furthermore, this is the first meta-analysis in which subgroup analysis for Neer 3-part and 4-part fractures was possible and showed no differences in operative versus nonoperative treatment.

This review showed similar pooled effects of observational studies and RCTs for the primary and secondary outcome measures. This finding is similar to previous meta-analyses in orthopaedic trauma surgery including both study designs.[1,2,19,41,42] As such, this review speaks to the growing potential of observational studies in orthopedic trauma surgery and contributes to the expanding discussion about the value of different study designs.[13]

In this review, the major reintervention rate included every additional surgery except for implant removal because of patient preference, implant-related irritation, or a stiff shoulder. Therefore, the major reintervention rate in this review is a surrogate marker for severe complications (e.g. implant failure, deep infection, nonunion, impingement, or avascular necrosis) after operative and nonoperative treatment of displaced proximal humerus fractures. This is the first review to show significantly more severe complications requiring surgical re-intervention after operative treatment of displaced proximal humerus fractures. These procedures add up to the additional surgery for implant removal for 21% of the patients for a less serious indication.

Another new finding is the higher risk of nonunion for nonoperatively treated patients. RCTs and observational studies alone were not able to detect a significant difference in this outcome. This demonstrates the added value of increasing study power by

including observational studies in order to detect rare outcomes. It is important to note that this difference is supported by the sensitivity analysis including only high-quality RCTs and observational studies (Table 2).

This review found no difference in the rate of avascular necrosis between the nonoperative and operative management. However, it should be noted that three of the 15 studies reporting on avascular necrosis had a follow-up of 12 months while avascular necrosis can be detected up to two years of follow-up. For this outcome measure, the pooled effect of observational studies was significantly different than the pooled effect of RCTs. However, in the sensitivity analysis with high quality studies, this contrasting result did not yield and pooled effects of both study designs were similar again. This demonstrates the importance of evaluating the quality of the included studies (Table 2). Therefore, including a study in a meta-analysis should be based on the quality of the study regardless of the study design.[41] Generally, RCTs will be of higher quality and thus included for analysis, however, a high quality observational study should be chosen over a low quality RCT.

The results of this systematic review and meta-analysis should be interpreted in the light of several limitations. First, the results of the meta-analysis may be influenced by missed studies in the database search or by publication bias. However, an extensive search was performed using multiple databases, and the citations and references of included studies were also screened. Furthermore, a funnel plot of the primary outcome measure did not suggest possible bias due to selective publication. Second, results of observational studies are more heterogeneous than those of RCTs in the meta-analysis of the Constant-Murley score. Still, it should be noted despite heterogeneity in mean differences of the observational studies, the observed effects all are within a range of the Constant-Murley score which is clinically nonimportant.[47] Third, in the analysis of functional outcome, we did not distinguish between 12 or more than 12 months of follow-up since prior studies have shown the greatest increase in functional outcome takes place in the first six months and no significant improvement is to be expected after 12 months.[9,10,31,32,35] This is further supported by an additional sensitivity analysis that showed no differences in functional outcome at 12 months and at 24 or more months. Fourth, the Neer classification for proximal humerus fractures is the most frequently used classification system in the literature even though it has been considered to have important limitations. However, no other system for evaluating these fractures is consistently more reliable than the Neer classification.[6] Fifth, The majority of the included studies are European and only three studies described patients from Northern America, let alone other continents. However, subgroup analyses revealed no differences for the primary and secondary outcome measures between these continents (data not shown).

Finally, it should be noted that the majority of studies in this review excluded patients with pathological fractures, open fractures, fractures of skeletal immature patients, and other sustained injuries to the affected arm. As a result, recommendations from this review are not applicable to these patients.

Although we acknowledge the vast amount of existing systematic reviews on this topic[14,16,34,48], we feel that the several unique qualities of this meta-analysis contribute to the existing knowledge. Strengths of this study include the consistent results of the different sensitivity analyses for time of publication, type of osteosynthesis, and arthroplasty. Furthermore, by including observational studies in addition to the highly selective patient population of RCTs, the analyzed patients may be more representative of patients encountered in daily clinical practice and also improve generalizability of our results. We also demonstrated that findings were consistent across study designs with respect to different outcome measures. Although no subgroup analysis could be performed on elderly patients > 65 years old, the mean age of all patients in this review was 68 years old with a relatively small standard deviation for the majority of the included studies; therefore, we feel confident that recommendations from this review apply to the average elderly patient. Finally, this is the largest meta-analysis in the literature with the highest number of patients available for analysis of proximal humerus fractures.

CONCLUSIONS

We recommend nonoperative treatment for the average elderly patient (aged >65 years) with a displaced proximal humerus fracture. Pooled effects of observational studies were similar to those of RCTs, and the inclusion of observational studies improves the generalizability of findings.

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APPENDICES

Appendix 1. Search Syntax

Date of search: March 30th, 2017

Searchstring PubMed/MEDLINE (n= 660)

(Humeral Fractures[MeSH Terms] OR Shoulder Fractures[MeSH Terms] OR ((humeral[Title/Abstract] OR humerus[Title/Abstract] OR humeri[Title/Abstract] OR humor[Title/Abstract] OR (upper[Title/Abstract] AND arm[Title/Abstract] AND bone[Title/Abstract]) OR (upperarm[Title/Abstract] AND bone[Title/Abstract])) AND fractur*[Title/Abstract])) AND (proximal[Title/Abstract] OR sub-capital[Title/Abstract] OR subcapital[Title/Abstract] OR neck[Title/Abstract]) AND (surgery[subheading] OR Fracture Healing[MeSH Terms] OR Fracture Fixation[MeSH Terms] OR Surgical Procedures, Operative[MeSH Terms] OR orthopedics[MeSH Terms] OR orthopedics[Title/Abstract] OR orthopaedics[Title/Abstract] OR orthopedic[Title/Abstract] OR orthopaedic[Title/Abstract] OR surgery[Title/Abstract] OR surgical[Title/Abstract] OR operative[Title/Abstract] OR operate[Title/Abstract] OR operating[Title/Abstract] OR operated[Title/Abstract] OR operation[Title/Abstract]) AND (conservative[Title/Abstract] OR conventional[Title/Abstract] OR non-operative[Title/Abstract] OR non-surgical[Title/Abstract] OR non surgical[Title/Abstract] OR nonoperative[Title/Abstract] OR Physical Therapy Modalities[MeSH Terms] OR sling[Title/Abstract] OR collar[Title/Abstract] OR cuff[Title/Abstract] OR bandages[Title/Abstract] OR bandage[Title/Abstract])

Searchstring Embase (n= 866)

('humerus'/exp OR humerus:ti,ab OR humeri:ti,ab OR humer:ti,ab OR humor:ti,ab OR 'corpus humeri':ti,ab OR 'upper arm bone':ti,ab OR 'upperarm bone':ti,ab OR humeral:ti,ab) AND ('fracture'/exp OR fracture:ti,ab OR fractured:ti,ab OR fractures:ti,ab) AND (proximal:ti,ab OR 'sub capital':ti,ab OR 'subcapital':ti,ab OR neck:ti,ab) AND ('surgery'/exp OR surgery:ti,ab OR surgical:ti,ab OR operative:ti,ab OR operation:ti,ab OR 'Fracture Healing':ti,ab OR 'Fracture fixation':ti,ab OR 'Surgical Procedures':ti,ab OR orthopedics:ti,ab OR orthopedic:ti,ab OR orthopaedics:ti,ab OR orthopaedic:ti,ab OR operate:ti,ab OR operating:ti,ab OR operated:ti,ab) AND ('conservative treatment'/exp OR 'conservative treatment':ti,ab OR conservative:ti,ab OR conventional:ti,ab OR 'non-operative':ti,ab OR nonoperative:ti,ab OR non-surgical:ti,ab OR 'non surgical':ti,ab OR sling:ti,ab OR collar:ti,ab OR cuff:ti,ab OR bandages:ti,ab OR bandage:ti,ab)

Searchstring CENTRAL (The Cochrane Library) (n=166)

humerus AND fracture AND (proximal OR neck OR sub capital OR subcapital)

Searchstring CINAHL (n= 102)

(humerus OR humeri OR humer OR humor OR corpus humeri OR upper arm bone OR upperarm bone OR humeral) AND (fracture OR fractured OR fractures) AND (proximal OR sub capital OR neck OR subcapital) AND (surgery OR surgical OR operative OR operation OR Fracture Healing OR Fracture fixation OR Surgical Procedures OR orthopedics OR orthopedic OR orthopaedics OR orthopaedic OR operate OR operating OR operated) AND (conservative treatment OR conservative OR conventional OR non-operative OR nonoperative OR non-surgical OR non surgical OR sling OR collar OR cuff OR bandages OR bandage)

APPENDIX 2. MINORS assessment criteria

Criteria	2	1	0
A clearly stated aim	Aim or hypothesis including outcomes have been reported	Aim or hypothesis have been reported without a clear outcome	Not reported
Inclusion of consecutive patients	Explicit inclusion and exclusion criteria have been reported	Unclear or poor description inclusion and exclusion criteria have been reported	Not reported
Prospective collection of data	Prospective	Retrospective	Not reported
Endpoints appropriate to the aim of the study	Outcomes are appropriate to the aim of the study	Outcomes are not appropriate to the aim of the study	Not reported
Unbiased assessment of the study endpoint	Blind evaluation of objective outcomes and double-blind evaluation of subjective outcomes	One or more outcomes have been blinded	No blinding / not reported
Follow-up period appropriate to the aim of the study	≥ 1 year	< 1 year	Not reported
Loss to follow-up less than 5%	≤ 5%	> 5% and ≤ 20%	Not reported / >20%
Prospective calculation of the study size	Power analysis has been performed	Explanation for the number of included patients without a power analysis	Not reported / not performed
An adequate control group	Plate or intramedullary fixation compared with a conservative treatment	Not applicable	Not reported
Contemporary groups	Study group and controls have been managed during the same time period	Study group and controls have not been managed during the same time period	Not reported / unclear discription
Baseline equivalence of groups	Baseline characteristics have been described for both groups and are comparable	Baseline characteristics have not been described thoroughly or are not comparable	Not reported
Adequate statistical analyses	Statistical analysis has been described including the type of test	Inadequate statistical analysis	Not reported

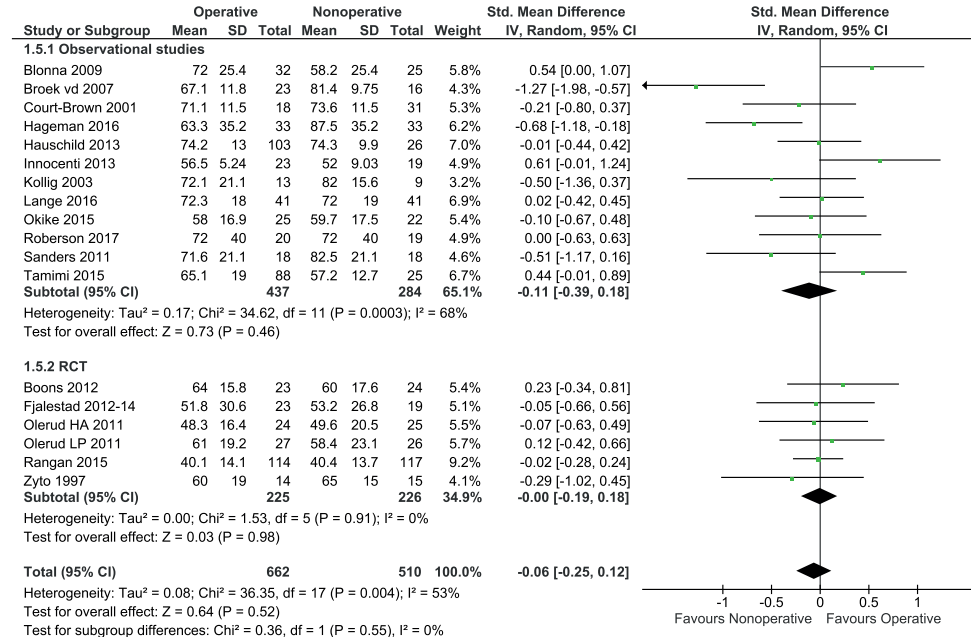
Criteria	Blonna 2009	Boons 2012	vd Broek 2007	Court-Brown 2001	Fjalestad 2005	Fjalestad 2012-14	Hageman 2016	Hauschild 2013	Ilchman 1998	Innocenti 2013	Kollig 2003	Lange 2016	Nourai 2014	Okike 2015	Olerud 2011a	Olerud 2011b	Rangan 2015	Robertson 2017	Sanders 2011	Stableforth 1984	Tamimi 2015	Zyto 1997
A clearly stated aim	2	2	2	1	1	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2
Inclusion of consecutive patients	2	2	2	2	1	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2
Prospective collection of data	0	2	0	2	1	2	0	2	0	2	0	0	2	0	2	2	2	0	0	2	0	2
Endpoints appropriate to the aim of the study	2	2	2	2	1	2	2	2	1	2	2	2	1	2	2	2	2	2	2	1	2	2
Unbiased assessment of the study endpoint	1	1	1	1	1	1	1	1	0	0	0	0	0	0	1	1	1	0	1	0	0	1
Follow-up period appropriate to the aim of the study	2	2	1	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2
Loss to follow-up less than 5%	1	1	1	0	0	2	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	2
Prospective calculation of the study size	0	2	0	0	0	1	0	1	0	0	0	0	0	0	1	1	2	0	0	0	0	0
An adequate control group	2	2	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	1	2
Contemporary groups	2	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2
Baseline equivalence of groups	2	2	1	2	1	2	2	2	2	2	0	2	0	1	2	2	2	2	2	2	1	2
Adequate statistical analyses	2	2	0	2	2	2	2	2	1	2	0	2	1	2	2	2	2	2	2	0	2	2
Total quality score MINORS	**18**	**22**	**13**	**18**	**14**	**22**	**17**	**21**	**14**	**19**	**12**	**16**	**13**	**16**	**21**	**21**	**22**	**16**	**18**	**16**	**14**	**21**

APPENDIX 3. Quality assessment of all included studies in a systematic review of proximal humerus fractures comparing operative to nonoperative treatment

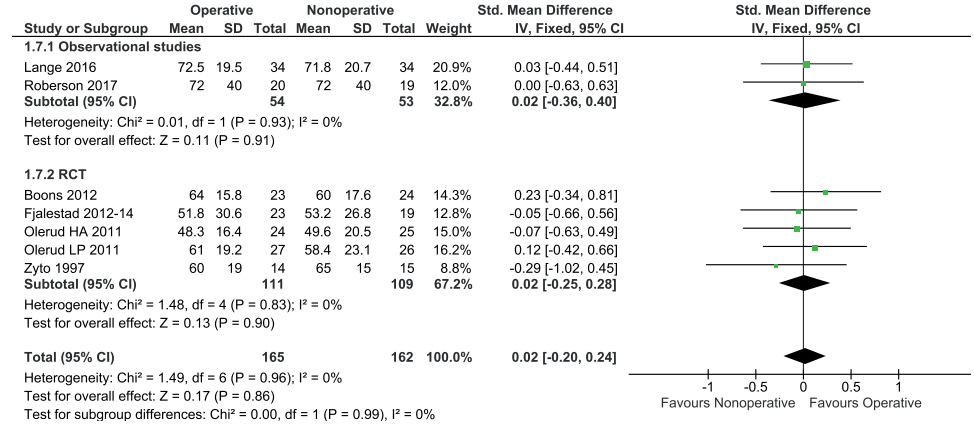
APPENDIX 4. Outcome measures in a systematic review of proximal humerus fractures comparing operative to nonoperative treatment

Study		Constant score (± SD)	Revision surgery	Non-union	AVN	DASH score (± SD)	Implant removal
Blonna 2009	Operative	72 (25.4)	0	0	NR	15.0 (3.0)	32
	Nonoperative	58.2 (25.4)	0	0		30.5 (5.1)	
Boons 2012	Operative	64 (15.8)	1	2	0	NR	0
	Nonoperative	60 (17.6)	1	3	2		
vd Broek 2007	Operative	67.1 (11.8)	3	0	0	NR	5
	Nonoperative	81.4 (9.8)	0	1	0		
Court-Brown 2001	Operative	NR	NR	1	NR	NR	NR
	Nonoperative			4			
Fjalestad 2005	Operative	NR	NR	1	3	NR	NR
	Nonoperative			5	2		
Fjalestad 2012-14*	Operative	51.8 (30.6)	1	1	12	NR	7
	Nonoperative	53.2 (26.8)	1	2	15		
Hageman 2016	Operative	63.3 (35.2)	5	NR	1	22 (13.9)	2
	Nonoperative	87.5 (35.2)	2		0	10.3 (13.9)	
Hauschild 2013	Operative	74.2 (13)	NR	1	1	NR	NR
	Nonoperative	74.3 (9.9)		0	0		
Ilchman 1998	Operative	NR	4	NR	9	NR	NR
	Nonoperative		1		7		
Innocenti 2013	Operative	56.5 (5.2)	0	NR	0	NR	23
	Nonoperative	52 (9.0)	0		0		
Kollig 2003	Operative	72.1 (21.1)	NR	NR	NR	NR	NR
	Nonoperative	82 (15.6)					
Lange 2016	Operative	72.3 (18)	13	NR	NR	NR	NR
	Nonoperative	72 (19)	0				
Noureai 2014	Operative	NR	NR	NR	NR	NR	NR
	Nonoperative						
Okike 2015	Operative	58 (16.9)	8	0	10	26.5 (17.8)	NR
	Nonoperative	59.7 (17.5)	2	2	3	25.1 (18.2)	
Olerud 2011a	Operative	48.3 (16.4)	2	0	0	30.2 (18.3)	1
	Nonoperative	49.6 (20.5)	1	1	3	36.9 (21.3)	
Olerud 2011b	Operative	61 (19.2)	4	1	3	26.4 (25.2)	5
	Nonoperative	58.4 (23.1)	1	1	2	35 (26.8)	
Rangan 2015	Operative	NR	11	0	4	NR	NR
	Nonoperative		11	5	1		
Roberson 2017	Operative	NR	3	NR	NR	NR	0
	Nonoperative		0				
Sanders 2011	Operative	NR	3	0	8	NR	7
	Nonoperative		0	1	5		
Stableforth 1984	Operative	NR	1	NR	NR	NR	1
	Nonoperative		0				
Tamimi 2015	Operative	65.1 (19)	NR	NR	NR	33 (21.8)	NR
	Nonoperative	57.2 (12.7)				38.4 (19.2)	
Zyto 1997	Operative	60 (19)	NR	1	1	NR	1
	Nonoperative	65 (15)		0	0		

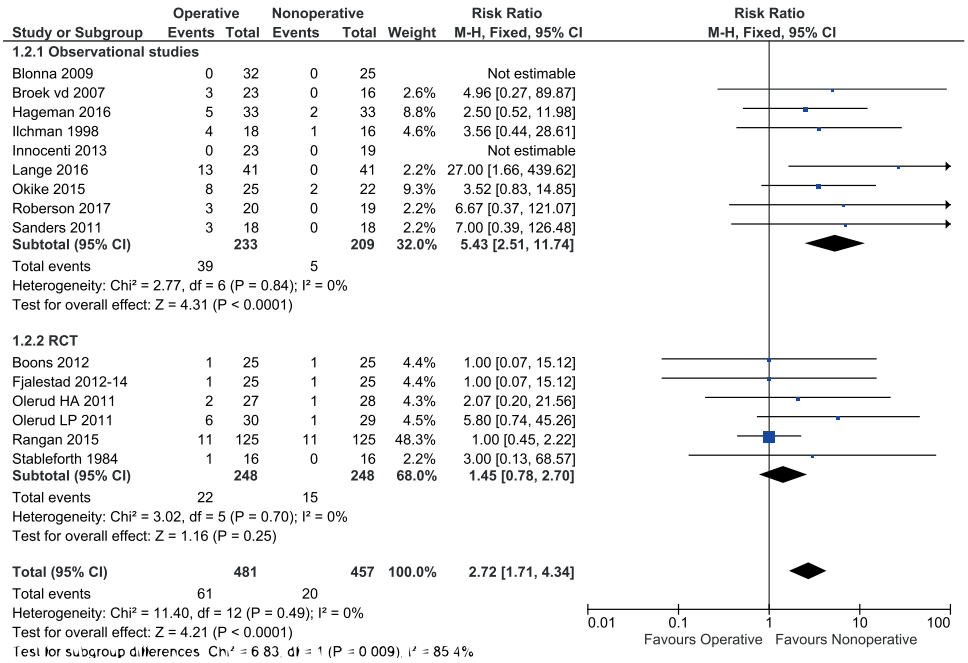
*In this analysis Fjalestad 2012 and 2014 were seen as one study as both studies describe the same patient cohort
AVN avascular necrosis; NR not reported; SD standard deviation



APPENDIX 5. Standardized mean difference of functional outcome scores in a systematic review of proximal humerus fractures comparing operative to nonoperative treatment.



