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ABSTRACT

Introduction: The number of operatively treated clavicle fractures has increased over the past decades. Consequently, this has led to an increase in secondary procedures required to treat complications such as fracture-related infection (FRI). The primary objective of this study was to assess the clinical and functional outcome of patients treated for FRI of the clavicle. The secondary objectives were to evaluate the healthcare costs and propose a standardized protocol for the surgical management of this complication.

Methods: All patients with a clavicle fracture who underwent open reduction and internal fixation (ORIF) between 1 January 2015 and 1 March 2022 were retrospectively evaluated.

This study included patients with an FRI who were diagnosed and treated according to the recommendations of a multidisciplinary team at the University Hospitals Leuven, Belgium.

Results: We evaluated 626 patients with 630 clavicle fractures who underwent ORIF. In total, 28 patients were diagnosed with an FRI. Of these, eight (29%) underwent definitive implant removal, five (18%) underwent debridement, antimicrobial treatment and implant retention, and fourteen patients (50%) had their implant exchanged in either a single-stage procedure, a two-stage procedure or after multiple revisions. One patient (3.6%) underwent resection of the clavicle. Twelve patients (43%) underwent autologous bone grafting (tricortical iliac crest bone graft ($n = 6$), free vascularized fibular graft ($n = 5$), cancellous bone graft ($n = 1$)) to reconstruct the bone defect. The median follow-up was 32.3 (P_{25}-P_{75}: 23.9–51.1) months. Two patients (7.1%) experienced a recurrence of infection. The functional outcome was satisfactory, with 26 out of 28 patients (93%) having full range of motion. The median healthcare cost was € 11.506 (P_{25}-P_{75}: € 7.953–23.798) per patient.

Conclusion: FRI is a serious complication that can occur after the surgical treatment of clavicle fractures. In our opinion, when treated adequately using a multidisciplinary patient-specific approach, the outcome of patients with an FRI of the clavicle is good. The median healthcare costs of these patients are up to 3.5 times higher compared to non-infected operatively treated clavicle fractures. Although not studied individually, we consider factors such as the size of the bone defect, condition of the soft tissue, and patient demand important when it comes to guiding our surgical decision making in cases of osseous defects.

Introduction

Fractures of the clavicle are common, with recent large national studies demonstrating an incidence ranging between 59.3 and 101 per 100,000 persons per year [1–3]. The number of operatively treated displaced clavicle fractures has increased over the course of the past decades [4]. This can be attributed to recent studies demonstrating lower non-union rates, faster return to function and less pain for operatively treated displaced fractures of the clavicle compared to non-operatively treated fractures [5–10]. However, high quality evidence on

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the superiority of surgical treatment of displaced midshaft clavicle fractures with respect to long term functional outcome is still lacking [8–10].

With the number of surgeries increasing, the number of secondary procedures will increase as well. One of the most important indications for such a secondary procedure is a fracture-related infection (FRI) [8,11]. FRI is a serious complication that is often related to orthopedic trauma. Studies showed that it has a major impact on the patient's quality of life [12] and can increase hospital-related healthcare costs by up to eight times compared to non-infected fractures [13]. Although studies focusing on infection after operatively treated displaced midshaft clavicular fractures are scarce, infection rates ranging between 0.4% and 7.8% have been reported [14–17]. As scientific data related to the management of FRI after the operative treatment of clavicular fractures is limited, standardized treatment protocols are almost nonexistent. The importance of standardized treatment protocols – based on a multidisciplinary team (MDT) approach – has recently been addressed by the *FRI Consensus Group* [18].

The primary objective of this study is to retrospectively evaluate the clinical and functional outcome of patients treated for FRI of the clavicle. The secondary objectives are to evaluate the healthcare costs of patients treated for FRI of the clavicle and propose a standardized protocol for the surgical management of this complication.

Methods

Study and patient characteristics

This retrospective study was conducted at the University Hospitals Leuven, which is a designated level-1 trauma referral center in Belgium. The protocol has been approved by the hospital's Ethics Committee (S66740). Between 1 January 2015 and 1 March 2022, 626 patients with 630 fractures underwent open reduction and internal fixation with plate and screw osteosynthesis for a clavicular fracture. These patients were identified from the operating theater logbooks. Of the identified patients, the data were retrieved from the hospital electronic patient file system and included in the study's database if they met the inclusion criteria. Inclusion criteria were: patients of sixteen years of age and older who were diagnosed with an FRI of the clavicle according to the criteria of the FRI consensus definition [19,20]. Exclusion criteria were: index surgery outside the study period (i.e., before 1 January 2015 or after 1 March 2022), noninfected fractures, non-operatively treated fractures and pathological fractures. Patients who were initially treated elsewhere for primary fracture fixation but who were later referred to our center for treatment of FRI were also included in this study.