APPENDIX 6. Subgroup analyses looking at standardized mean difference for functional outcome measures including only studies reporting on Neer 3-part or 4-part fractures in a systematic review of proximal humerus fractures comparing operative to nonoperative treatment.

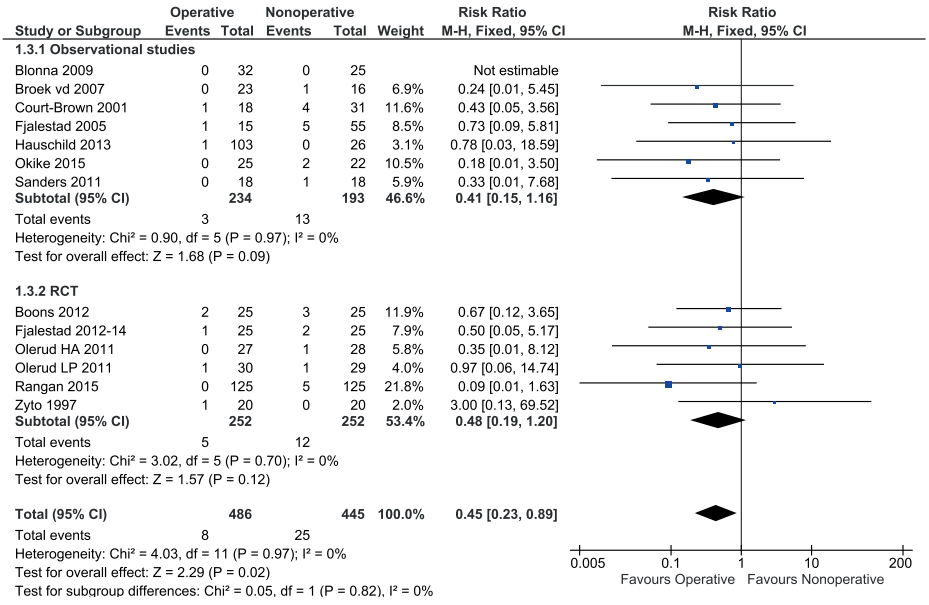


APPENDIX 7. Revision surgery in a systematic review of proximal humerus fractures comparing operative to nonoperative treatment

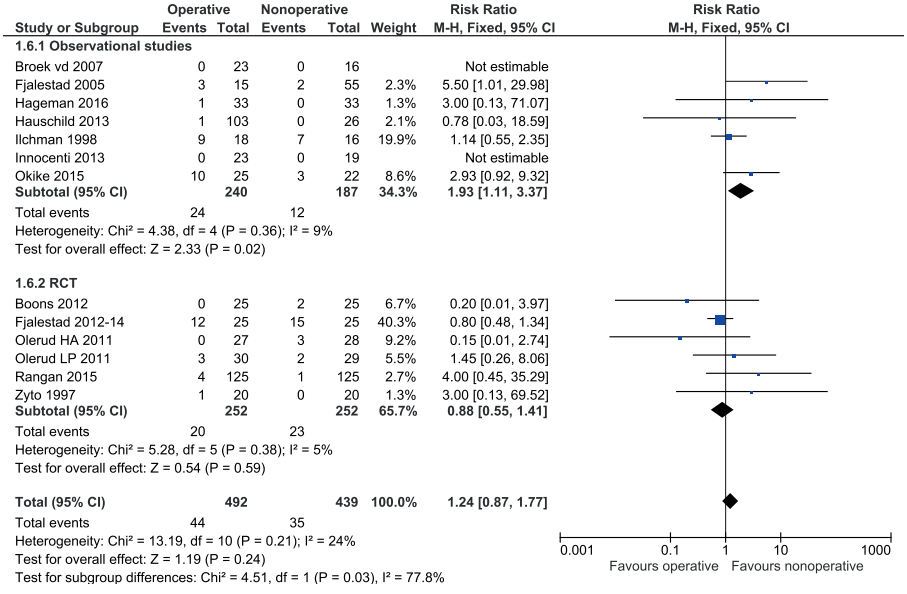
APPENDIX 8. Impact of different methods to handle zero-event data in a meta-analysis of operative versus nonoperative treatment of proximal humerus fractures and major reintervention

Method	Observational studies OR (95% CI)	RCT OR (95% CI)	Total OR (95% CI)
Mantel-Haenzel*	5.46 (2.29, 13.01)	1.37 (0.85, 2.77)	2.32 (1.34, 4.02)
Inverse variance - no correction	3.76 (1.30, 10.91)	1.32 (0.64, 2.71)	1.83 (1.01, 3.33)
Inverse variance - with correction	4.64 (2.03, 10.62)	1.37 (0.68, 2.77)	2.29 (1.30, 7.28)
DerSimonian Laird with correction	4.75 (1.43, 15.73)	1.71 (0.57, 5.13)	2.96 (1.26, 7.00)

* Method used in meta-analysis; OR odds-ratio; CI confidence interval
In a model with correction 0.5 is added to every table of the 2x2 table



APPENDIX 9. Nonunion in a systematic review of proximal humerus fractures comparing operative to nonoperative treatment



APPENDIX 10. Avascular necrosis in a systematic review of proximal humerus fractures comparing operative to nonoperative treatment

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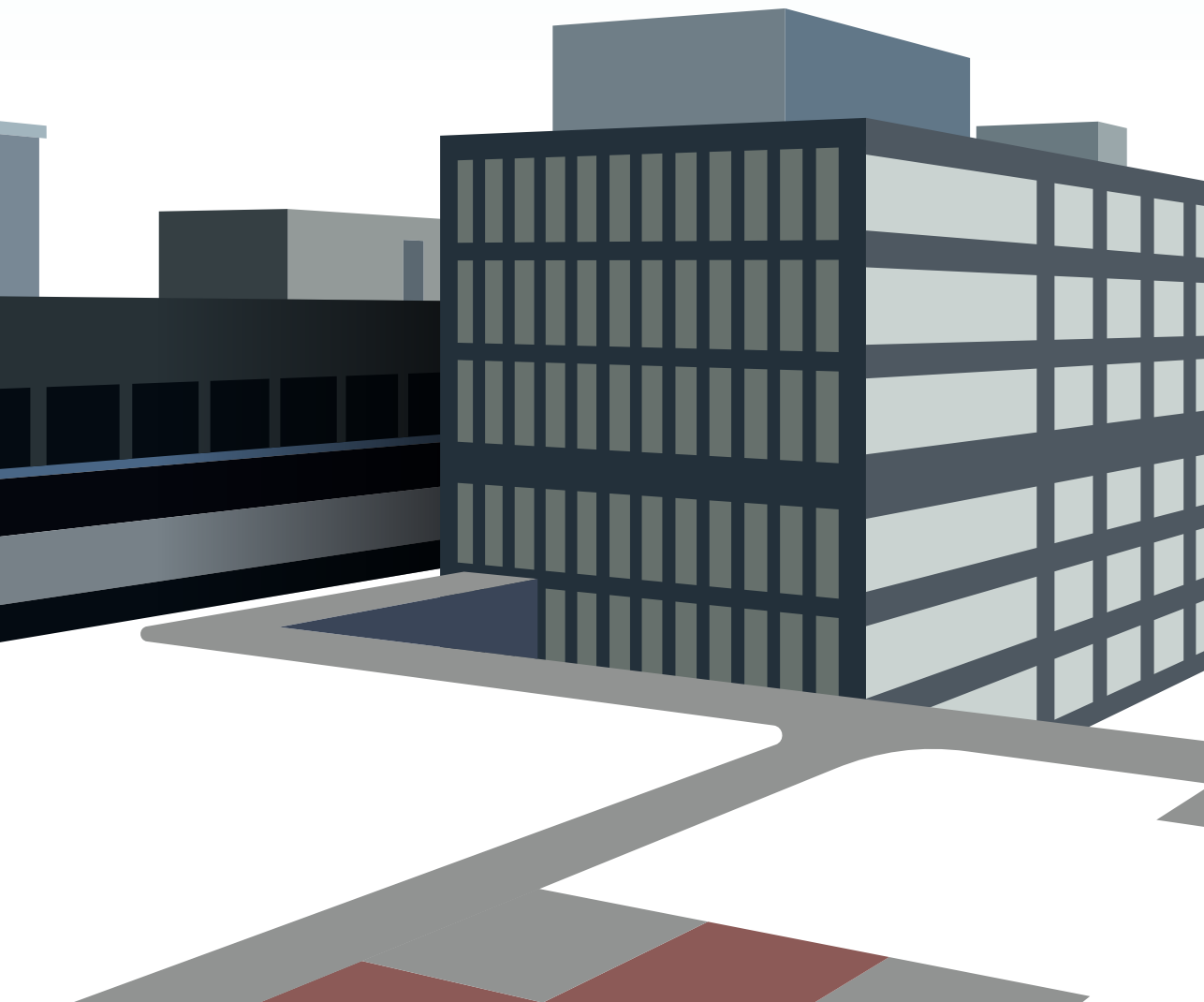

CHAPTER 8

Long-term follow-up after MIPO Philos plating for proximal humerus fractures

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ABSTRACT

Introduction: Minimally invasive plate osteosynthesis (MIPO) has been described as a suitable technique for the treatment of proximal humerus fractures, but long-term functional results have never been reported. The aim of this study was to describe the long-term functional outcome and implant related irritation after MIPO for proximal humerus fractures.

Methods: A long-term prospective cohort analysis was performed on all patients treated for a proximal humerus fracture using MIPO with a Philos plate (Synthes, Switzerland) between December 2007 and October 2010. The primary outcome was the QuickDASH score. Secondary outcome measures were the Subjective Shoulder Value (SSV), implant related irritation and implant removal.

Results: Seventy-nine out of 97 patients (81%) with a mean age of 59 years were available for follow-up. The mean follow-up was 8.3 years (SD 0.8). The mean QuickDASH score was 5.6 (SD 14). The mean SSV was 92 (SD 11). Forty out of 79 patients (50,6%) had implant removal, and of those, 27/40 (67,5%) were due to implant related irritation. On average, the implant was removed after 1.2 years (SD 0.5). In bivariate analysis there was an association between the AO classification and the QuickDASH ($p = 0.008$).

Conclusion: Treatment of proximal humerus fractures using MIPO with Philos through a deltoid split approach showed promising results. A good function can be assumed due to the excellent scores of patient oriented questionnaires. However, about one third of the patients will have a second operation for implant removal due to implant related irritation.

INTRODUCTION

Proximal humerus fractures are very common and account for 5% of all fractures in the emergency department, with an incidence of 82 per 100,000 people [1-6]. The incidence has an unipolar distribution with a typical patient being relatively fit, female and more than 80 years old [7]. Most patients are treated non-operatively while one out of five will undergo surgery even though no clear benefit of operative treatment has been shown [6,8,9].

The standard approach for osteosynthesis of proximal humerus fractures is the deltopectoral approach, which generally is considered the open approach [1,10-12]. Over the past decade, there has been an increasing interest in minimally invasive plate osteosynthesis (MIPO) of proximal humerus fractures through the deltoid split approach [10,13-19]. Previously reported possible advantages of MIPO are: less soft tissue stripping and a lower risk of injury to the ascending branch of the anterior circumflex humeral artery resulting in lower rates of avascular necrosis (AVN) and shorter operation time [10,15,16,18]. Possible disadvantages are risk of damage to the axillary nerve [10] and, in case of a later shoulder prosthesis, the need for a different second surgical approach. Several studies have reported on the short-term results of this technique [10,14,15,19,20]. Although long-term results of the open approach for proximal humerus fracture treatment have been reported, little is known about the long-term results after MIPO with Philos [12,21].

The aim of this study was to analyze the long-term functional outcome after MIPO with Philos for proximal humerus fractures. Additionally we assessed implant related irritation and implant removal.

METHODS

Study design

Between December 2007 and October 2010, 191 patients with a proximal humerus fracture were treated with MIPO through a 'deltoid split' approach in our center using the Philos® system (Synthes, Switzerland). Patients were operated by 16 different surgeons. Two of these surgeons performed 50% of all operations. In 2013 Acklin et al. published prospectively gathered data on the short-term outcome of 97 of these patients available for follow-up [10]. In the current study, this cohort was approached and analyzed again to obtain long-term outcome on these patients. Exclusion criteria

were death, a second trauma to the operated arm, inability to answer questions, or absence of written consent. This study was approved by the Cantonal Ethic Committee Zürich (KEK-ZH-Nr. 2017-00428).

Operative procedure and indications

All patients were treated in a MIPO technique. In beach chair position a minimally invasive anterolateral deltoid split approach was performed. After reduction of the humeral head and non-absorbable suture insertion in the tendons of the rotator cuff, a five hole Philos® plate was inserted. This was done sub-muscular, either percutaneously or with a radiolucent aiming device, under Langenbeck protection to preserve the axillary nerve. The plate was fixed to the humeral head with 4 locking screws and, depending on bone quality, with two to four conventional or locking screws to the shaft. The non-absorbable sutures were then knotted to the plate for additional stabilization and to prevent secondary dislocation.

Postoperatively, patients were allowed immediate active-assisted mobilization without sling immobilization. Abduction of more than 90° was not allowed in the first six weeks.

Indications for operative treatment were a varus displacement of >20°, a valgus displacement of >40°, an increased reclination >30°, a lateral displacement of > ½ diaphyseal diameter, and/or displacement of the major and/or minor tubercle of >5-10mm.

Baseline characteristics and outcome measures

Baseline characteristics were obtained from the prospectively collected data by Acklin et al. [10]. All patients were contacted by phone by an independent study nurse to assess shoulder function using the QuickDASH questionnaire [22] and the Subjective Shoulder Value (SSV) [23]. Implant removal was assessed using the algorithm of Hulsmans et al. [24]. If patients could not be reached after a minimum of five phone call attempts, their contact person and general practitioner were approached for contact details and the internet was searched for an alternative telephone number. A letter was sent to patients who could not be reached by phone, asking the patient to contact us. Patients were considered lost to follow-up if all these attempts were unsuccessful.

The primary outcome measure was shoulder function as measured by the QuickDASH score [22]. The QuickDASH is a validated measure for disability of the arm, shoulder and hand and provides a summative score on a 100-point scale, where a higher score indicates more disability. A QuickDASH score of less than 15 is considered an excellent result and a score of >40 indicates poor shoulder function [25].

Secondary outcome measures were SSV and implant related irritation or implant removal. The SSV is a subjective value for shoulder function determined by the patient after answering the following question: "What is the overall percent value of your shoulder if a completely normal shoulder represents 100%?", with 100% indicating the best function [23]. The SSV has shown a reliable agreement with the validated Constant Score for measuring shoulder function [26]. Implant removal and implant related irritation were discussed and analysed using the algorithm of Hulsmans et al., developed to analyse the presence of implant related irritation [24]. In addition, all patients were asked if they have had re-operations or were diagnosed with AVN in another hospital.

Statistical analysis

Data were described using frequencies and percentages for dichotomous and categorical variables, mean and standard deviation (SD) for normally distributed continuous data, and median and interquartile range (IQR) for non-normally distributed continuous data. In bivariate analysis, the association patients characteristics with the QuickDASH and SSV were assessed using a Mann-Whitney test for dichotomous variables (age), a Kruskal-Wallis test for ordinal variables (AO classification [27] and trauma mechanism) and a Spearman's rank correlation coefficient for continuous variables (age). A p value < 0.05 was considered significant which was tested using non-parametrical tests. The analyses were performed with SPSS, version 22.0 (IBM Corp., Armonk, NY) for Windows.

RESULTS

Informed consent was obtained from all individual participants included in the study. A total of 79 (81%) patients were available for follow-up and included for analysis (Figure 1). The mean age at the time of accident was 59 (SD ± 13) years and 37 (47%) patients were male (Table 1). The most common trauma mechanism was injury during skiing or snowboarding (51%). There were 16 (20%) type A, 33 (42%) type B, and 30 (38%) type C fractures according to the AO classification [27]. There were no significant differences in age, trauma mechanism, and AO classification of patients available for follow-up as compared to the initial cohort (data not shown). The mean follow-up duration was 8.3 years (SD 0.8).

The mean QuickDASH score was 5.6 (SD 14) and the mean SSV was 92 (SD 11) (Table 2). A total of 40/79 (50,6%) patients had implant removal on average 1.2 years (SD 0.5) after the initial osteosynthesis (Table 2). Twenty-seven of the 79 (34,2%) patients had implant removal due to implant irritation and 13/79 (16,5%) patients requested implant removal without implant irritation.

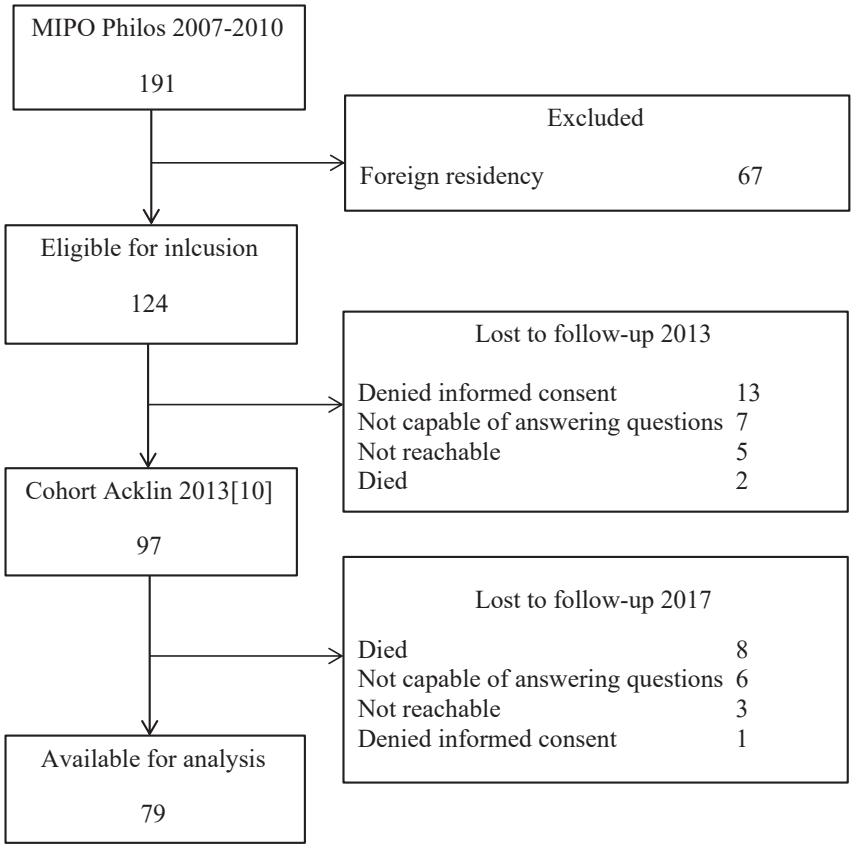

FIGURE 1. Flowchart patient inclusion

In bivariate analysis, there was a significant difference between AO fracture type and QuickDASH score with a mean of 0.4 (SD 0.9) for type A, 4.6 (SD 9.4) for type B and 9.5 (SD 20) for type C fractures ($p = 0.008$) (Table 3). There was no association of age or trauma mechanism with the QuickDASH score and also no association of age, trauma mechanism or AO classification with the SSV.

Previously published short-term follow-up of this cohort by Acklin et al. showed that all fractures were healed and no hardware failure occurred on follow-up radiographs. The mean radiological follow-up was 18 ± 6 months. There was a small but significant progression of varus displacement visible on last follow-up radiographs compared to postoperative evaluation (40°±8 and 41°±8; p= 0.015, respectively. Secondary screw perforation occurred in seven (7%) patients on average 7 weeks postoperatively and

required operative screw(s) replacement. Four patients (4%) had axillary nerve injury with atrophy of the anterior border of the deltoid muscle, however, without clinical consequences.

Furthermore, eight (8%) patients developed some degree of radiological AVN (grade 3-5) in short term follow-up. With a mean 99 months follow-up, five patients with AVN were available for long-term follow-up. The mean time to diagnosis was 16.7 months, the mean radiological follow-up was 34 months. They had a mean QuickDASH of 21 (SD 29) and a mean SSV of 72 (SD 12) which was significantly worse compared to patients without diagnosis of AVN in short-term follow-up (p=0.001 and p<0.001, respectively). One patient with a QuickDASH of 73 was offered a reversed arthroplasty but she refused. One patient with AVN grade 5 with a QuickDASH score of 13 and a SSV of 60 is considering a reversed arthroplasty. Of all patients with AVN three had a screw perforation of the head and four had their implant removed. At long-term follow-up there were no new reported cases of AVN based on the interview.