Study variables

Patient files were screened for the following data: sex, age at time of initial infection surgery, body mass index (BMI), Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association (AO/OTA) fracture classification, fracture type (open/closed), American Society of Anesthesiologists (ASA) classification, initial fracture fixation device type, time to onset of FRI, treatment method, type of bone graft used and the total number of surgeries related to the treatment of infection. Patients were classified based on the definitive treatment method, i.e., definitive implant removal; Debridement, Antimicrobial therapy, and Implant Retention (DAIR); exchange of the implant in either a single-stage, a two-stage or a multiple-stage revision approach; resection of the clavicle. Patients who underwent exchange of the implant were subclassified in the following groups: 1) exchange of the implant without structural bone grafts; 2) exchange of the implant with autologous cancellous bone grafts (ACBG); 3) exchange of the implant with bone reconstruction using a tricortical autologous iliac crest bone graft (ICBG) or 4) exchange of the implant and reconstruction with a free vascularized fibular bone graft (FVFG). Furthermore, the duration of follow-up and both the clinical and functional outcome were recorded.

Definitions and outcome measures

The classification of fractures was based on the AO/OTA classification. This was evaluated using a standard radiograph (X-ray) and/or computed tomography (CT) scan. The overall management of the FRI patient was based on the recommendations of a multidisciplinary team. The MDT was composed of at least orthopedic/trauma surgeons, plastic surgeons, microbiologists, infectious disease specialists, radiologists, pharmacists, physiotherapists and specialist nurses. All decisions and agreements made by the MDT were documented in the patient's electronic medical record. Recurrence of infection was defined as the recurrence of a confirmatory sign according to the FRI consensus definition, within the follow-up period after cessation of surgical and antimicrobial treatment [19,20].

Clinical outcome

Outcome was based on clinical, functional and radiological evaluation during the last follow-up visit. During physical examination patients were monitored for signs of infection and shoulder function was assessed using the AO neutral 0-method: active anteflexion (40 – 180°) and scapular abduction (0 – 180°) [21]. Full range of motion (FROM) was defined as reaching 180° in both planes. Evaluation of bone healing was performed by a musculoskeletal radiologist and an experienced trauma surgeon and was based on plain X-rays, and/or CT-scans in case osseous reconstruction was required.

Healthcare costs and utilization

The patient's total healthcare costs are the sum of four main hospital-related cost categories: honoraria, materials, hospitalization (cost of daily patient care), and pharmaceuticals [22]. In summary, honoraria mainly consist of fees related to medical activities, mainly based on a fee-for-service principle (i.e., surgery, consults, and imaging). Material-related costs refer to the actual implants and other required materials. The hospitalization-related costs are the sum of the patient's actual length-of-stay multiplied by the day-based care fee. The day-based care fees were €647, €620, €670, €664, €650, €686 and €765 for 2015, 2016, 2017, 2018, 2019, 2020 and 2021, respectively. Pharmaceutical costs are all costs for received drugs and blood products. All costs were allocated with prices of 2015.

Statistical analysis

Study data was collected and managed using REDCap electronic data capture tool hosted at University Hospitals Leuven, Belgium [23]. Data was analyzed using Rstudio for Windows version 4.1.2. (RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA URL http://www.rstudio.com/). Counts and percentages were used to report descriptive statistics of categorical variables. The Shapiro-Wilk test was performed to test normality of continuous variables. Normally distributed variables were reported using mean and standard deviation (SD) and the median and inter-quartile range (P_{25}-P_{75}) were used for non-normally distributed variables.

Results

Patient characteristics

Out of the 626 patients with 630 clavicle fractures, 28 FRI patients, with a median age of 42.0 (22.5 - 49.5) years were included in this study. The infection rate in the group of patients initially treated in our center for their fracture was 2.9% ($n = 18$). Ten patients (1.6%) were initially treated for a clavicle fracture in another center and were later referred to

Table 1
Baseline patient characteristics.