TABLE 1. Baseline characteristics

Variable	Baseline cohort (n=79) n (%)
Age (mean, SD)	59 (13)
Male	37 (47)
ASA	
1	28 (35)
2	49 (62)
3	2 (2.5)
4	0 (0)
Dominant hand side	31 (39)
Trauma mechanism	
Ski / Snowboard	40 (51)
Low energy	29 (37)
Traffic accident	6 (7.6)
Other	4 (5.1)
AO Classification	
A	16 (20)
B	33 (42)
C	29 (38)
Follow-up time in years (mean, SD)	8.3 (0.8)

SD standard deviation

TABLE 2. Outcome measures

Variable	Mean (SD)	Median (IQR)
Functional outcome		
QuickDASH	5.6 (14)	0 (0 - 4.5)
Subjective Shoulder value	92 (11)	97 (90 - 100)
Implant related irritation / removal (n, %)		
Implant not removed, no irritation	34 (44)	
Implant not removed, irritation but implant removal not necessary	1 (1.3)	
Implant not removed, irritation, no request for removal due to fear of surgery	2 (2.6)	
Implant not removed, irritation, considering removal	0 (0)	
Implant removed routinely or on patient's request without irritation	13 (17)	
Implant removed due to implant irritation	27 (35)	
Duration till removal of PHILOS plate in years	1.2 (0.5)	

SD standard deviation, IQR interquartile range

TABLE 3. Bivariate analysis

	QuickDASH			SSV		
Variable	Mean (SD)	Median (IQR)	P value	Mean (SD)	Median (IQR)	P value
Age continous (coefficient)	0.139		0.223	-0.002		0.988
Age categorical						
Age < 65	3.8 (13)	0 (0 - 2.3)	0.06	94 (8.7)	98 (90 - 100)	0.209
Age > 65	8.4 (16)	2.3 (0 - 6.8)		89 (13)	95 (80 - 100)	
Trauma mechanism						
Ski / Snowboard	2.0 (3.1)	0 (0 - 2.3)	0.232	95 (6.6)	99 (90 - 100)	0.155
Low energy	8.5 (17)	0 (0 - 6.8)		89 (13)	95 (80 - 100)	
Traffic accident	20 (33)	5.7 (2.3 - 14)		83 (16)	90 (75 - 90)	
Other	1.1 (1.3)	1.1 (0 - 2.3)		93 (5.4)	93 (89 - 98)	
AO						
A	0.4 (0.9)	0 (0 - 0)	0.008	93 (7.7)	95 (89 - 100)	0.844
B	4.6 (9.4)	0 (0 - 4.5)		93 (10)	98 (90 - 100)	
C	9.5 (20)	2.3 (0 - 6.8)		91 (12)	97 (85 - 100)	

SD standard deviation, IQR interquartile range

In total, one patient received a reversed arthroplasty. This was because of a symptomatic malunion. The major tubercle was not anatomically reduced and healed with a cranial step. At 80 months follow-up this patient had a QuickDASH of 31 and a SSV of 65. Two other new reported complications occurred. Two patients developed a recurrent shoulder dislocation of whom one was operated for a rotator cuff repair.

DISCUSSION

MIPO with Philos has been described as a suitable technique for the treatment of proximal humerus fractures, but long-term functional results have never been reported. The aim of this study was to describe the long-term functional outcome and implant related irritation after MIPO for proximal humerus fractures. In our cohort, we found a very good QuickDASH score and SSV representing an excellent functional outcome at more than 8 years of follow-up after MIPO with Philos for proximal humerus fractures. For this long-term follow-up we used patient reported questionnaires but were not able to obtain an objective clinical and radiological examination. Forty of the 79 patients (50,6%) had implant removal, and of those, 27/40 (67,5%) were due to implant related irritation. We found a mean QuickDASH score of 5.6 and a mean SSV of 92, which can be considered an excellent outcome. In 2013, Acklin et al. reported the one-year follow-up of this cohort and found a Constant score of 75 (SD 11) that corresponded to a shoulder function of 91% compared to the uninjured side. Other studies presenting one or two year follow-ups reported mean DASH scores ranging from 14.5 to 26 after MIPO and 31 to 32 after an open procedure [1,4,14,17,20]. It is still debated whether further improvement of shoulder function is to be expected 12 months after treatment. Hirschmann et al. found only a slight improvement after one year [28]. Other studies published no further improvement at longer follow-up [12,29].

Few studies have reported on long-term follow-up after operative treatment of proximal humerus fractures but almost all studies investigated the open approach. Ockert et al. investigated 43 patients who were operated on using the open approach with a median follow-up of 10 years and reported a mean DASH score of 24 [12]. Most patients had an excellent outcome while 16% of the patients were considered to have a poor outcome. Bahrs et al. analysed 77 patients with a mean follow-up of eight years; eight patients were operated on using MIPO and 68 via an open approach [21]. They found a good mean DASH score of 12 with 77% of the patients having an excellent/good result and 23% having a satisfactory or worse result. No difference in Constant score between surgical approaches nor a correlation with the variables age and AO classification was found.

More than half of the patients had their implant removed. The majority (68%) because of implant related irritation and 32% requested implant removal because they did not want the material in their shoulder for the rest of their lives. Our findings are in line with Ockert et al. who reported a 40% implant removal rate [12]. They also found a significant improvement of functional outcome after implant removal. Similarly, another study reported improvement of shoulder function after implant removal among patients with implant related irritation treated with MIPO Philos plating [30]. In our study, we did not have sufficient data to report on improvement of shoulder function after implant removal. However, based on the study of Acklin et al., the high rate of implant removal in our cohort might have been beneficial for the excellent long-term results [30].

Results of different operative treatments should be put into perspective with regard to the conservative treatment for proximal humerus fractures. In a Cochrane review of eight randomized and quasi-randomized controlled trials the authors conclude that there was no evidence that supported the benefit of operative treatment of proximal humerus fractures [8]. But these results have to be interpreted with caution as the results did not cover two-part tuberosity fractures, fractures in young people, high-energy trauma, fracture-dislocations and head splitting fractures. Recently, the five-year follow-up results of the PROFHER trial, the most influential trial leading to conclusions in the Cochrane review, were published in which patients with a proximal humerus fracture were randomized between conservative and operative treatment [29]. In this medium-term follow-up study, the results of 109 patients were reported and no differences in Oxford Shoulder Score and EQ-5D-3L Score were observed. They concluded that there is no evidence that supports the trend of increased surgery for patients with displaced proximal humerus fractures. Nevertheless, there are major shortcomings in this study. First, the study is designed as a superiority study. Only 32% of the screened patients were included (e.g. several patients with clear indication for surgery were excluded). In 11% of cases, fairly inexperienced surgeons (e.g. registrars) performed the operation and 17% were operated on with something other than a plate (e.g. hemi-arthroplasty). So these results raise serious doubts. In addition, Kruithof et al. presented the long-term follow-up of conservatively treated patients with proximal humerus fractures between 2000 and 2013 [2]. After exclusion, there was data of 410 patients with a good median DASH score of 6.67 at a follow up of 7.5 years. Sub-analysis revealed a significant better outcome of patients younger than 65 years old at the time of injury. They concluded that long-term functional outcome and quality of life were good in most patients after proximal humeral fractures.

Our study has several limitations that need to be addressed. First, we report on a subgroup of the original cohort that could have led to bias and limited generalizability

of the study results. However, compared to the original cohort there were no differences in baseline characteristics in terms of age, trauma mechanism and AO-classification. Second, our hospital is situated in a recreational area in the mountains. Therefore, as compared to other hospitals, our patient population consists of younger and many relatively fit patients who were injured during outdoor sports activities. Therefore, our results might not be applicable to the typical proximal humerus fracture patient (female and > 65 years of age) [7]. Nevertheless, in bivariate analysis there was no association of age or trauma mechanism with functional outcome. Third, the sample size in this study is small and as this was a single center study, no appropriate control group was available. Furthermore, in this long-term follow-up study, we used telephone interviews in order to get sufficient follow-up. Therefore we were not able to perform a clinical examination of the shoulder or obtain long-term radiological follow-up. Consequently, no radiological data is available to report on the actual number of patients that developed AVN or implant failure. It can be argued to what extent radiological grade of AVN translates to limitations experienced by the patient [31], although, it seems that patients diagnosed with radiological AVN do have a worse functional outcome in this cohort. In addition, a possible disadvantage of the deltoid-split approach is second deltopectoral incision should a prosthesis be necessary in the future. However, this occurred only once in our patient sample. Finally, more than half of the patients were operated by two trauma surgeons dedicated to shoulder surgery while 14 different surgeons operated the other patients, which could have resulted in a performance bias. However, bivariate analysis did not show a difference in functional outcome of patients treated by the two surgeons versus patients treated by the 14 other surgeons. This possibly reflects the effect of in-hospital training and standardized procedure with the introduction of the MIPO technique and postoperative protocol in our hospital.

The results of this study can be of guidance when discussing treatment options for a proximal humerus fracture. The challenge for the future will be to determine which patient will benefit from operative treatment and which patient should be treated conservatively. We recommend operative treatment with MIPO for fit and active patients with a displaced proximal humerus fracture.

CONCLUSION

Treatment of proximal humerus fractures using MIPO with Philos through a deltoid split approach showed promising results. A good function can be assumed due to the excellent scores of patient oriented questionnaires. However, about one third of the patients will have a second operation for implant removal due to implant related irritation.

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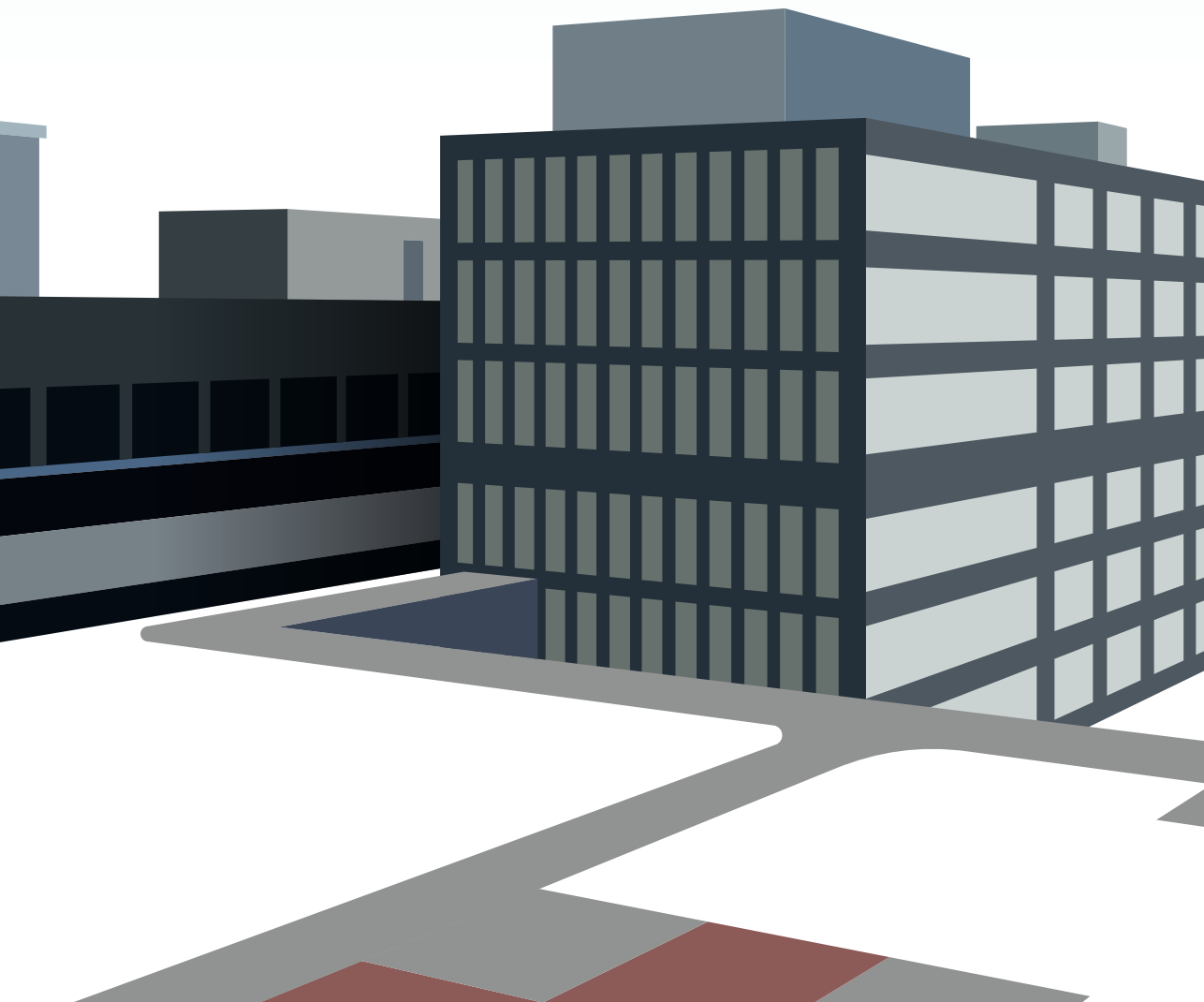

CHAPTER 9

Operative treatment of proximal humeral fracture-dislocations through an anterolateral deltoid split approach

Submitted

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ABSTRACT

Introduction: Proximal humeral fracture-dislocations (PHFD) are a special entity in proximal humeral fracture treatment. The aim of this study is to present our minimally invasive plate osteosynthesis (MIPO) technique through an anterolateral deltoid split approach. In addition, we performed a retrospective cohort study analyzing the patient reported functional outcome and complications.

Materials and Methods: A single center cohort study was performed. All patients operated through a deltoid split approach for PHFD between 2009 and 2016 were eligible for inclusion. The primary endpoint was subjective shoulder function measured with QuickDASH and subjective shoulder value (SSV). Secondary endpoints were complications and implant-related irritation.

Results: 28 patients were included. The mean age was 49 (SD ± 10.3). The mean follow-up was 48 months (SD ± 23.7). The mean QuickDASH score was 6.8 (SD ±7.8) and the mean SSV was 86 (SD ±14.6). Four patients had a conversion into a reversed arthroplasty (14%), one patient (4%) a shortening of secondary perforated screws, four patients an early re-osteosynthesis (14%), four patients (14%) developed an AVN and in one patient damage of the axillary nerve was observed. 21 patients (75%) had their implant removed.

Conclusions: Patient reported functional results after humeral head preservation and internal fixation of PHFDs through an anterolateral deltoid spilt approach are promising. However, there is a high rate of re-operations either because of complications or for implant removal.

INTRODUCTION

Proximal humeral fractures are very common and account for 4% of all fractures [1]. Proximal humeral fracture-dislocations (PHFDs) are a special entity in proximal humeral fracture treatment. PHFDs occur infrequently, with an incidence of 1-2% of all proximal humeral fractures [1]. PHFD is defined as a proximal humeral fracture with a dislocation of the humeral head either anterior or posterior to the glenoid fossa [2]. Non-dislocated fractures most often occur in the elderly population and are often treated conservatively [3,4]. PHFD occur more often in the younger, active population and are related to high-energy injuries [1,2,5]. Treatment is primarily operative and traditionally suggested to be arthroplasty, especially in the elderly patient [6-8]. With the introduction of angular stable screws new implants have been developed. A shift towards operative treatment of proximal humeral fractures in general has been observed [9-11]. PHFDs in younger patients have been suggested to be treated with a head preserving osteosynthesis, generally via an 'open' deltopectoral approach [2,5]. Trikha et al [2] suggested the deltopectoral approach for anterior dislocations and the deltoid split approach for posterior dislocations. Plate positioning and the window to the rotator cuff is challenging through the deltopectoral approach. Even more with difficult fracture patterns. Therefore, we adopted the 'minimally invasive' anterolateral deltoid split approach [3] for both anterior and posterior PHFDs.

The aim of this study was to present our technique for open reduction and internal fixation (ORIF) of PHFDs through an anterolateral deltoid split approach. Furthermore, we present the functional results and complications after osteosynthesis of these severe injuries.

MATERIALS AND METHODS

Patient population

After approval from our institutional review board, a retrospective cohort study for PHFD was performed. All patients with a PHFD (AO 11-B3 or 11-C3) [12] who were operated on with ORIF between 2009 and 2016 through an anterolateral deltoid split approach were eligible for inclusion. In our hospital young and active patients with a PHFD are treated with an osteosynthesis through an anterolateral deltoid split approach. Elderly and geriatric patients with a PHFD are treated with an arthroplasty.

Baseline characteristics, operation time, image-intensifier time, follow-up data and complications were obtained from electronic patient files. All patients were analyzed

either during regular outpatient visits or by telephone by an independent research fellow to assess shoulder function using the QuickDASH questionnaire [13] and the Subjective Shoulder Value (SSV) [14]. Implant removal was assessed using the algorithm of Hulsmans et al [15] and conversion to a shoulder arthroplasty was recorded. If patients could not be reached after a minimum of five telephone call attempts, their contact person and general practitioner were approached for contact details and the internet was searched for an alternative telephone number. If patients could not be reached by phone a letter was sent, asking the patient to contact us. Patients were considered lost to follow-up if all these attempts were unsuccessful.

Exclusion criteria were death, a second trauma to the operated arm, inability to answer questions and absence of informed consent.

This study was approved by the Cantonal Ethic Committee in Zurich (KEK-ZH-Nr. 2017-00554).

Operative technique

Until 2009 the classical 'open' deltopectoral approach was used to perform ORIF of PHFDs. This approach is well known and accepted [16]. After the introduction of and with growing experience in using the deltoid split approach [10,17] for proximal humeral fractures, we changed our approach for PHFD from deltopectoral to deltoid split.

As the deltoid split technique has not been described for PHFD, it is described in further detail:

After general anesthesia, patients are positioned in beach-chair position. Under antibiotic prophylaxis, an anterolateral deltoid split approach is performed. The incision starts at the end of the anterolateral acromion and runs down anterolateral about 5-7cm in length depending on the size of the shoulder. After blunt dissection through the deltoid muscle, the subacromial bursa is opened and partially resected to provide a better view onto the fracture site. The axillary nerve is protected by straight submuscular/periosteal dissection and the use of a rectangular retractor. Further access to the fracture fragments and the reduction techniques depend on the specific fracture pattern:

A. In 3- or 4-part fractures (**Fig.** 1) where the dislocated head fragment is separated from the tuberosity/ies, the approach provides direct access to the underlying tuberosities with the attached rotator-cuff, hiding the dislocated head fragment. The greater tuberosity is found either direct beneath the incision or slightly

posterior. The lesser tuberosity lies anterior. Access to the glenoid cavity is achieved either at the lower margin of the greater tuberosity by lifting it up, or through the fracture gap between the two tuberosities. Both tuberosities can be held apart using a small self-retaining retractor. Most often the dislocated head is found anterocaudally at the lower border of the now well-visible glenoid cavity. From the fracture side opposite to the articular surface a Schanz screw (4.5 or 5mm diameter) is inserted directly into the center of the head fragment. This is done under direct vision and using the fluoroscopy controlling insertion depth (**Fig.** 2a). Attaching a T-handle on this firmly inserted Schanz screw allows for direct manipulation and reduction of the head fragment. It is very often impacted behind the border of the glenoid and has to be moved sideward (anterocaudal) for decompaction. This allows correct reduction into the glenoid cavity (**Fig.** 2b). The unstable fragment is held in place using a 2.0mm K-wire which is inserted through the head fragment into the glenoid for temporary trans-fixation (**Fig.** 2c).

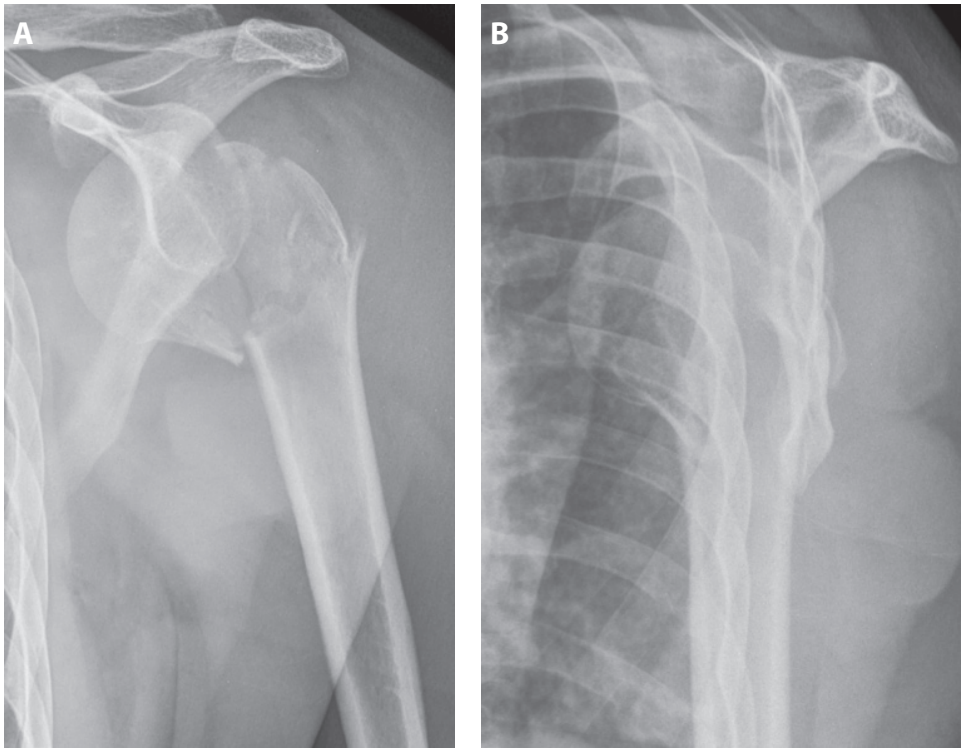

FIGURE 1. X-rays from anterior-inferior proximal humeral fracture-dislocation on AP (1a) and Neer (1b) view.

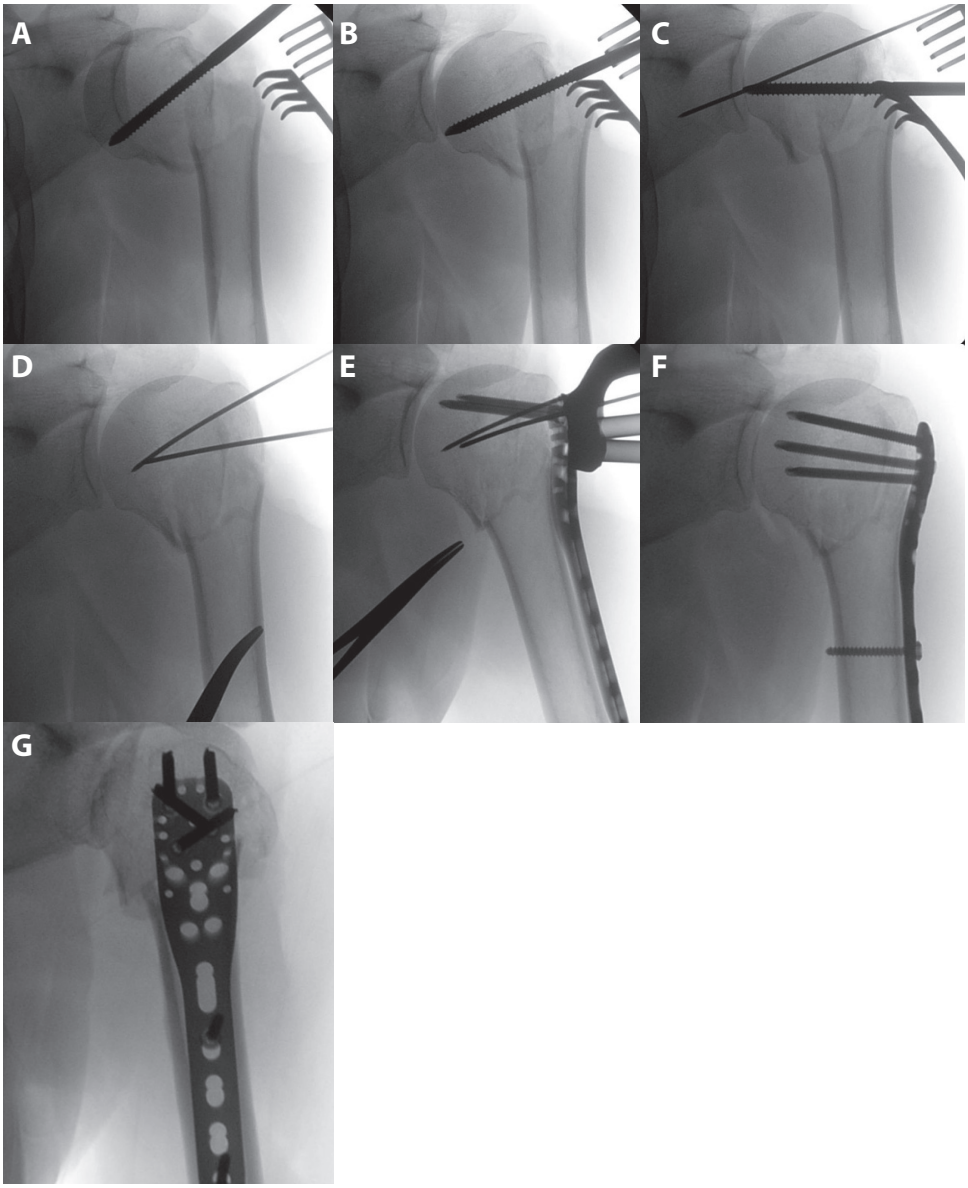

FIGURE 2. Intraoperative images of the osteosynthesis with a PHILOS plate through an anterolateral deltoid split approach. 2a insertion of a Schanz-screw in the humeral head. 2b reduction of the humeral head in the glenoid fossa using the Schanz-screw with T-handle. 2c temporary retention of the humeral head with a transfixation on to the glenoid using a K-wire. 2d reconstruction of the humeral head and temporary fixation with K-wires. 2e insertion of the PHILOS plate using the aiming device with proximal fixation with 2 angular stable screws. 2f and 2g final x-rays after PHILOS plate fixation with proximally 4 angular stable screws and distally 2 conventional screws in AP and lateral view fixation

The Schanz screw is removed. Strong FiberWire sutures are placed at the base of the rotator-cuff tendons at the greater (supraspinatus and infraspinatus tendon) and, if fractured as well, at the lesser tuberosity (subscapular tendon). Using these sutures and smaller K-wires as joy-sticks, the tuberosities are now reduced to the head fragment and held in place by further inserting these K-wires into the head fragment (**Fig.** 2d). The reduction is checked by fluoroscopy. The 3-/4-part fracture-dislocation is now converted to a non-dislocated 2-part fracture. The next step is to reduce the shaft fragment to the head using indirect manipulation of the arm. Often the fist of the surgeon is put into the axilla as a hypomochlion to lateralize the displaced shaft onto the head fragment. Angulation of the arm helps for correct alignment. If possible, a strong 2.0mm K-wire is inserted from the top of the greater tuberosity medially downwards over the sub capital fracture level into the proximal medial part of the shaft fragment for temporary retention. For distal tunneling, blunt dissection is done underneath the deltoid muscle straight on the anterolateral aspect of the humeral shaft to protect the axillary nerve. The axillary nerve is further protected using a rectangle 'Langenbeck' retractor. After inserting the previously described FiberWire sutures through the corresponding marginal plate holes, the 5-hole PHILOS-plate is then slid down using the guiding arm (**Fig.** 3) until the correct height of the proximal plate end is reached (fluoroscopic control) (**Fig.** 2e). The plate is fixed with four angular stable screws in the head and two to three conventional (in good bone) or angular stable (in osteoporotic bone) screws in the humeral shaft. Using the minimally invasive aiming device allows insertion of 4 angular stable screws proximally only. Insertion of more screws in the head puts the axillary nerve at risk via this approach. Reduction and fixation are checked under image intensifier (**Fig.** 2f and 2g). After removal of the aiming arm, the FiberWire sutures are tightly knotted over the plate for additional firm fixation of the tuberosities/ rotator cuff. After rinsing the wound, it is closed in layers.

B. In 2-part fractures, after splitting the deltoid muscle, the approach ends on the rotator cuff (supraspinatus tendon) that is under tension and still attached to the dislocated humeral head over the intact tuberosities. In this case, the greater tuberosity is located by the surgeons' index finger and the Schanz screw is inserted through the greater tuberosity into the head fragment. The reduction maneuver is the same as described above. Depending on the stability of the head fragment into the glenoid, a transfixation K-wire (2mm) is used. Further reduction onto the shaft fragment and plate fixation is performed as described above.

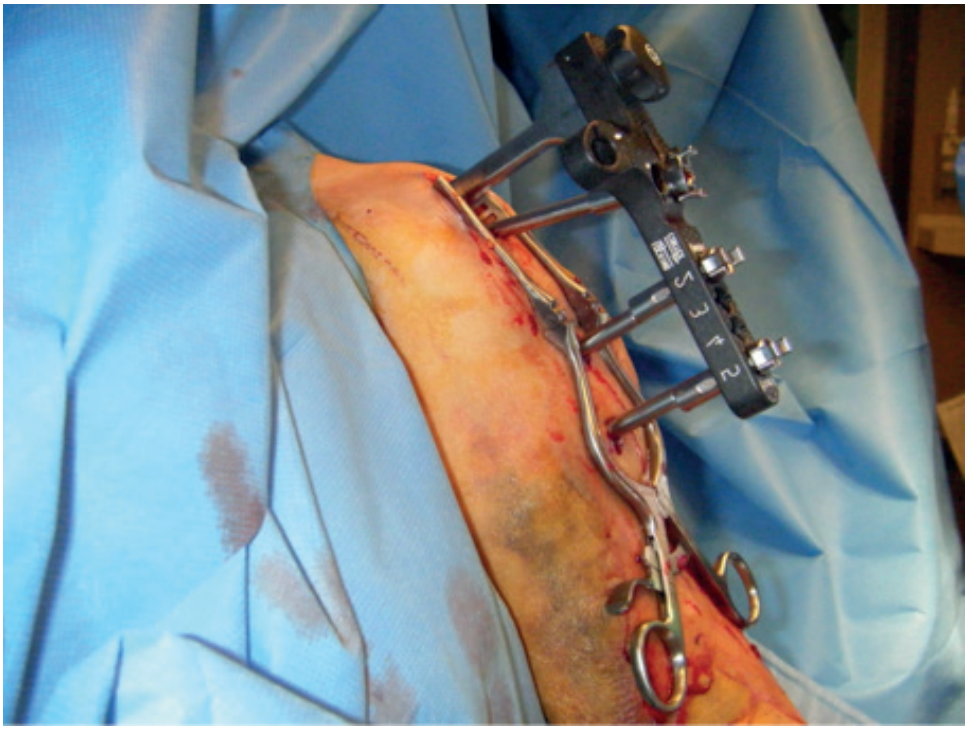

FIGURE 3. Plate and screw positioning with aiming arm

At the end of the operation, the stability of the osteosynthesis as well as the position of the head in the joint is tested clinically by careful manipulation of the upper arm. If in doubt, fluoroscopic control can be used. Depending on the stability, a sling for initial shoulder immobilization might be necessary; although, in most cases a stable situation is achieved by the reconstruction. Therefore, patients are allowed functional movement without weight bearing for the first 6 weeks. Abduction of more than 90 degrees and forced rotational movements are not allowed for the first 6 weeks. Physical therapy is started immediately postoperatively and is continued for the first 4-6 months. After six weeks, further mobilization and progressive weight bearing is allowed. X-ray controls are performed 2 days postoperative and then after 6 weeks, 12 weeks, 6 months and 1 year (**Fig.** 4a, 4b and 4c)). Implant removal is performed on patients' request or because of implant-related irritation (**Fig.** 5).

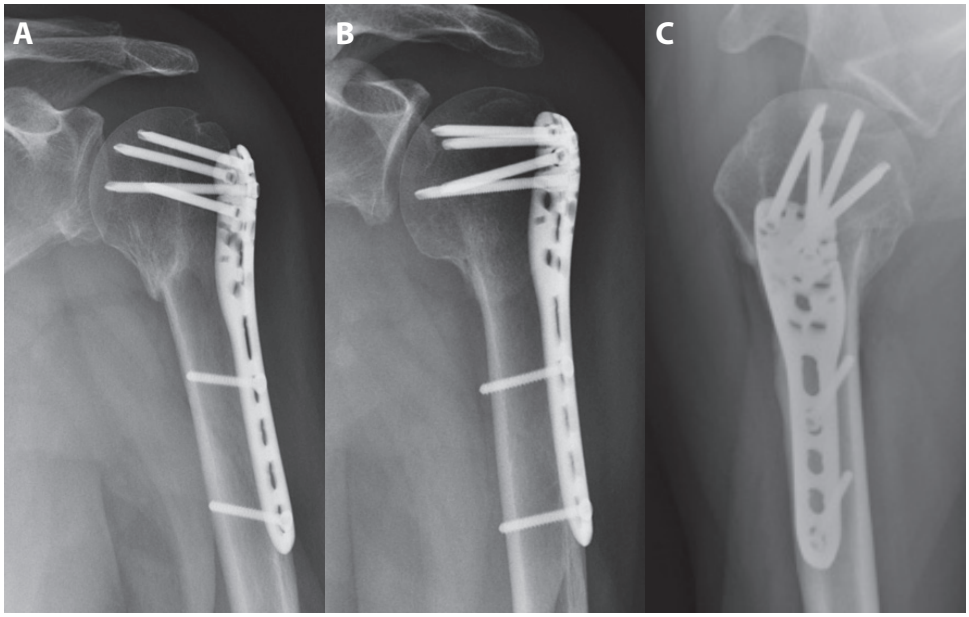

FIGURE 4. Six months follow-up with consolidated fracture in inner rotation (4a), external rotation (4b) and axial (4c) view.

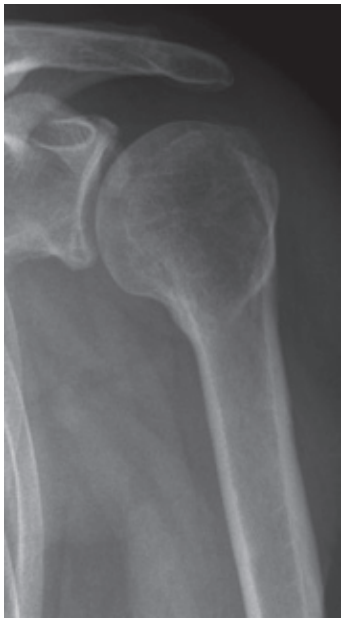

FIGURE 5. AP follow-up x-ray after 3 years

Outcome measures

The primary outcome measure was the patient reported shoulder function as measured by the QuickDASH and SSV score [14,18]. The QuickDASH score is a validated measure for disability of the arm, shoulder and hand. This is a summative score on a 100-point scale. A QuickDASH score of less than 15 is considered an excellent result and a score of >40 reflects a poor shoulder function [13]. The SSV is a patient reported outcome measure determined by answering the following question: "What is the overall percent value of your shoulder if a completely normal shoulder represents 100%?", with 100% indicating the best function [14]. Secondary outcome measures were conversion into a shoulder arthroplasty, implant-related irritation or implant removal and complications. Implant removal and implant-related irritation were discussed and analyzed using the algorithm of Hulsmans et al [15], developed to analyze the presence of implant-related irritation.

Complications were divided in short-term and long-term complications [19]. Short-term complications like insufficient reduction and wound related complications as superficial or deep infections were analyzed using the electronic patient files. Superficial infection was defined as redness, swelling and/or purulent discharge from the wound that could be treated with antibiotics. Infections were considered deep if surgical debridement was performed together with antibiotic therapy. Long-term complications like symptomatic avascular head necrosis (AVN), screw perforation, nonunion, implant breakage or loosening were also recorded. The incidence of symptomatic AVN was diagnosed during regular follow-up and it was discussed during the telephone interviews if this was diagnosed by any other doctor. An unsuccessfully healed proximal humerus by radiograph 6 months after surgery with clinical evidence of pain was considered a nonunion.

Actions taken because of complications like re-osteosynthesis, shortening of screws and/or conversions into a shoulder arthroplasty were noted [19].

Statistical analysis

Data were described using frequencies and percentages for dichotomous and categorical variables, mean and standard deviation (SD) for normally distributed continuous data. Continuous variables were compared using Mann-Whitney U-test for non-normal distributed data. A p value < 0.05 was considered significant. The analyses were performed with SPSS, version 22.0 (IBM Corp., Armonk, NY) for Windows.

RESULTS

After informed consent was obtained, a total of 28 patients were available for follow-up and included for analysis (**Fig.** 6). The mean age at the time of accident was 49 (SD ± 10.3) years old and 25 (89%) patients were male (**Table** 1). The most common trauma mechanism was injury during skiing or snowboarding (57%). There were 4 (14%) type B3 and 24 (86%) type C3 fractures according to the AO classification [12]. 17 patients had an anterior fracture-dislocation and 11 a posterior fracture-dislocation. The mean operation time was 101 minutes (SD ± 42.5). The mean follow-up duration was 48 months (SD ± 23.7).

The mean QuickDASH score was 6.8 (SD ± 7.8) and the mean SSV was 86 (SD ± 14.6) (**Table** 2). 21 patients (75%) had their implant removed, 8 (29%) due to implant-related irritation.

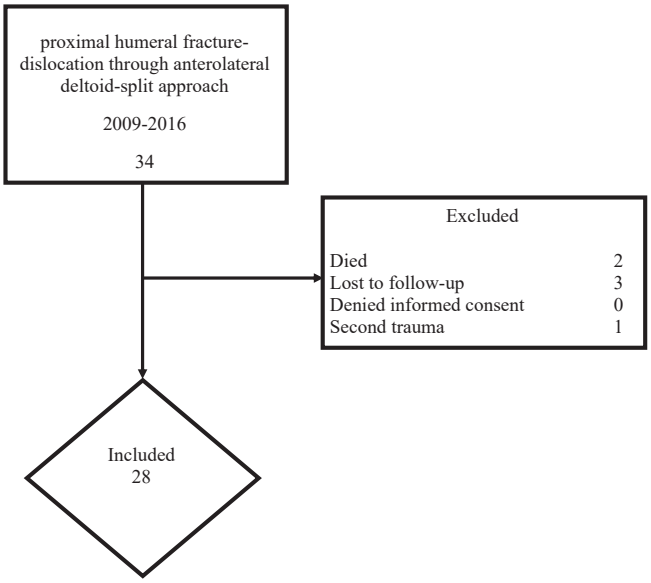

FIGURE 6. Flow-chart of patient inclusion

Several complications occurred (**Table** 3). Six patients had short-term complications. One patient had a repetitive pull-out of the Schanz screw from the humeral head that required a second deltopectoral approach and four patients had an insufficient primary reduction that resulted in an early re-osteosynthesis (14%). These are classified

as treatment related adverse events. In one patient damage to the anterior branch of the axillary nerve was observed, a soft tissue related adverse event [19]. There was full recovery after 6 months.

Five patients had long-term complications. One patient (4%) had an implant related complication with a secondary perforated screw tip leading to an osteoarthritis, which was treated by implant removal first and a reversed arthroplasty one month later. Four patients developed an AVN, a fracture related adverse event. Three of them, with a mean age of 59 years, got a conversion into a reversed arthroplasty (11%). AVN was diagnosed at an average of 19 months (SD ± 12.8) follow-up. Sub-analysis shows that patients who develop an AVN have a significant poorer functional outcome according to the QuickDASH (p=0.009) and a poorer SSV (p=0.083) (**Table** 4).

TABLE 1. Baseline characteristics (N=28)

Variable	n (%)
Age, mean (SD)	49 (10.3)
Male	25 (89)
Side	
right	16 (57)
left	12 (43)
Dominant side	
right	25 (89)
left	3 (11)
Trauma mechanism	
Ski / Snowboard	16 (57)
Low energy	6 (20)
Traffic accident	2 (7)
Other	4 (14)
AO classification	
B3	4 (14)
C3	24 (86)
ASA classification	
1	15 (54)
2	11 (39)
3	2 (7)
4	0
Operation time, minutes, mean (SD)	101 (42.5)
Image intensifier time, seconds, mean (SD)	128 (105)
Time to operation, days, mean (SD)	0.5 (2.13)
Follow up time, months, mean (SD)	48 (23.7)

SD standard deviation

TABLE 2. Results

Variable	N=28
Functional outcome	
QuickDASH, mean (SD)	6.8 (7.8)
SSV, mean (SD)	86 (14.6)
Implant related irritation / removal, n (%)	
Implant not removed, no irritation	7 (25)
Implant not removed, irritation but implant removal not necessary	0
Implant not removed, irritation, no request for removal due to fear of surgery	0
Implant not removed, irritation, considering removal	0
Implant removed on patient's request without irritation	13 (46)
Implant removed due to implant irritation	8 (29)

SD standard deviation

TABLE 3. Complications

Complication groups	Patient cohort N=28 n (%)
Local complications	
Implant/device	2 (8)
Secondary screw perforation	1 (4)
Implant loosening	0
Implant breakage	0
Other	1 (4)
Bone/fracture/cartilage	8 (28)
Loss of reduction	0
Impaction	0
Nonunion	0
Avascular necrosis	4 (14)
Other	4 (14)
Soft tissue of musculoskeletal system	1 (4)
Bursitis	0
Other	1 (4)
Wound/other soft tissue	0
Superficial infection	0
Deep infection	0
Heamatoma	0
Other	0

TABLE 4. Functional results with and without AVN

	AVN		
Variable	**Yes (N=4) mean (SD)**	**No (N=24) mean (SD)**	**P-value**
QuickDASH	18.9 (11.9)	4.9 (5.21)	**0.009**
SSV	71 (24.3)	89 (11.4)	0.082

SD standard deviation

DISCUSSION

Osteosynthesis of PHFDs can be performed through a minimally invasive anterolateral deltoid split approach. Above we described our operation technique for MIPO of PHFD. Our results show that osteosynthesis for PHFD through the deltoid split approach can lead to good patient reported functional outcomes. However, 36% of the patients required a re-operation for either conversion into an arthroplasty, shortening of perforating screws or a revision-osteosynthesis. Furthermore, with a total of 75%, we found a very high implant removal rate.