	$N = 28$
Sex	
Female	6 (21.4)
Male	22 (78.6)
Age (years)	42.0 (22.5–49.5)
BMI (kg/m^2)	24.1 (22.3–27.4)
ASA classification	
1	15 (53.6)
2	12 (42.9)
3	1 (3.6)
Referral	
Yes	10 (35.7)
No	18 (64.3)
AO/OTA fracture classification	
15.2A	14 (50.0)
15.2B	4 (14.3)
15.2C	7 (25.0)
15.3A	2 (7.1)
15.3C	1 (3.6)
Open fracture	
No	28 (100)
Yes	0 (0)
Initial primary fixation device	
Plate and screw osteosynthesis	27 (96.4)
Screw osteosynthesis	1 (3.6)
Time to onset of FRI (days)	55 (37–132)

Data are shown as median (P_{25}-P_{75}) or as n (%). Inter-quartile range 25th and 75th percentile; BMI: body mass index; ASA classification: American Society of Anesthesiology classification; AO/OTA: Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association; FRI: fracture-related infection.

our center for treatment of the FRI. The cohort consisted of 22 males (79%) and six females (21%). Nearly all patients were classified as either ASA 1 ($n = 15$, 54%) or ASA 2 ($n = 12$, 43%) and one patient was classified as ASA 3 (3.6%). Out of all 630 clavicle fractures, only three patients suffered an open fracture, none of them developed an FRI. Most fractures ($n = 25$, 89%) were midshaft and a minority ($n = 3$; 11%) was classified as lateral clavicle fractures. Simple diaphyseal clavicle fractures (15.2A) were most common ($n = 14$, 50%), followed by comminuted diaphyseal fractures (15.2C) ($n = 7$, 25%) and diaphyseal wedge fractures ($n = 4$, 14%), as described in Table 1.

In 27 cases (96%) the initial fracture fixation was done using a plate and screw osteosynthesis while one patient (3.6%) was treated with screw osteosynthesis alone. In all cases, at least one pathogen was identified through culture. Twenty-three cases were monomicrobial and five cases were polymicrobial. The most frequently cultured pathogens were *Cutibacterium acnes* followed by *Staphylococcus. aureus* and *S. epidermidis* (Fig. 1).

Antimicrobial treatment

As standard of care, patients undergoing initial fracture surgery were given 2 g cefazolin (single dose) intravenously before the operative intervention. In case of confirmed or suspected infection, antimicrobial therapy was not initiated until intraoperative cultures were obtained. Empirical therapy consisted of vancomycin and piperacillin/tazobactam intravenously. As soon as the culture results were available this was switched to (oral) targeted therapy. The treatment duration for patients followed the hospital's guidelines at that time, with a total of six weeks after implant removal and 12 weeks after implant retention or replacement. Local antibiotic therapy (gentamicin and vancomycin) using polymethylmetacrylate (PMMA) cement as a carrier was given to ten patients as part of staged revision surgery before definitive reconstructive surgery with a bone graft. One patient declined to follow the recommended six-week oral antibiotic regimen and instead received oral antibiotics for two weeks after implant removal. At the final follow-up (at 55 months), this patient had an asymptomatic non-union and refused further treatment.

Surgical treatment

Eight patients (29%) underwent definitive implant removal, five patients (18%) underwent a DAIR approach, and one patient (3.6%) underwent resection of the clavicle after multiple revisions. Fourteen patients (50%) were treated with an exchange of the implant (Table 2).

This was done in a single-stage approach in three patients, a two-stage approach in seven patients and four patients required multiple revisions before definitive osteosynthesis could be performed. Twelve patients (43%) received an autologous bone graft: ICBG ($n = 6$) (Fig. 2), FVFG ($n = 5$), ACBG ($n = 1$)) to reconstruct the bone defect. An overview