The indication for operative or conservative treatment of proximal humeral fractures in general is still under debate [3,4,10]. However, the indication for operative treatment of PHFD, either with arthroplasty or osteosynthesis, seems accepted [2,5,6]. A literature search did not reveal any publications about conservative treatment for PHFDs. The standard approach for osteosynthesis of proximal humeral fractures in general is the open deltopectoral approach [20]. Over the past decade, there has been increasing interest in the deltoid split approach for proximal humeral fracture treatment [10,11,17,21]. With our growing experience in the deltoid split approach for proximal humeral fractures, we started using this approach for difficult cases like fracture-dislocations. In our experience, using this approach, the operative procedure itself becomes easier to perform. The "window" for access to the dislocated head fragment as well as to the tuberosities (esp. the greater, usually posteriorly displaced) is much more direct and "inline" compared to the deltopectoral approach. This facilitates the reduction of these fragments, especially the greater tuberosity. The plate itself is placed directly underneath the approach, what makes the insertion of the proximal screws easier. Another advantage, however hypothetical, might be a positive influence on the blood supply of the humeral head which may reduce the incidence of AVN. Through

an anterolateral deltoid split approach there is a smaller risk of damaging the anterior circumflex artery compared to the deltopectoral approach. However, this potential benefit cannot be concluded from this study but might be analysed in future studies.

The functional outcome in this study is comparable to two other larger studies on PHFDs [2,5]. Soliman et al [5] published the results of osteosynthesis of 39 patients who were younger than 40 years old. They analyzed four-part PHFD that were treated with ORIF through a deltopectoral approach with either K-wire or locking plate fixation. With an average Constant score of 77, after a mean follow-up of 26 months, they concluded that rigid fixation could lead to satisfactory results. In addition, Trikha et al [2] reported on 33 PHFDs treated patients through a deltopectoral approach for anterior dislocations and through a deltoid-split approach for posterior dislocations. In their mean-aged cohort of 35 years old, they found a mean Constant score of 78 after a mean follow-up of 40 months. They concluded that young patients can achieve a good functional outcome after locking plate fixation. Our study, in combination with current literature, supports the choice for primary osteosynthesis of PHFDs, especially in young and active patients.

Several complications have occurred and need to be discussed. As published by Robinson et al. there is a high rate of AVN of the humeral head after ORIF of PHFDs [22]. They found a radiological AVN in 6 out of 30 patients (20%) treated with ORIF. Three of these patients were asymptomatic and treated conservatively. The other three were converted into a hemiarthroplasty. Our rate of AVN is comparable with literature [2,5,22]. In our series four patients (14%) were diagnosed with an AVN, of whom three were converted into an arthroplasty. As shown in Table 4, patients who develop an AVN have a poorer functional outcome. Even though Schliemann et al. [23] showed good functional results for reversed total shoulder arthroplasty after AVN. According to Hertel [24] and the nature of the fracture-dislocation, one can expect avascularity of the humeral head. However, a primarily avascular head does not necessarily result in a symptomatic AVN [25]. Radiological AVN can develop without any symptoms and stay asymptomatic or revascularization may occur [22,25]. Therefore, the clinical symptomatic (and not only radiological) AVN seems most relevant. In our analysis we assumed that patients with complaints, possibly because of AVN, have contacted us or another specialist and that x-rays have been made. A possible AVN would have been diagnosed and the patient would know this. Therefor we discussed this actively in the telephone interviews. We are aware however, that, despite the fact that 22 patients had partly or complete outpatient follow-up in our clinic, this might have resulted in an underestimation of AVN.

Besides AVN, several other complications occurred. One patient had screw perforation of the humeral head. The shoulder was converted into a reversed arthroplasty.

Temporary axillary neuropraxia occurred in one patient. One patient had a conversion of a deltoid split approach into an open approach due to failure to retrieve the humeral head. Furthermore, four patients needed a re-osteosynthesis after insufficient primary fixation. All the re-operations were performed through the deltoid split approach. Compared to the above mentioned other studies on the operative treatment of PHFDs our complication rates are equal [2,5].

We analyzed our implant removal rates using the algorithm of Hulsmans et al [15]. This analysis revealed a high rate of implant removal. 21 patients (75%) had their implant removed, of whom eight (29%) were due to implant-related irritation. Included in these 21 patients are the four patients with shoulder arthroplasty. One of these patients had no irritation of the implant and only one patient had the implant removed at the same time as the reversed shoulder arthroplasty was implanted. We assume the high rate of removed implants reflects our young population as thirteen patients had their implant removed on request without irritation. Unfortunately, we don't have pre- and postoperative functional data before and after the implant removal.

Several limitations regarding this study need to be addressed. First of all, this is a retrospective study that has the usual 'retrospective' drawbacks. Second, a selection was made. Patients who were primarily treated with an arthroplasty for a PHFD were not included. Unfortunately, we were not able to include these patients as they are not recorded in our trauma registry. However, as discussed above, our indication for osteosynthesis of PHFD is in young and active patients. Less active elderly and geriatric patients are treated with an arthroplasty. In addition, our study population is younger than many other studies about proximal humeral fracture treatment in general. This is partially caused by our geographical location in the mountains with young and active patients as can be concluded from the trauma mechanisms. They might have better bone quality and therefore better results. Another limitation is that we used telephone interviews in order to get sufficient follow-up. This resulted in a high rate of follow-up, but we were not able to perform a clinical examination of the shoulder or to obtain long-term radiological follow-up. And lastly, 18% of the patients with a PHFD treated through an anterolateral deltoid split approach were lost to follow-up.

CONCLUSIONS

Patient reported functional results after open reduction and internal fixation of PHFDs using the deltoid split approach, analyzed with patient-oriented questionnaires are promising. In 86% preservation of the humeral head was successful. However, there is a high rate of re-operations either because of complications or for implant removal.

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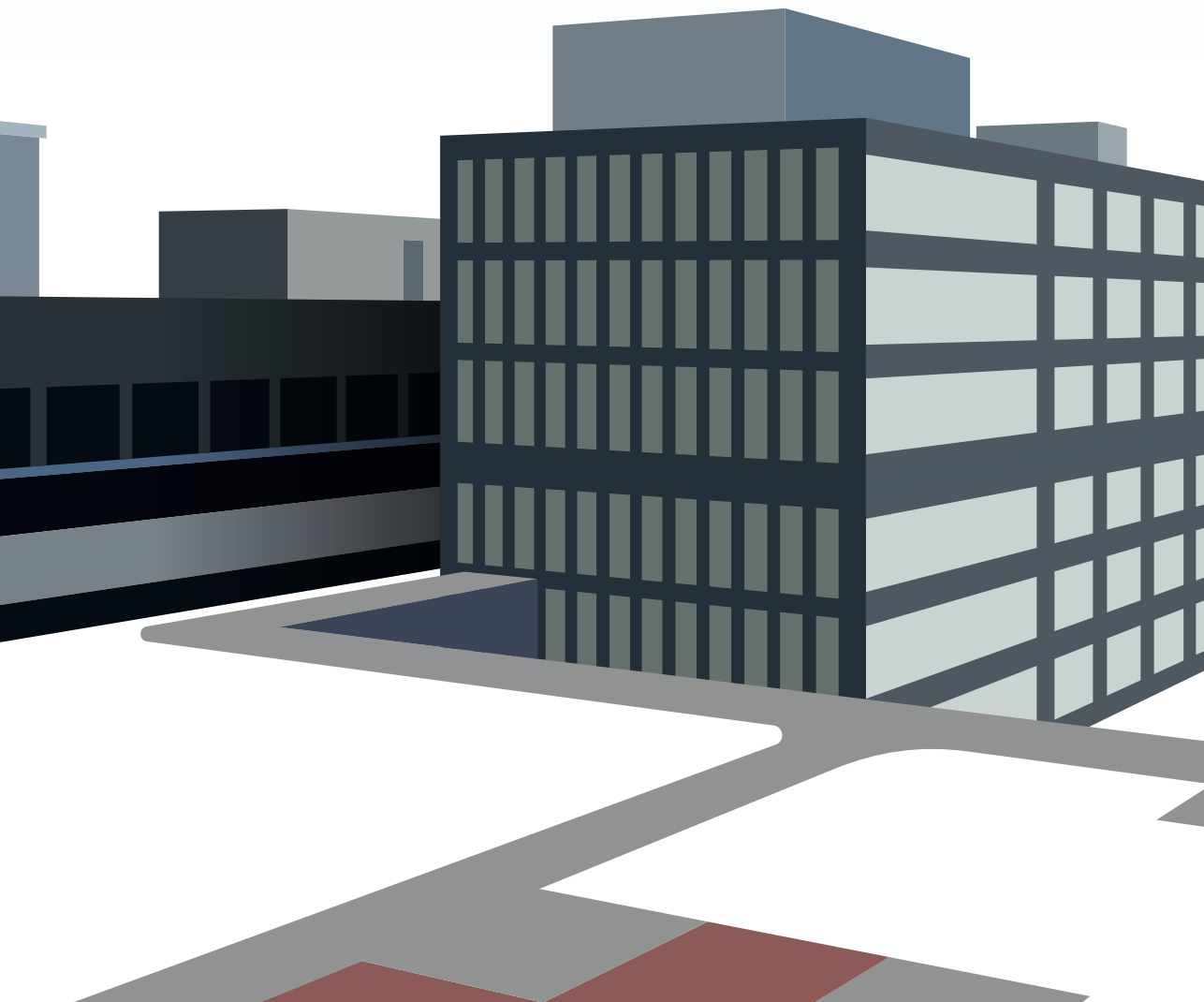

CHAPTER 10

Proximale humerusfracturen: Conservatief of operatief behandelen?

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SAMENVATTING

- Proximale humerusfracturen komen steeds vaker voor.
- Patiënten met een proximale humerusfractuur worden van oudsher conservatief behandeld. De laatste decennia zijn echter diverse nieuwe implantaten voor osteosynthese en protheses van de schouder ontwikkeld en is de operatieve behandeling van proximale humerusfracturen toegenomen.
- Recente literatuur waarin de conservatieve en de operatieve behandeling van proximale humerusfracturen vergeleken wordt, laat echter geen verschil zien in functionele uitkomsten. De trend om vaker operatief te behandelen berust dus niet op wetenschappelijk bewijs.
- In dit artikel presenteren wij de huidige stand van zaken en proberen wij een genuanceerd beeld te geven van wie niet, maar ook wie mogelijk wél profiteert van een operatieve behandeling van de proximale humerusfractuur.

ABSTRACT

Proximal humerus fractures; conservative or surgical treatment?

- There is an increasing incidence of proximal humerus fractures.
- Patients with proximal humerus fractures have traditionally been treated conservatively. During the past decades, however, various new osteosynthetic and prosthetic implants have been developed for the shoulder and surgical treatment of proximal humerus fractures has increased.
- However, recent literature in which conservative and surgical treatment of proximal humerus fractures is compared has shown no difference in functional outcome. The trend towards more frequent surgical treatment is thus not based on scientific evidence.
- In this article, we present the current state of affairs and attempt to give a nuanced picture of who will not, but also who might profit from surgical treatment of a proximal humerus fracture.

U bent 60 jaar en tijdens uw jaarlijkse wintersportvakantie in Zwitserland valt u op uw rechter schouder. Een röntgenfoto laat een proximale humerusfractuur met valgusimpactie en een gedislokeerd tuberculum majus zien (figuur 1a). U krijgt het advies en aanbod om een operatie te ondergaan. Vervolgens telefoneert u met een bevriende traumachirurg in Nederland voor aanvullend advies. Die zegt dat, gezien de huidige literatuur, een operatie niet nodig is en adviseert een conservatieve behandeling. Is er dan niemand gebaat bij een operatieve behandeling van zijn of haar proximale humerusfractuur? Waarom krijgt u dan in Zwitserland toch een operatie aangeboden? Welke patiënten kunnen wél baat hebben bij een operatie?

Het doel van dit artikel is om bovenstaande vragen te beantwoorden en een genuanceerd beeld te schetsen van de huidige stand van zaken bij de behandeling van de proximale humerusfractuur.

EPIDEMIOLOGIE, DIAGNOSTIEK EN CLASSIFICATIE

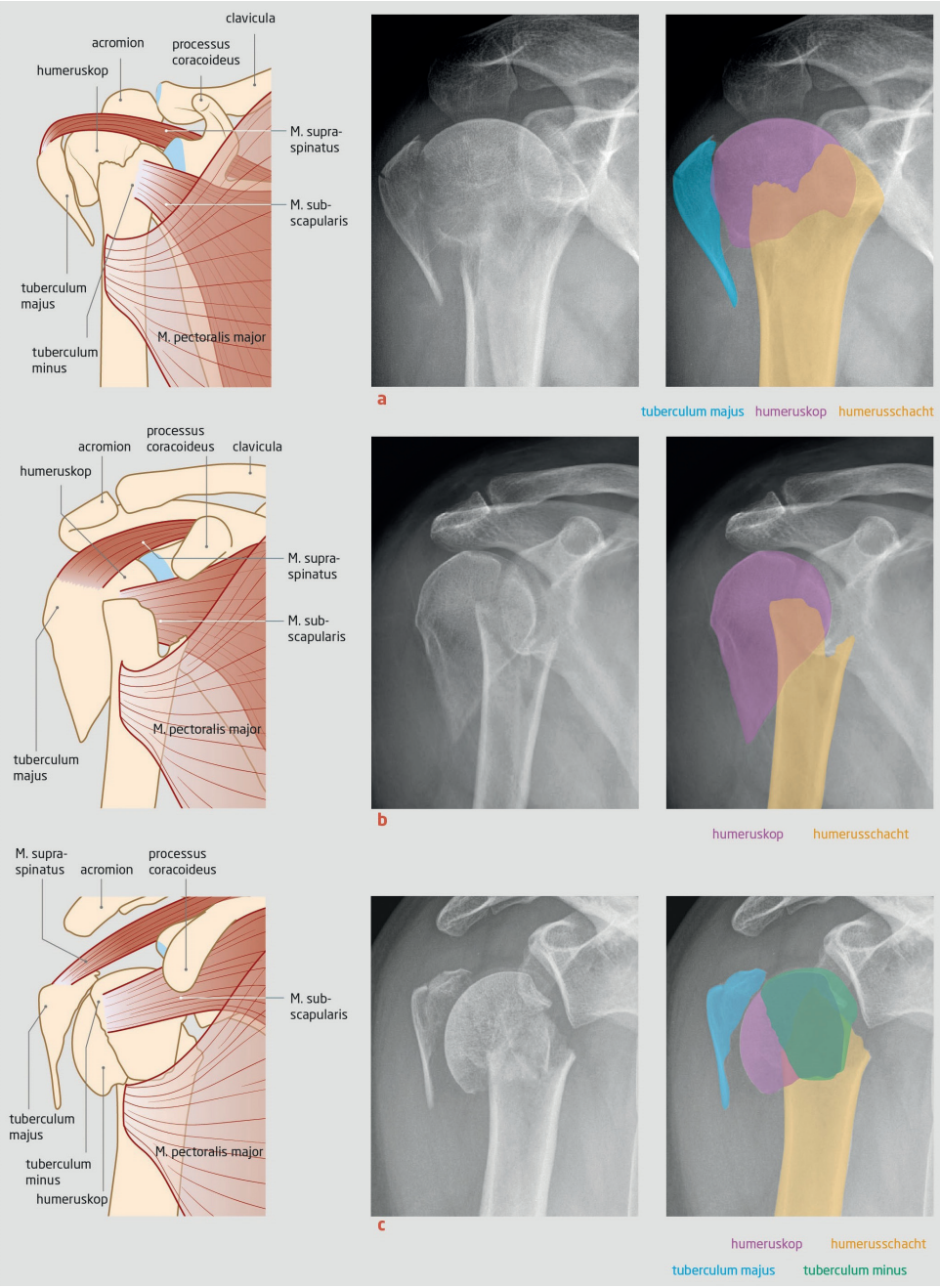
De incidentie van proximale humerus- en claviculafracturen in Nederland neemt toe: van 93 per 100.000 in 2004 tot 115 per 100.000 in 2012.[1] Met een groeiende bevolking en toenemende vergrijzing zullen proximale humerusfracturen in de toekomst nog vaker voorkomen; zij zullen niet alleen medisch, maar ook maatschappelijk een toenemende belasting zijn voor ons gezondheidszorgsysteem.

Van oudsher wordt gesproken over 'subcapitale humerusfracturen'. Deze naamgeving is gewijzigd in 'proximale humerusfracturen', aangezien veel fracturen van de proximale humerus niet alleen subcapitaal zijn, maar meer fragmenten van de humeruskop betreffen. De proximale humerus breekt meestal volgens een kenmerkend patroon van 2 tot 4 fragmenten. Deze fragmenten zijn de humeruskop met het gewrichtsvlak, tuberculum majus, tuberculum minus en de humerusschacht (figuur 1). Deze fracturen ontstaan meestal door een val met uitgestrekte arm of direct op de schouder. Bij klinische verdenking op een proximale humerusfractuur wordt een röntgenopname gemaakt in 2 richtingen. Bij gedislokeerde intra-articulaire fracturen heeft CT toegevoegde waarde.

Proximale humerusfracturen kunnen worden geclassificeerd volgens de indeling van Neer,[2] van de AO/OTA of van Hertel. Geen van deze classificaties is duidelijk de betere. Deze classificaties vertonen alle drie een aanzienlijke inter- en intraobserver-variabiliteit.[3,4]

BEHANDELING

De behandeling van proximale humerusfracturen is van oudsher conservatief vanwege slechte resultaten van operatieve behandeling met conventionele implantaten.[5] Conservatieve behandeling bestaat uit immobilisatie in een polysling of mitella gedurende 4-6 weken. Na 2-3 weken begint de patiënt met pendelbewegingen en na 6 weken gaat hij of zij actief oefenen onder begeleiding van een fysiotherapeut.[6] Met de komst van nieuwere, zogenoemde 'hoekstabiele' implantaten en protheses is er een trend ontstaan om sneller te gaan opereren. De vraag is of deze trend gerechtvaardigd is en of de resultaten met deze nieuwere implantaten inderdaad beter zijn dan die van de conservatieve behandeling.



FIGUUR 1. Voorbeelden van proximale humerusfracturen. De proximale humerus breekt meestal volgens een kenmerkend patroon van 2 tot 4 fragmenten. (a) fractuur met 3 fragmenten; (b) fractuur met 2 fragmenten; (c) fractuur met 4 fragmenten.

Conservatieve versus operatieve behandeling

De laatste jaren is er veel onderzoek gepubliceerd over de behandeling van proximale humerusfracturen.[6-12] De meest toonaangevende studie tot op heden is de PROPHER-trial, een Engelse gerandomiseerde, gecontroleerde trial (RCT).[8] In deze studie werden patiënten met een gedislokeerde proximale humerusfractuur van ten minste het collum chirurgicum (zie uitleg) gerandomiseerd tussen een conservatieve en een operatieve behandeling. Als de patiënt lootte voor een operatieve behandeling was het de keuze van de behandelend chirurg welk implantaat hij zou gebruiken: een plaatosteosynthese, penosteosynthese of een hemiprothese. Na 2 jaar was er geen verschil tussen de twee groepen in de uitkomsten op de Oxford Shoulder Score en de Short-Form 12. Hieruit volgt de begrijpelijke conclusie dat de trend dat gedislokeerde proximale humerusfracturen steeds vaker operatief behandeld worden, niet berust op wetenschappelijk bewijs voor een betere uitkomst.

Er kunnen echter wel een paar kanttekeningen geplaatst worden bij de PROPHER-studie. Van de 1250 patiënten die aanvankelijk gescreend werden, zijn er uiteindelijk slechts 250 gerandomiseerd. Onder de geëxcludeerde patiënten waren er 87 met 'een duidelijke operatie-indicatie', zonder dat deze indicatie werd toegelicht; dit is een duidelijk voorbeeld van selectie. Verder werden de 109 geopereerde patiënten geopereerd door 66 verschillende chirurgen in 30 verschillende klinieken. 82 patiënten kregen een plaatosteosynthese, 4 een penosteosynthese en 10 een hemiprothese. Deze diversiteit in behandeling en vooral het grote aantal verschillende chirurgen met een lage 'case load' (nog geen 2 operaties per chirurg) doet twijfels rijzen bij de expertise en ervaring van de chirurgen in deze studie. Zo liet een recente publicatie zien dat de case load per chirurg waarschijnlijk van invloed is op het resultaat van de behandeling bij patiënten met een proximale humerusfractuur.[10]

Geen verschil in functionele uitkomsten

Ook de meest recent gepubliceerde systematische review en meta-analyse van RCT's en observationele studies toont geen verschil aan in de functionele uitkomst na conservatieve dan wel operatieve behandeling van proximale humerusfracturen (figuur 2).[6]

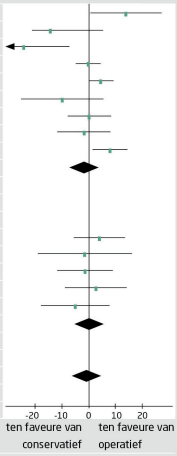
De functionele uitkomst werd gemeten met de Constant-Murley score.[13] Dit is een score tussen 0 en 100 die wordt opgebouwd uit subscores voor de pijn, de functionaliteit en de kracht van de schouder; een hogere score staat voor een betere functionele uitkomst. In deze meta-analyse werden studies geïncludeerd waarin de conservatieve en operatieve behandeling (osteosynthese of prothese) met elkaar waren vergeleken. Zowel RCT's als

observationele studies werden geïncludeerd en methodologisch beoordeeld volgens de MINORS-criteria.[6] De in- en exclusiecriteria van deze studie zijn weergegeven in de tabel.

TABEL. In- en exclusiecriteria voor studies in een meta-analyse[2]. Voor deze meta-analyse werden RCT's en observationele onderzoeken naar de behandeling van proximale humerusfracturen gebruikt

Inclusiecriteria	**Exclusiecriteria**
• proximale humerusfractuur • vergelijking conservatieve versus operatieve behandeling • functionele resultaten en complicaties als uitkomstmaten	• publicatie in andere taal dan Engels, Nederlands of Duits • geen volledige tekst beschikbaar • er zijn patiënten jonger dan 18 jaar geïncludeerd • brieven, notulen of casuïstiek • operatieve behandeling met externe fixatie

eerste auteur van de studie	operatie	conservatieve behandeling		
	Constant-Murley-score; gemiddelde (SD)	Constant-Murley-score; gemiddelde (SD)	gewicht; %	MD (95%-BI)
cohort				
Blonna	72 (25,4)	58,2 (25,4)	5,5%	13,80 (0,51-27,09)
v.d. Broek	67,1 (11,8)	81,4 (9,75)	9,1%	-14,30 (-21,09- -7,51)
Hageman	63,3 (35,2)	87,5 (35,2)	4,1%	-24,20 (-41,18- -7,22)
Hauschild	74,2 (13)	74,3 (9,9)	10,5%	-0,10 (-4,66-4,46)
Innocenti	56,5 (5,24)	52 (9,03)	10,5%	4,50 (-0,09-9,09)
Kollig	72,1 (21,1)	82 (15,6)	4,7%	-9,90 (-25,24-5,44)
Lange	72,3 (18)	72 (19)	8,4%	0,30 (-7,71-8,31)
Okike	58 (16,9)	59,7 (17,)5	7,3%	-1,70 (-11,57-8,17)
Tamimi	65,1 (19)	57,2 (12,7)	9,4%	7,90 (1,53-14,27)
subtotaal (95%-BI)			69,4%	-1,50 (-7,33-4,33)
test voor totaal effect: Z = 0,50 (p = 0,61)				
RCT				
Boons	64 (15,8)	60 (17,6)	7,4%	4,00 (-5,55-13,55)
Fjalestad	51,8 (30,6)	53,2 (26,8)	4,0%	-1,40 (-18,77-15,97)
Olerud HA	48,3 (16,4)	49,6 (20,5)	7,0%	-1,30 (-11,67-9,07)
Olerud LP	61 (19,2)	58,4 (23,1)	6,4%	2,60 (-8,86-14,06)
Zyto	60 (19)	65 (15)	5,9%	-5,00 (-17,52-7,52)
subtotaal (95%-BI)			30,6%	0,40 (-4,76-5,56)
test voor totaal effect: Z = 0,15 (p = 0,88)				
totaal (95%-BI)			100%	-0,87 (-5,13-3,38)
test voor totaal effect: Z = 0,40 (p = 0,69)				



MD = gemiddelde-verschil.

FIGUUR 2. Proximale humerusfractuur conservatief of operatief behandelen? Vergelijking van de resultaten van conservatieve versus operatieve behandeling. Forestplot van de functionele uitkomsten van de behandeling, gemeten met de Constant-Murley-score (bewerking van een eerder gepubliceerde figuur).[2]

Volgens deze meta-analyse geeft operatieve behandeling van proximale humerusfracturen een hoger risico op majeure re-interventies en een lager risico op een non-union gevonden. Een sensitiviteits-analyse toonde geen verschil aan voor implantaat, studies die na 2005 waren gepubliceerd of studies van hoge kwaliteit (arbitrair gedefinieerd als MINORS > 16). Gezien de gemiddelde leeftijd van de geïncludeerde patiënten (68 jaar, met een relatief kleine standaarddeviatie) lijken deze resultaten vooral van toepassing op de 'oudere' patiënt. Verder is opvallend dat 75% van de geanalyseerde patiënten vrouw was, wat bijdraagt aan de ontwikkeling van een stereotype voor de patiënt met een proximale humerusfractuur: ouder en van het vrouwelijke geslacht.[6,14] In het ontwikkelen van een stereotype patiënt en het projecteren van deze stereotypie op de gehele populatie, schuilt echter een gevaar. Het kan andere, niet-vergelijkbare patiënten tekort doen.

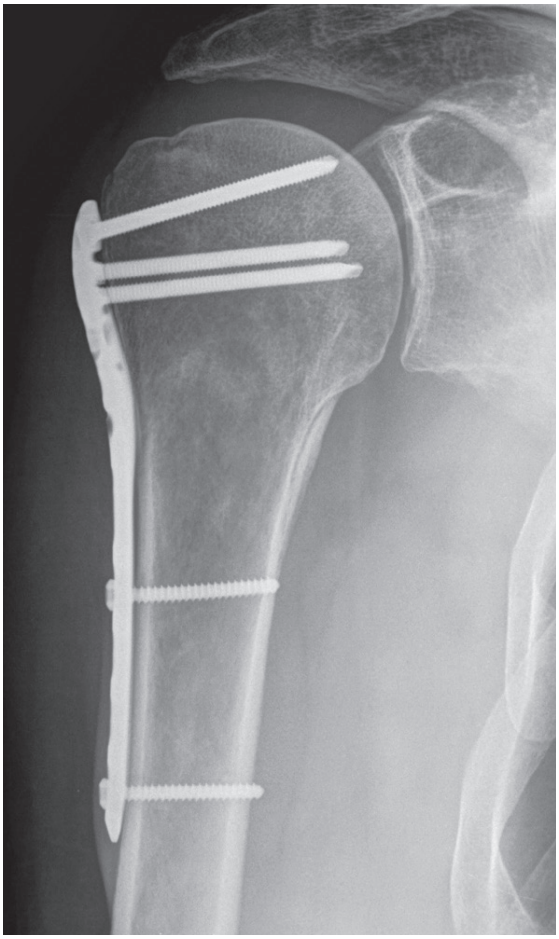
Wij concluderen dat er in ieder geval genoeg wetenschappelijk bewijs is voor het uitgangspunt dat patiënten met een niet tot weinig gedislokeerde proximale humerusfractuur en oudere of multimorbide patiënten met een proximale humerusfractuur conservatief behandeld dienen te worden.

Wie dan toch operatief behandelen?

Is er dan niemand gebaat bij een operatieve behandeling van zijn of haar proximale humerusfractuur? Wie doet het wél beter na een operatie?

Met de komst van hoekstabiele implantaten zijn er naast de bekende conservatieve behandeling nieuwe behandelmogelijkheden ontwikkeld met bijvoorbeeld plaat- of penosteosynthese (figuur 3).[8-10] Deze ontwikkeling heeft ook geleid tot minimaal-invasieve technieken die voordelen bieden boven de klassieke open behandeling van fracturen, maar deze zijn technisch lastig en hebben een langere leercurve. Een prothese kan uitkomst bieden bij de behandeling van proximale humerusfracturen. De voordelen van operatie zijn een vroege functionele nabehandeling, minder kans op non-union en een anatomische reconstructie of prothese, wat in theorie zou moeten leiden tot een betere functioneel resultaat.[6,10]

In de meeste studies naar de behandeling van proximale humerusfracturen worden open fracturen, luxatiefracturen, pathologische fracturen en proximale humerusfracturen bij multitraumapatiënten aangevoerd als exclusiecriteria.[6,8] Hiermee lijkt het algemeen geaccepteerd te zijn dat patiënten met deze fracturen geopereerd dienen te worden, al is dit niet bij elke indicatie onderzocht. Verder worden ook jonge patiënten vaak geopereerd, hoewel dat niet wordt ondersteund door wetenschappelijk bewijs.



FIGUUR 3. Röntgenfoto van de rechter schouder van de patiënt in figuur 1a, 2 dagen na osteosynthese met een Philos-plaat.

Luxatiefracturen zijn speciale proximale humerusfracturen waarbij het gewrichtsvlak van de humeruskop naar anterieur of posterieur geluxeerd is. Over het algemeen wordt bij deze patiënten een prothese geadviseerd als zij ouder zijn;[15] bij jongere en anderszins fitte patiënten wordt een osteosynthese aanbevolen. Hoewel bekend is dat osteosynthese een hoog risico op een avasculaire kopnecrose geeft, leidt deze ingreep bij veel patiënten tot een goed functioneel resultaat. Bij 20% van de patiënten is later echter alsnog een prothese nodig.[15]

Dat niet-gedislokeerde proximale humerusfracturen conservatief behandeld worden, staat niet ter discussie. Ook de geriatrische patiënt met multimorbiditeit en een

gedislokeerde proximale humerusfractuur wordt conservatief behandeld. Wij vinden het echter niet gerechtvaardigd om een harde leeftijdsgrens te stellen zonder te kijken naar de activiteitsgraad van de patiënt.

Een prospectieve Zwitserse studie bij patiënten met een proximale humerusfractuur die met een Philos-plaat werden behandeld, liet een goed functioneel resultaat na gemiddeld 1,5 jaar zien (gemiddelde Constant-score: 75, 91% van de contralaterale zijde).[9] In deze studie werden 97 patiënten geanalyseerd die gemiddeld 62 jaar oud waren ten tijde van het ongeluk. Bij 50% van de patiënten was het traumamechanisme een ski- of snowboardongeval. 91% van de patiënten paste in ASA-klasse 1 of 2. Het gaat hier dus, in vergelijking met andere studies, om een relatief jong, fit en actief patiëntencohort. Kijk nu nog eens terug naar de casus aan het begin van het artikel: wat betekenen deze resultaten voor u, met uw gebroken schouder? Want u bent natuurlijk fit en actief.

Nadelen van opereren

Naast de algemene nadelen en complicaties van operaties in het algemeen, zoals bloeding en wondinfectie, zijn er ook operatie-specifieke complicaties. Bekende complicaties zijn schroefperforatie door de humeruskop, avasculaire kopnecrose, implantaatgerelateerde irritatie en letsel van de N. axillaris.[9,10] In een studie naar deze complicaties werden 282 patiënten geanalyseerd, van wie 108 in Nederland waren geopereerd en 174 in Zwitserland.[10] Bij deze analyse werden er 196 complicaties bij 127 patiënten geturfd. Bij 80 patiënten werden 132 heroperaties verricht, waaronder verwijdering van het osteosynthesemateriaal. De meest voorkomende complicatie was schroefperforatie door de humeruskop. Dit kwam voor bij 65 patiënten (23%), wat veel is in vergelijking met de 7% uit eerdere literatuur.[9] De plaat werd verwijderd bij 51 patiënten (18%). Avasculaire kopnecrose komt even vaak voor bij conservatief behandelde als bij operatief behandelde patiënten.[6]

Verschillen Nederland en Zwitserland

Het is duidelijk dat er een verschil is tussen Nederland en Zwitserland als het gaat om de keuze voor een conservatieve dan wel operatieve behandeling van proximale humerusfracturen. Waar in Nederland 12% van de patiënten met een clavicula- of schouderfractuur operatief behandeld wordt, ligt dat getal in Zwitserland alleen al voor proximale humerusfracturen veel hoger.[1,12] Een vragenlijstonderzoek onder Duitse, Oostenrijkse en Zwitserse ziekenhuizen liet zien dat in de meeste ziekenhuizen meer dan 40% van de patiënten met een proximale humerusfractuur operatief behandeld wordt.[12] Doet het ene land het nu beter dan het andere?

In de eerder genoemde vergelijkende studie tussen Nederland en Zwitserland bleek dat patiënten in Nederland gemiddeld na 5 dagen worden geopereerd, in Zwitserland na een halve dag.[10] In die studie was er een trend naar een minder goede repositie van het tuberculum majus in Nederland. Opvallend was ook het grotere aantal complicaties in Nederland. Verder gingen een lagere leeftijd en een anatomische repositie van het tuberculum majus gepaard met minder complicaties.[10] Mogelijk dat het vaker en eerder doen van deze ingreep bijdraagt aan een lager complicatierisico.

TOEKOMSTIG ONDERZOEK

Momenteel wordt een studieopzet geschreven voor een internationale, multicentrische, observationele cohortstudie naar de behandeling van proximale humerusfracturen. In de geplande studie worden alle patiënten met een proximale humerusfractuur prospectief geïdentificeerd. Patiënten zullen worden geïncludeerd vanuit 4 perifere ziekenhuizen uit 2 landen met een voorkeur voor een operatieve (Zwitserland) dan wel conservatieve behandelstrategie (Nederland).

Inclusie zal plaatsvinden op basis van 'agree to disagree'.[16] Hiertoe zal elke patiënt afzonderlijk worden beoordeeld door een expertpanel dat bestaat uit 6 traumachirurgen vanuit deze centra die zijn geblindeerd voor de behandeling; de behandeling begint overigens al voordat het expertpanel zijn oordeel geeft. Als de meerderheid van de Zwitserse chirurgen voor een operatieve behandeling kiest en de meerderheid van de Nederlandse chirurgen voor conservatieve behandeling, kan de patiënt worden geïncludeerd. Zodoende zullen er twee vergelijkbare groepen worden gecreëerd, waarna beide behandelingen met elkaar kunnen worden vergeleken.

CONCLUSIE

De resultaten van de besproken meta-analyse laten zien dat patiënten met niet of weinig gedislokeerde proximale humerusfracturen conservatief kunnen worden behandeld. Ook gedislokeerde proximale humerusfracturen bij oudere, osteoporotische en multimorbide patiënten kunnen goed conservatief worden behandeld.

Andere studies laten zien dat oudere patiënten met een luxatiefractuur in aanmerking komen voor een prothese en jongere patiënten met een luxatiefractuur voor een osteosynthese. Bij patiënten met een gedislokeerde proximale humerusfractuur die nog actief en fit zijn, is er in Europa geen consensus over het te voeren beleid. Verder onderzoek moet uitwijzen voor welke patiënt een operatie zinvol is.

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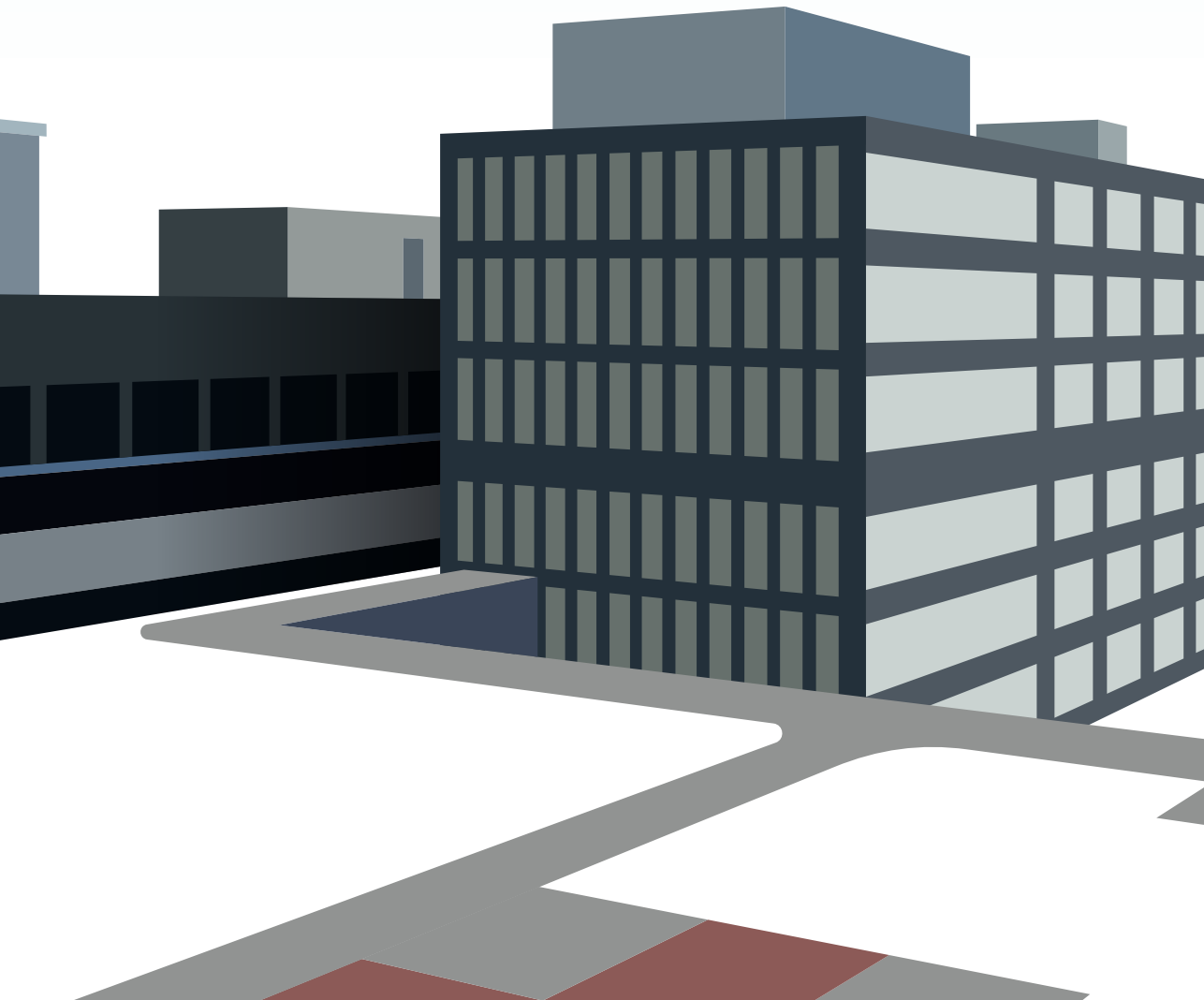

CHAPTER 11

Discussion and future perspectives

UNSOLVED FRACTURES?

Clavicle fractures and proximal humeral fractures are very common[1-4] and both orthopedic and trauma surgeons treat these fractures on a regular basis. Despite many years of medical development and research, there is still an ongoing debate about the best treatment modalities of these fractures.[5-9] Either operative or non-operative treatment and if treated operatively by means of which technique are still issues that have to be solved.

In this thesis we discuss controversies concerning the treatment of clavicle fractures. For displaced clavicle fractures, the indication for operative treatment, especially for the active and demanding patient seems clear.[6-8, 10, 11] However the discussion on technical improvement is still ongoing.

This thesis also aims to facilitate future discussion on which patient with a proximal humeral fracture could benefit from operative treatment and which patient should be treated non-operatively. The key to success will be patient selection.

CLAVICLE FRACTURES

Clavicle fractures are very common fractures with an incidence of 30 per 100,000 and represent 2.6% - 4% of all fractures.[1, 12, 13] Fractures of the clavicle shaft have the highest incidence and account for 69% of all clavicle fractures. Lateral clavicle fractures and medial clavicle fractures have a lower incidence and account for 28% and 3% respectively.[1]

For decades, clavicle fractures were treated primarily conservatively.[14, 15] However, non-union rates after conservative treatment appear higher than previously reported, in addition to a presumed better functional outcome following surgical treatment.[7, 11, 12, 16, 17] This has led to a paradigm shift during the last 15-20 years towards an increase in operative treatment. Ongoing interest in the literature regarding the optimal treatment for these fracture types seems to have led to an increase in scientific data favoring operative treatment.[11, 13, 16-20]

There is little discussion that non-displaced and stable clavicle fractures are treated non-operatively. This conservative treatment consists of a shoulder sling (collar and cuff) for 6 weeks, 2-3 weeks fixed and 3 weeks intermediate use. The main purpose of this sling is patient comfort during the initial phase. As soon as pain subsides, usually after 2-4 weeks, physiotherapy may start with passive range of motion (ROM) exercises

followed by active ROM and strengthening exercises preventing abduction more than 90 degrees for 6 weeks.[16, 18, 21-26] After 6 weeks, free movement and progressive strain is allowed.

Medial clavicle fractures

Medial clavicle fractures, as mentioned before, are rare and mostly occur after a high energy trauma.[27] As these fractures are rare, little evidence is available about the best treatment. Displaced medial clavicle fractures may lead to up to 14-20% of non-unions compared to 7% for non-displaced medial clavicle fractures.[18, 25] Therefore, operative treatment for displaced medial clavicle fractures can be considered according to recent literature.[5, 19, 26, 28, 29] Several operative techniques and implants for open reduction and internal fixation (ORIF) of medial clavicle fractures have been described. Fixation with inverted LCP™ Superior Anterior Clavicle Plate with lateral extension is mostly used.[19] As presented in this thesis, we suggest the radial (VA)-LCP™ Distal Humerus Plate as a solution for intra-articular fractures or extra-articular fractures with a small medial fragment.[5] As far as we know, no anatomical shaped medial clavicle plate has been developed yet. The functional outcome of the operative treatment of displaced medial clavicle fractures as published in three retrospective studies showed good to excellent results. Therefore, we propose operative treatment for (one shaft width) displaced medial clavicle fractures.

Clavicle shaft fractures

Many midshaft clavicle fractures, and most certainly the non-displaced midshaft clavicle fractures, can be treated conservatively. More has become known about the benefits of operative treatment for displaced midshaft clavicle over the last few decades: less chance of non-union (1-2%), faster return to work in an active population and a better short-term functional outcome.[7, 11-13, 16, 20, 21, 23] Functional outcomes after one year are equally good in both groups.[7, 8, 11, 17, 20, 21] Operative treatment may consist of (percutaneous) intramedullary fixation (IMF), either antegrade or retrograde, or plate fixation (PF). Several studies regarding this topic have recently been published.[10, 30-32] Some studies show a faster recovery and better short-term functional outcome at three to six months after plate fixation.[10, 30] Benefits of IMF compared to PF include, besides the obvious smaller scar, shorter operation time, fewer infections, fewer major re-interventions and a lower re-fracture risk after implant removal.[6, 30, 32] One of the disadvantages and complications of operative treatment in general is implant related irritation, encountered in both treatment modalities in up to 70%.[30, 33] This is why we conducted two studies on this topic. Implant related irritation after IMF could be caused by telescoping of the nail at the entry side.[10, 34] Unfortunately the application

of an end cap with the aim to prevent this telescoping did not result in less implant-related irritation as the end cap is in itself bulky.[34] Furthermore, we found more major re-interventions after the application of an end cap. We therefore concluded that end caps should not be used. In the other study presented in this thesis, we found the degree of fracture comminution to be a strong predictor of slower recovery, poorer functional outcome and more implant-related irritation.[30, 35] This effect has not been seen after plate fixation. Because of our results, supported by the results of other studies, we advocate IMF for non-comminuted displaced midshaft clavicle fractures only.[6, 30, 35] Bedsides complications, possible implant removal is a clear disadvantage of operative treatment resulting in secondary operations. Wide ranges of implant removal rates are reported ranging from 17-82%.[13, 17 30, 33] This is something that has to be clearly mentioned when discussing treatment options with patients.

We propose non-operative treatment for all non-displaced and slightly displaced fractures with bony contact. Operative treatment should be discussed with and offered to patients with a displaced midshaft clavicle fracture presenting the above-mentioned advantages and disadvantages resulting in shared decision making. Especially young and highly demanding active people who prefer a low non-union risk and early functional movement will benefit from this operative treatment. Simple fractures can be treated with IMF. Comminuted fractures should be treated with PF.

Lateral clavicle fractures

Stable fractures (Neer I and III) as well as fractures at or medially from the cc-ligaments that are non-displaced can be treated conservatively. Operative treatment is warranted for displaced unstable fractures (Neer IIa, IIb and V) as conservative treatment results in up to 33% non-unions.[24, 36] Until now, many different treatment options like K-wire fixation, locking plate fixation, hook plate fixation, coracoid-clavicle screw fixation and (arthroscopical) button fixation have been proposed. However, in current literature, none of these options have proved to be the golden standard to date.[36-38] No randomized controlled trials (RCT) are available and most studies have been reporting on small series. In this thesis we compared the functional outcomes of instable lateral clavicle fractures treated with a clavicle hook plate and the LCP™ Superior Anterior Clavicle Plate with lateral extension. We found no difference in patient-oriented functional outcome. However the LCP™ Superior Anterior Clavicle Plate with lateral extension has a lower implant removal rate compared to the clavicle hook plate. More recently, coracoclavicular button fixation, either open, minimally invasive or arthroscopically,

has been described.[39-41] These newer techniques seem promising, but, as only very little evidence on these techniques exists, future comparative studies are necessary to determine their clinical value.

Stable Neer I and III fractures as well as non-displaced instable Neer IIA, IIB and V lateral clavicle fractures can be treated non-operatively. Unstable and displaced Neer IIA, IIB and V lateral clavicle fractures should be treated with pre-shaped locking plate fixation whenever sufficient stable fixation in the lateral fragment is possible. For fractures with a small lateral fragment, where stable fixation is not possible, a hook plate can be used.

PROXIMAL HUMERAL FRACTURES

The proximal humerus fracture is the third most common fracture seen in the elderly with an incidence of 82 per 100,000 per year with an annual increasing rate of 13.7% per year over the last 33 years.[3, 4] The typical patient is a female aged 65 or over.[42] However, this fracture can also be seen in young and active people.[43] For instance, fracture-dislocations, a rare entity in proximal humeral fractures, often occur after high energy trauma and in younger people.[44, 45] In general, 75% of patients are treated non-operatively, and one out of five will undergo surgery depending on fracture type and displacement.[46]

Depending on factors such as patient age, activity and fracture pattern, operative treatment options include intramedullary fixation, (minimally invasive) ORIF or arthroplasty of the glenohumeral joint. Non-operative treatment usually starts with immobilization followed by passive and active rehabilitation.[46] Despite the fact that the available literature is inconclusive regarding the superiority of either treatment option, it is common practice to attempt joint saving operative procedures in younger patients.[46, 47] Additionally, there is no consensus whether surgery is beneficial for the older patient with a displaced proximal humerus fracture.

In addition there appears to be a difference in the treatment of proximal humeral fractures between different countries.[2, 48] In a Dutch epidemiological study, Beerekamp et al. found that in the Netherlands, 12% of all clavicle and shoulder fractures are treated operatively.[2] This is in great contrast to a survey presented by Tepass et al. who showed that in Germany, Austria and Switzerland 94%, 53% and 73% of all hospitals treat more than 40% of all proximal humeral fractures operatively.[48] The reason for this difference is unclear and only hypothetical answers like 'cultural difference, difference in fracture

types or population' can be given. Interestingly, Beeres et al. showed by analyzing the functional results and complications in the Netherlands and Switzerland that the results were better in the country that performed more of these operations.[49]

Available literature does not provide a clear answer to the question: 'which patient with a proximal humeral fracture will benefit from an operative treatment and which patient is better off without an operation in general?' The Cochrane review on the treatment of proximal humeral fractures by Handoll et al. did not show any difference in outcome between these treatment modalities.[47] However these results have to be interpreted with caution as the results did not cover two-part tuberosity fractures, fractures in young people, high-energy trauma, fracture-dislocations and humeral head splitting fractures. Furthermore, the most influencing trial in this analysis, the PROPHER trial, has several shortcomings.[50] Only 32% of the screened patients were included (e.g. several patients with clear indication for surgery were excluded). In 11% of cases, fairly inexperienced surgeons (e.g. registrars) performed the operation and 17% were operated on with something other than a plate (e.g. hemi-arthroplasty).

In this thesis we have performed a review and meta-analysis of randomized controlled trials and observational studies comparing the operative and non-operative treatment of proximal humeral fractures.[51] This meta-analysis did not show a benefit for either the operative or the non-operative treatment when analyzing the functional outcome. Consequently we concluded that proximal humeral fractures should be treated conservatively. The question rises, however, as to which patient benefits from operative treatment of these fractures, and the challenge remains patient selection.

As with most reviews and meta-analyses, the more patients that are included the more heterogeneous the groups become. Due to the fact that the mean functional outcomes are compared, it always results in half of the patients falling above and half of them below this mean. Therefore it is interesting and necessary to know who these patients are. For instance, who are these patients who do better with the non-operative treatment and who are these patients that are doing worse after surgery? And off course vice versa!

As discussed above, proximal humeral fracture-dislocations are a rare entity in proximal humeral fractures. These fractures mostly occur after a high-energy trauma.[44, 45] In these fractures the humeral head is dislocated either anteriorly or posteriorly out of the glenohumeral fossa. The indication for operative treatment of these fractures seems clear. No literature about the conservative treatment of these fractures is available. In elderly patients these fractures should be treated with a prosthesis.[44, 45] In young and active people an attempt for preservation of the humeral head with an osteosynthesis

should be performed. Trikha and Soliman already presented relatively good results after ORIF in young patients.[44, 45] In this thesis we presented our technique of the minimally invasive plate osteosynthesis of these fracture-dislocations with comparable results. However, patients should be informed about a high rate of reoperations. Twenty percent will eventually end up with a secondary shoulder prosthesis.

Combining the available evidence, it is clear that there is a great role for conservative treatment of proximal humeral fractures. Non- or slightly-displaced proximal humeral fractures should be treated non-operatively. Elderly and frail patients with displaced fractures can also be treated non-operatively. In cases of severe persisting pain, a prosthesis can be discussed with these patients. Fracture-dislocations should be treated operatively: in elderly patients with a prosthesis and in young and active people with an osteosynthesis. No consensus is available for young and active patients with a displaced proximal humeral fracture. No specific studies concerning this group of patients have been published. Even without evidence, many trauma surgeons tend to operate on these patients.

FUTURE PERSPECTIVES

Regarding clavicle fractures, the advantages and disadvantages of either an operative or non-operative treatment have become clearer during the last two decades. The decision between these treatment modalities has to be made in a shared decision making model where the treating surgeon and the patient decide together. Future studies will have to focus on new implants and or techniques, especially for the medial and lateral fractures.

In proximal humeral fracture treatment, the challenge lies in the patient selection. It is clear that many patients can be treated non-operatively. However there might be a possible benefit of an operative treatment in active and young patients. This is an area that has to be explored. A proposed study model is a study that is based on 'agree to disagree'. This model allows a comparison of 'borderline' patients with a proximal humeral fracture. Patients who are treated non-operatively in the Netherlands (and based on x-rays and clinical case would have been treated operatively in Switzerland) will be compared to patients who are operated on in Switzerland (and who would have been treated non-operatively in the Netherlands according to an expert panel).

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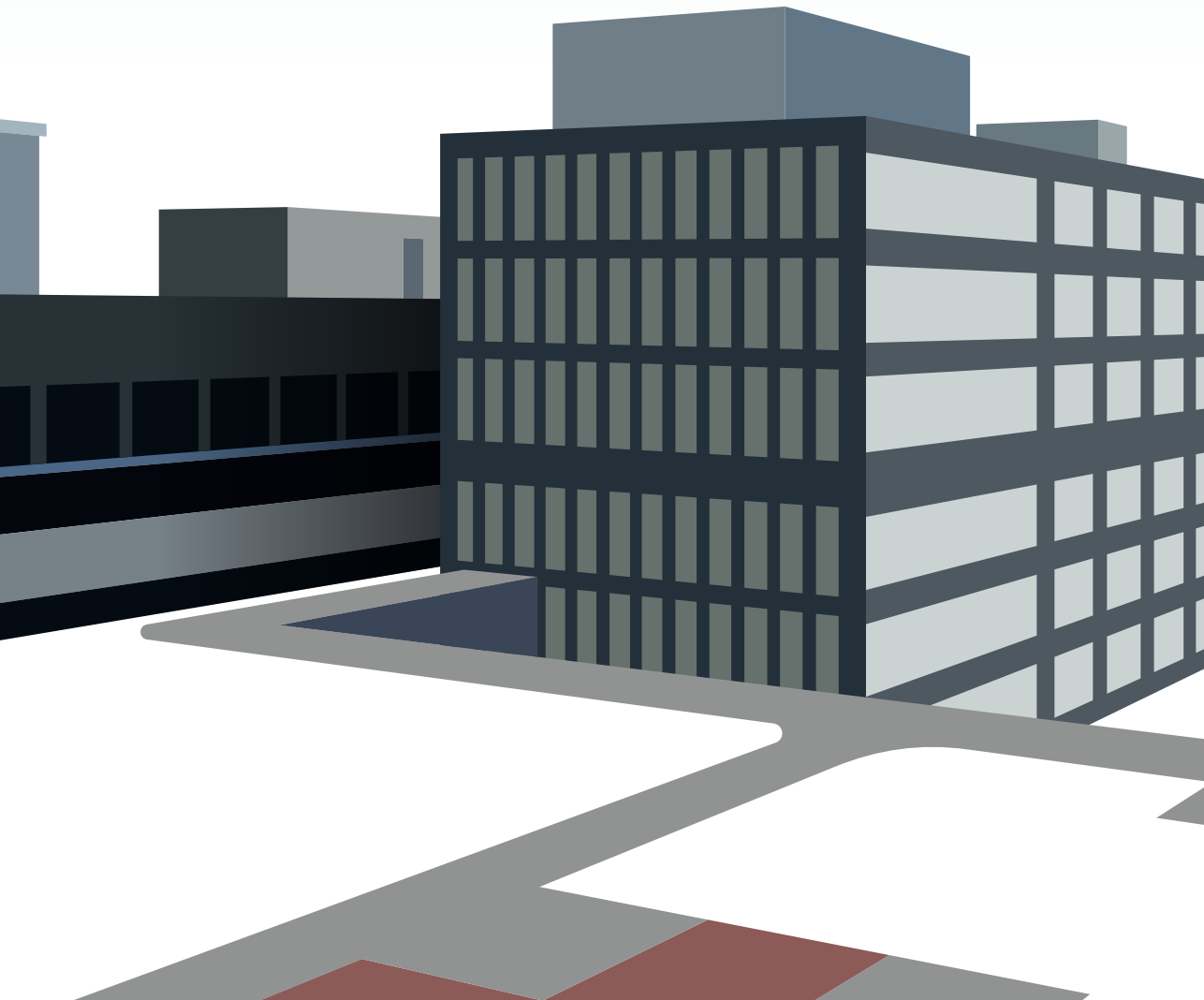


CHAPTER 12

Summary

Clavicle and proximal humeral fractures are very common and used to be treated non-operatively. The last two decades we have seen a shift however towards more operative treatment. Despite many trials and other studies, until now there is still an ongoing debate about what the best treatment modality is for these fractures. 'Patient selection' together with 'shared decision making' are hot topics and are probably the key to future indications for operative or non-operative treatment of these fractures. This thesis presents several studies that aim to provide further evidence that can aid in making a decision for the best treatment for every single patient. Part 1 addresses clavicle fractures and Part 2 covers the topic of proximal humeral fractures.

PART 1: CLAVICLE FRACTURES

In **chapter 2** the treatment of displaced medial clavicle fractures is discussed. Medial clavicle fractures are rare injuries and historically treated non-operatively. Displaced medial clavicle fractures, however, have a higher incidence of delayed- or non-union compared to non-displaced medial clavicle fractures and might benefit from operative treatment. We described a technique for treating intra-articular fractures or extra-articular fractures with a small medial fragment with the radial (VA)-LCP™ Distal Humerus Plate (DePuy Synthes, Switzerland). Furthermore, we have shown that operative treatment of these fractures, as measured with the QuickDASH and Subjective Shoulder Value, can result in an excellent functional outcome.

Implant-related irritation is a well known and technique specific complication seen in patients treated with intramedullary fixation for clavicle fractures. **Chapter 3** describes a study where we tried to to identify predictors for developing implant-related irritation in patients with displaced midshaft clavicle fractures treated with elastic stable intramedullary nailing. A retrospective analysis with multivariate analysis showed that comminuted and lateral diaphyseal fractures were found to be independent predictors for developing implant-related irritation. We therefore concluded that based on implant-related irritation, IM fixation might not be suitable for these types of fractures.

Chapter 4 is about another study on implant-related irritation after IM nailing of displaced midshaft clavicle fractures. We conducted an international study and compared a group of patients with the application of an end cap with a matched group without end cap over the end of the titanium nail to see if the application of an end cap could reduce the implant related irritation. This study showed that the end cap did not reduce the patient-reported implant-related irritation. Furthermore, in the end cap

group, there were more major revisions. Based on the results of this study, we concluded that no end caps should be used after intramedullary nailing for displaced midshaft clavicle fractures.

Lateral clavicle fractures are addressed in **chapter 5**. In this chapter we analyzed two different fixation methods for operative treatment of unstable Neer type II and type V lateral clavicle fractures (LCF), comparing the patient-reported functional outcome after open reduction and internal fixation with the clavicle hook plate (CHP) and the superior clavicle plate with lateral extension (SCPLE). Analysis of data from two Dutch hospitals showed that both the CHP and SCPLE are effective fixation methods for the treatment of unstable LCF, resulting in excellent patient-reported functional outcome and similar complication rates. The SCPLE however has a lower implant removal rate. Therefore we recommended that, if technically feasible, the SCPLE should be used for the operative treatment of unstable Neer type II and type V LCF.

In **chapter 6** we have brought the results of our own studies and the available literature together in a current concepts paper about clavicle fracture treatment. The operative and non-operative treatment options together with their indications for medial, shaft and lateral clavicle fractures are discussed. For all three anatomical locations, a treatment algorithm is proposed. In general, non-displaced fractures are treated conservatively. Operative treatment should be discussed with patients who have displaced fractures, especially in the young and active patient.

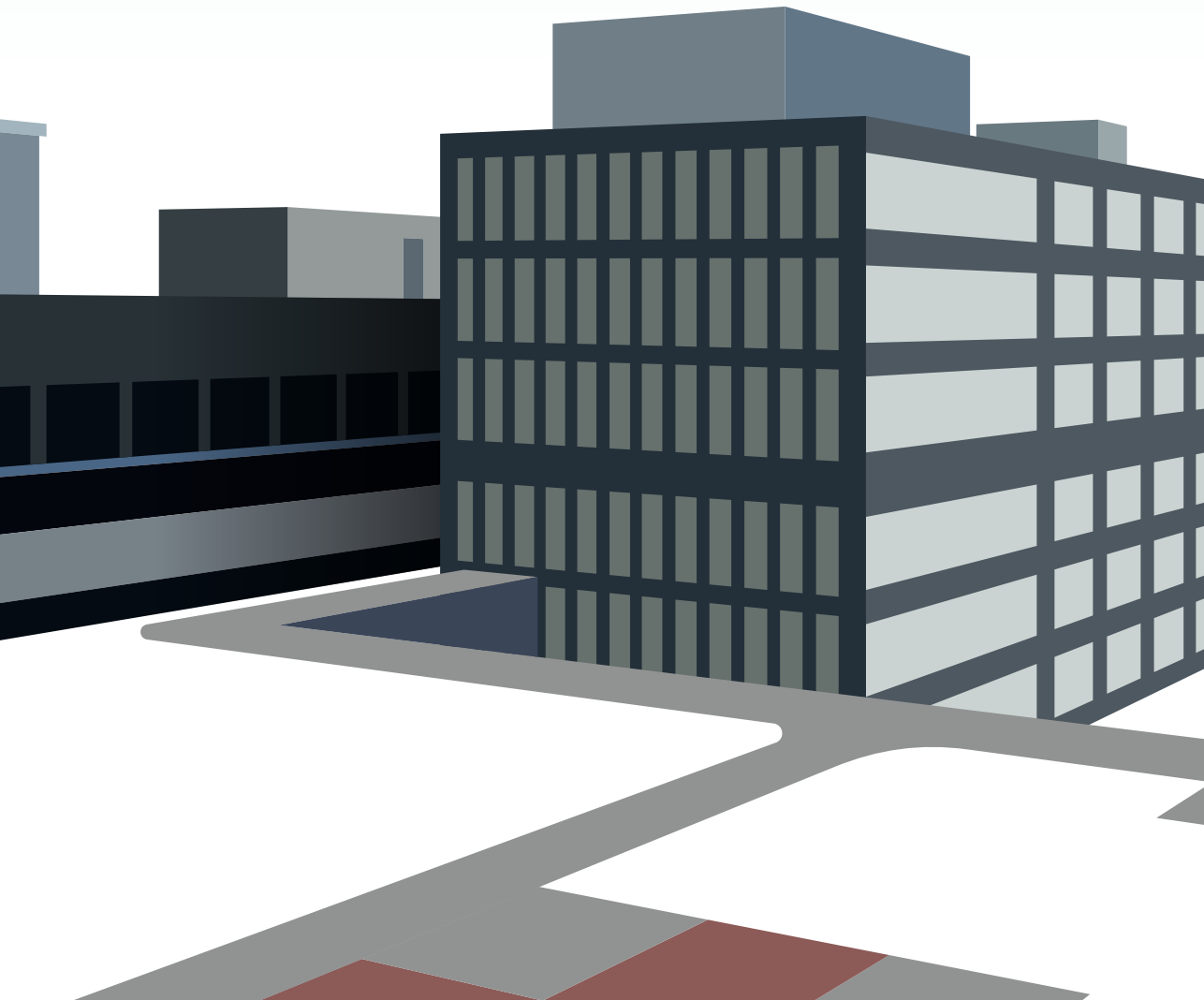
PART 2: PROXIMAL HUMERAL FRACTURES

As there is no consensus on the treatment for displaced proximal humeral fractures, **chapter 7** presents a systematic review and meta-analysis. The operative and non-operative treatments of displaced proximal humeral fractures were compared. Furthermore, a comparison was made of the effect estimates obtained from randomized controlled trials (RCT) and observational studies. Twenty-two studies were included and their quality was assessed using the Minors criteria. The primary outcome measure was physical function as measured by the absolute Constant-Murley score at least one year after operative or non-operative treatment. As we found no difference in functional outcome, we concluded that for the typical patient presenting with a displaced proximal humerual fracture—female and seventy years of age—we recommend the non-operative treatment. Pooled effects of observational studies were similar to those of RCTs and including observational studies led to more generalizable conclusions.

One of the developments in proximal humeral fracture treatment of the last two decades is the introduction of the minimally invasive plate osteosynthesis (MIPO). Although this technique has been described as suitable for the treatment of proximal humeral fractures, long-term functional results have never been reported. In **chapter 8** we studied the long-term functional outcome and implant-related irritation after MIPO for proximal humeral fractures. Analyzing 79 patients after a mean follow-up was 8.3 years, the patient reported functional outcome using the QuickDASH score and SSV showed promising results. However, about one third of the patients had a second operation for implant removal due to implant-related irritation.

Proximal humeral fracture-dislocations (PHFD) are a special entity in proximal humeral fracture treatment and are discussed in **chapter 9**. In these fractures, besides the fracture of the proximal humerus, the head of the humerus is dislocated either anteriorly or posteriorly. These fractures are generally treated operatively using an open deltopectoral approach. In this study we present our technique of MIPO of these special fractures through an anterolateral deltoid-split approach. In addition, we present our results reporting the patient-oriented functional outcome using the QuickDASH score and SSV, as well as our complications. Analysis of 28 patients through the MIPO approach showed promising results. In 86%, the humeral head was preserved. However, there is a high rate of re-operations either because of complications or for implant removal.

Proximal humeral fractures have an increasing incidence. Conservative treatment of these fractures has been standard of care for decades. Over the years, operative treatment has gained popularity and many new implants have been developed. However, recent literature comparing conservative and operative treatment of proximal humeral fractures did not show a difference in functional outcome between these treatment modalities. In **chapter 10** we present the current concepts of proximal humeral fracture treatment. In general, non- or slightly-displaced proximal humeral fractures are treated non-operatively. Also displaced proximal humeral fractures with elderly, osteoporotic and polymorbid patients can be treated conservatively. Older patients with a proximal humeral fracture-dislocation should be treated with a prosthesis, young and active patients with an osteosynthesis. For active and fit patients with a proximal humeral fracture there is no consensus about the treatment modality in Europe. Further research has to determine which patient will benefit from operative treatment and which patient will be better off with the non-operative treatment.



CHAPTER 13

Nederlandse samenvatting

Fracturen rond de schoudergordel
Onopgeloste fracturen?

Breuken van het sleutelbeen (clavicula) en van de schouder (proximale humerus) komen veel voor en worden van oudsher conservatief, dat wil zeggen zonder operatie, behandeld. De laatste twee decennia heeft er echter een omslag plaatsgevonden en worden deze fracturen vaak operatief behandeld. Ondanks vele trials en andere studies is er nog steeds een discussie gaande wat de beste behandeling is voor deze fracturen. 'Patiënten selectie' en 'shared decision making' zijn momenteel veel gehoorde en gelezen termen en waarschijnlijk van wezenlijk belang in de discussie wat voor welke patiënt de beste behandeling is. Dit proefschrift bevat meerdere studies die tot doel hebben aanvullend bewijs te leveren dat kan helpen bij deze beslissing. Deel 1 gaat over breuken van het sleutelbeen, deel 2 over breuken van de schouder.

DEEL 1: CLAVICULA FRACTUREN

Hoofdstuk 2 gaat over de behandeling van gedisloceerde mediale clavicula fracturen. Mediale claviculafracturen komen weinig voor en worden historisch gezien conservatief behandeld. Gedisloceerde mediale claviculafracturen hebben echter, vergeleken met niet gedisloceerde mediale claviculafracturen, een verhoogde kans op een vertraagd of niet genezende breuk, een delayed- of non-union. In dit hoofdstuk beschrijven we een techniek om intra-articulaire of extra-articulaire fracturen met een klein mediaal fragment te behandelen met de radiale (VA)-LCP™ Distal Humerus Plate (DePuy Synthes, Zwitserland). Verder laten we zien dat deze behandeling, gemeten met de QuickDASH score en de Subjective Shoulder Value (SSV), kan leiden tot goede functionele resultaten.

Implantaat gerelateerde irritatie is een bekende complicatie bij patiënten met een clavicula fractuur die met een intramedullaire titanium pen(netje) worden behandeld. **Hoofdstuk 3** beschrijft een studie waarbij gekeken is naar voorspellende factoren voor de implantaat gerelateerde irritatie na intramedullaire fixatie van gedisloceerde clavicula schacht fracturen. Een retrospectieve analyse met multivariate analyse liet zien dat laterale diafysaire fracturen een onafhankelijke voorspellende waarde hadden voor het ontwikkelen van implantaat gerelateerde irritatie. Hieruit concludeerden wij, dat op basis van implantaat gerelateerde irritatie, dit type fracturen minder geschikt zijn voor intramedullaire fixatie.

Hoofdstuk 4 gaat ook over implantaat gerelateerde irritatie na intramedullaire fixatie van gedisloceerde clavicula schacht fracturen. In een internationale vergelijkende studie hebben we een twee 'gematchte' groepen vergeleken waarbij bij de ene groep een end cap over het einde van het titatium pennetje is aangebracht en bij de ander niet. Een end cap is een titatium cap die over het uiteinde van een titatium pen in het bot gedraaid wordt. Vervolgens hebben we gekeken naar het wel of niet optreden van implantaat gerelateerde irritatie en complicaties. Deze studie liet zien dat het aanbrengen van een end cap niet resulteerde in minder implantaat gerelateerde irritatie. Wel waren er meer majeure revisies, dwz revisies van de osteosynthese in algehele narcose, in deze groep. Op basis daarvan hebben wij geconcludeerd dat er geen end caps moeten worden aangebracht bij de intramedullaire fixatie van gedisloceerde clavicula schacht fracturen.

Laterale claviculafracturen zijn het onderwerp van studie in **hoofdstuk 5**. In dit hoofdstuk hebben we twee operatieve fixatie methoden voor instabiele Neer type II en type V laterale clavicula fracturen (LCF) met elkaar vergeleken. De clavicula haakplaat enerzijds werd op basis van patiënt gerapporteerde functionele resultaten vergeleken met de 'LCP 2.7/3.5 superior clavicle plate with lateral extension' (DePuy Synthes, Zwitserland) (SPLE) anderzijds. Analyse van de gegevens uit twee Nederlandse ziekenhuizen liet zien dat beide implantaten effectieve fixatie methoden waren voor LCF en leidden tot goede functionele resultaten met vergelijkbare aantallen van complicaties. De SPLE moet echter in minder gevallen weer verwijderd worden. Daarom concludeerden wij dat, indien technisch haalbaar, de SPLE de voorkeur geniet voor de operatieve behandeling van LCF.

In **hoofdstuk 6** hebben we de resultaten van onze eigen studies met de beschikbare literatuur samengebracht in een 'stand van zaken' artikel over clavicula fracturen bij volwassenen. De operatieve en conservatieve behandelingsopties en hun indicaties van mediale- , schacht- en laterale clavicula fracturen worden beschreven. In het algemeen worden niet-gedisloceerde fracturen conservatief behandeld. Een operatieve behandeling moet besproken worden met patiënten met een gedisloceerde clavicula fractuur, met name bij jonge en actieve patiënten.

DEEL 2: PROXIMALE HUMERUS FRACTUREN

Aangezien er nog geen consensus is in de literatuur over wat de beste behandeling is bij proximale humerus fracturen hebben we in **hoofdstuk 7** een systematische review en meta-analyse uitgevoerd. Hierbij werd de conservatieve en operatieve behandeling bij gedisloceerde proximale humerus fracturen met elkaar vergeleken. Verder werd er

een vergelijking gemaakt van het effect van gerandomiseerd gecontroleerde trials en observationele studies. Tweeëntwintig studies werden geïncludeerd en beoordeeld met de Minors criteria. De primaire uitkomstmaat was het functionele resultaat, gemeten met de Constant-Murley score, minstens een jaar na de operatieve dan wel conservatieve behandeling.

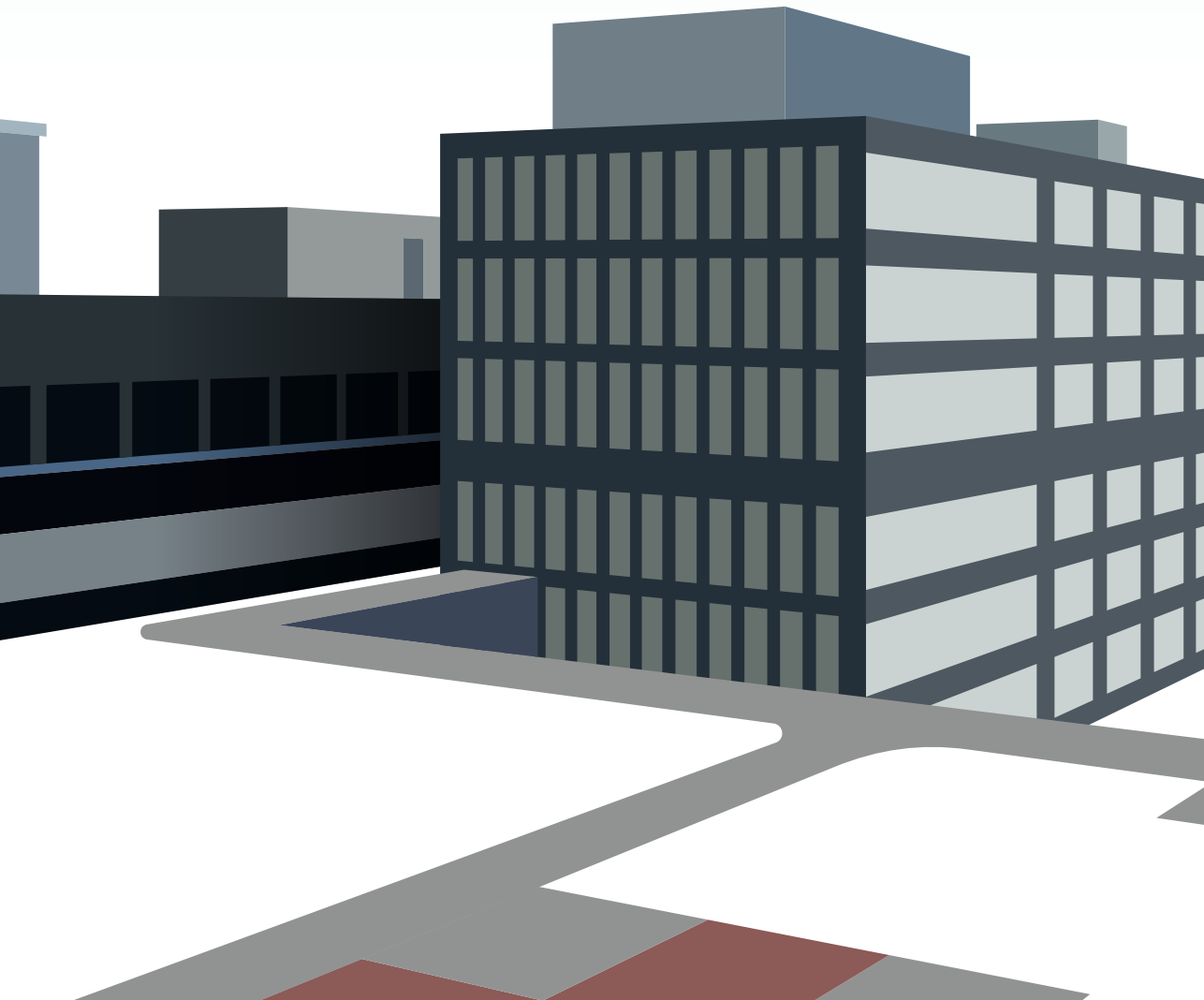
Aangezien we geen verschil in functioneel resultaat vonden, concludeerden we dat typische patiënt met een proximale humerus fractuur —vrouw en ouder dan 70— het beste af is met een conservatieve behandeling. Gepoolde effecten van observationele studies waren gelijk aan die van gerandomiseerd gecontroleerde trials. Het ook includeren van observationele studies resulteert in meer generaliseerbare conclusies.

Een van de ontwikkelingen in de behandeling van proximale humers fracturen van de laatste twee decennia is de introductie van de minimaal invasieve plaat ostesynthese (MIPO). Hoewel deze techniek al eerder beschreven is voor de behandeling van proximale humerus fracturen, zijn lange termijn resultaten nog niet bekend. In **hoofdstuk 8** analyseerden we de functionele lange termijn resultaten en implantaat gerelateerde irritatie na MIPO van proximale humerus fracturen. Deze analyse van 79 patiënten met een gemiddelde follow-up van 8,3 jaar liet, gemeten met de QuickDASH en SSV, veelbelovende resultaten zien. Echter, een derde van de patiënten had een tweede operatie nodig om vanwege implantaat gerelateerde irritatie de plaat te verwijderen.

Proximale humerus luxatie fracturen (PHLF) vormen een speciale entiteit binnen de proximale humerus fracturen en zijn onderwerp van studie in **hoofdstuk 9.** Bij deze fracturen is, naast het feit dat de proximale humerus gebroken is, de kop van de humerus naar anterieur of posterieur geluxeerd. Deze fracturen worden over het algemeen geopereerd via de deltopectorale benadering. In hoofdstuk 9 beschrijven we de MIPO techniek via een anterolaterale deltoid-split benadering voor deze frakturen. Verder presenteren we de functionele resultaten, gemeten met de QuickDASH en SSV, alsmede onze complicaties. Deze analyse van 28 patiënten met MIPO laat bemoedigende resultaten zien. In 86% van de patiënten kon de eigen humeruskop worden behouden. Echter, dit ging gepaard met een groot aantal re-operaties voor complicaties en implantaat verwijdering.

Proximale humerus fracturen komen steeds vaker voor. Patiënten met een proximale humerus fractuur worden van oudsher conservatief behandeld. De laatste decennia zijn echter diverse nieuwe implantaten voor het schoudergewricht ontwikkeld en is de operatieve behandeling van proximale humerus fracturen toegenomen. Recente literatuur waarin de conservatieve en de operatieve behandeling van proximale humerus

fracturen vergeleken wordt, laat echter geen verschil zien in functionele uitkomsten. De trend om vaker operatief te behandelen berust dus niet op wetenschappelijk bewijs. In **hoofdstuk 10** presenteren wij de huidige stand van zaken en proberen wij een genuanceerd beeld te geven van welke patiënt niet, maar ook welke patiënt mogelijk wél profiteert van een operatieve behandeling van de proximale humerus fractuur. In het algemeen worden niet- of weinig gedisloceerde proximale humerus fracturen conservatief behandeld. Oudere patiënten met een luxatie fractuur worden met een prothese behandeld, jonge en actieve patiënten met een osteosynthese. Voor de behandeling van actieve en jongere patiënten met een gedisloceerde proximale humerus fractuur is er nog geen consensus over de beste behandeling. Meer onderzoek is nodig om te bepalen wie wel en wie niet gebaat is bij een operatieve dan wel conservatieve behandeling van zijn of haar proximale humerus fractuur.



CHAPTER 14

Beoordelingscommissie

Curriculum Vitae

Dankwoord

Publications

BEOORDELINGSCOMMISSIE:

Prof. dr. I.H.R. Borel Rinkes
Prof. dr. M.H.J. Verhofstad
Prof. dr. F.C. Öner
Prof. dr. G.J. de Borst
Dr. E.J.M.M. Verleisdonk

CURRICULUM VITAE

Herman Frima was born on the 13th of August 1974 in Geldrop, Netherlands. After primary school, which he attended at the Vrije School, he went to gymnasium at the Lorenz Lyceum in Eindhoven. He studied medicine at the University Utrecht after which he enrolled in the tropical doctor training program in 2002. Before spending a year as tropical doctor at Nkhoma Mission Hospital in Malawi he was expedition doctor of the successful Vickspedition Ski800 (Dutch Cho Oyu Ski expedition, 8201m). After his return from Africa in 2005 Herman was trained in general surgery with a differentiation in visceral surgery at the Amphia Hospital in Breda (Dr. Van Geloven, Dr. Wijsman and Dr. Van der Laan) and the University Medical Centre Utrecht (Prof. Dr. Borel Rinkes). After an AO Trauma Fellowship in 2011 that he attended at the Kantonsspital Graubünden in Chur, Switzerland (Dr. Sommer), he specialized in trauma surgery in the Diakonessenhuis Utrecht/Zeist (Dr. Verleisdonk and Dr. Clevers). At the end of 2013 Herman and his family moved to Chur, Switzerland, where he has been working as a trauma surgeon at the Kantonsspital Graubünden. In September 2019 Herman will start as a trauma surgeon at the Northwest Hospital Group in Alkmaar, Netherlands.

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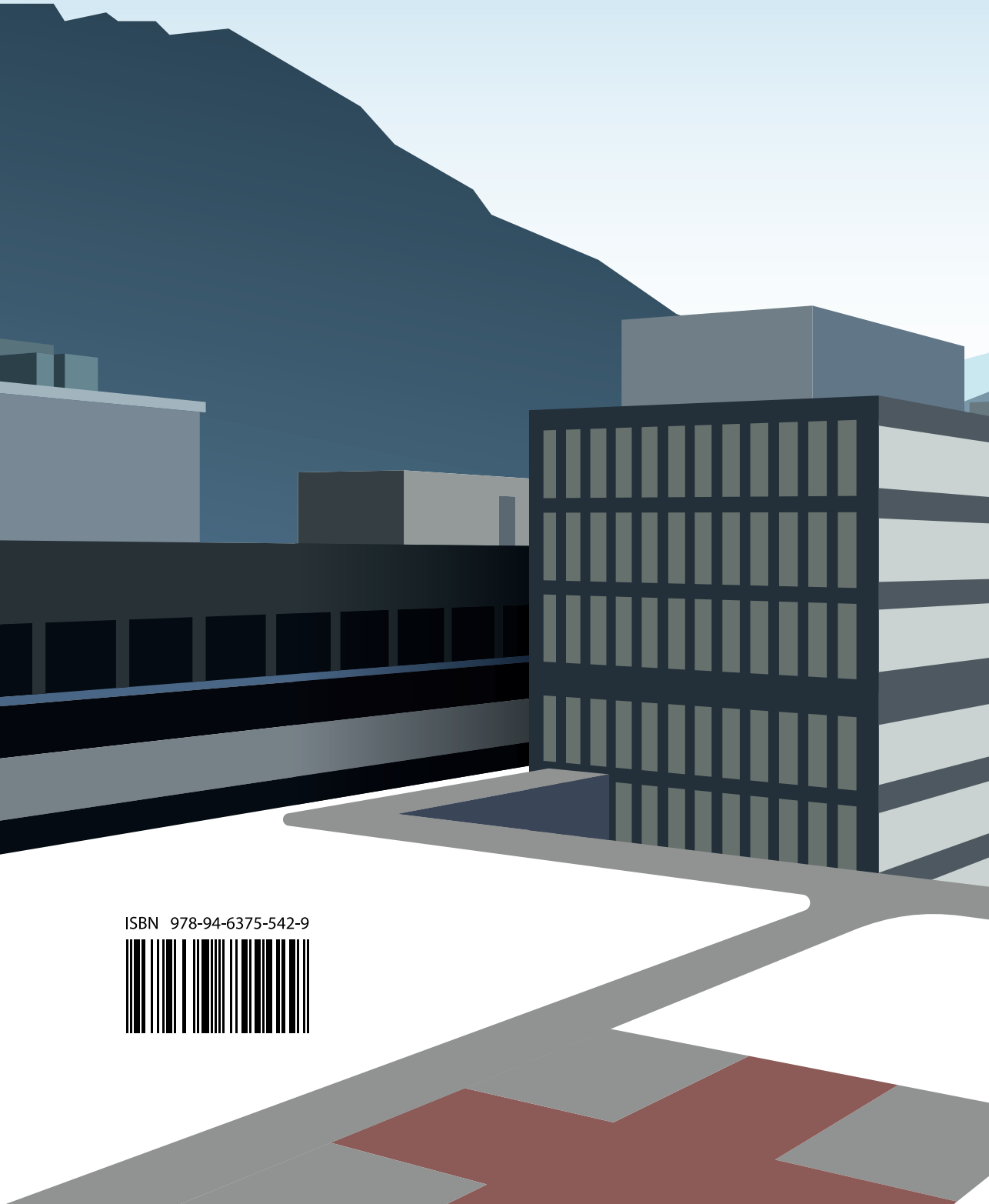

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