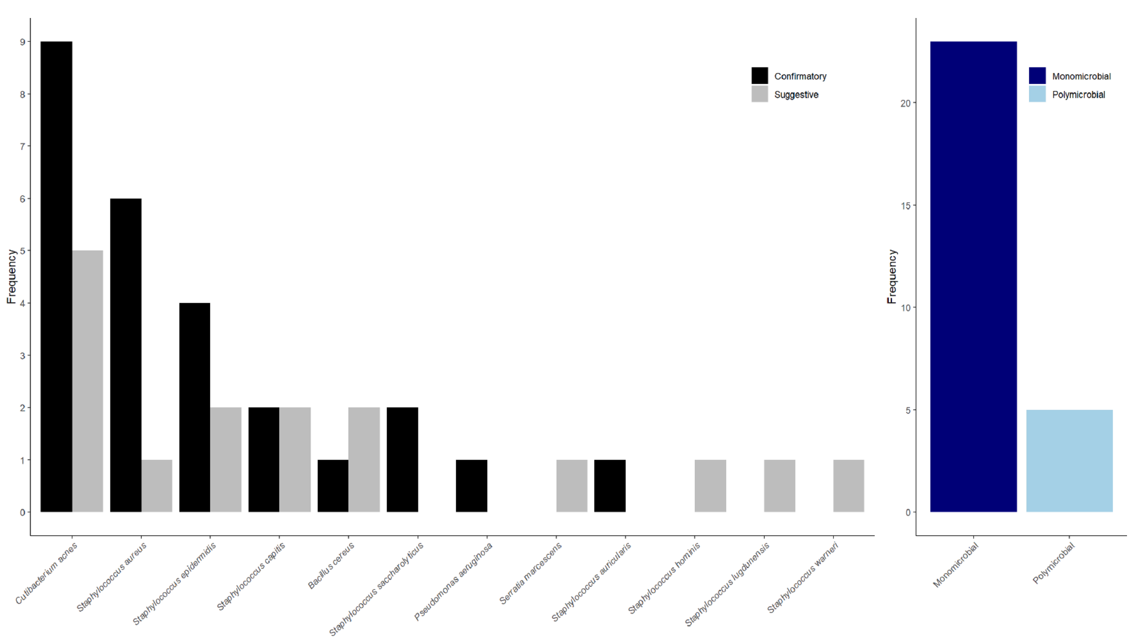

Fig. 1. An overview of the causative pathogens identified by microbiological culturing (left), and the number of monomicrobial and polymicrobial infections (right).

Table 2
Treatment strategies and outcome parameters.

	N = 28
Definitive FRI treatment	
DAIR	5 (17.9)
Implant removal	8 (28.6)
Exchange of implant	14 (50.0)
Single-stage revision	3 (10.7)
Two-stage revision	7 (25.0)
Multiple revisions	4 (14.3)
Resection of the clavicle	1 (3.6)
Bone graft	
None	16 (57.1)
Autologous cancellous bone graft	1 (3.6)
Tricortical autologous iliac crest graft	6 (21.4)
Free vascularized fibula graft	5 (17.9)
Number of reoperations median (min-max)	1 (0–19)
Duration of follow-up (months)	32.3 (23.9–51.1)
Outcome	
No recurrence infection	26 (92.9)
Recurrence of infection	2 (7.1)

Data are shown as median (P_{25}-P_{75}) or as n (%). FRI: fracture-related infection; DAIR: debridement, antimicrobial therapy and implant retention.

of the patients treated with a bone graft is presented in Table 3.

Figs. 3, 4 and 5 present a patient treated for an FRI of the clavicle, with a two-stage surgical approach for a 7 cm bone defect using a FVFG.

Clinical outcome

All FRI patients had at least twelve months of follow-up after cessation of surgical and antibiotic therapy. The median duration of follow-up was 32.3 months (P_{25}-P_{75}: 23.9–51.1). In 26 out of 27 patients (96%) fracture consolidation was achieved. One patient (3.7%) had an asymptomatic non-union. One patient who underwent resection of the clavicle was excluded from the evaluation of consolidation. FROM was achieved in 26 out of 28 patients (89%). Both of the patients who did not regain FROM, did have FROM prior to the fracture. One patient had FROM before the FRI occurred, while the other patient developed a frozen shoulder during the period between initial fracture treatment and the onset of FRI. One patient had slightly limited anteflexion (160°) and limited scapular abduction (130°) and the second patient had a slightly limited scapular abduction (160°).

Two patients (7.1%) suffered a recurrence of infection. One of these patients had a failed DAIR, five months after cessation of antimicrobial therapy. Here the fracture had healed, thus the implants were removed, and antimicrobial therapy was started. The patient remained infection-free during follow-up. The other patient underwent several complex surgical procedures with a massive allograft but presented with a fistula ten months later. Infection control was achieved after multiple surgical debridements, removal of the allograft and resection of the clavicle. This patient regained FROM and remained infection-free during follow-up.

Healthcare costs

The healthcare costs are related to the patients treated for clavicle fractures, which were complicated with an FRI. Of note, a total of ten patients that were initially managed for their fracture (and infection) at other hospitals before being referred to our hospital for infection treatment, were included in the cost analyses as well. Overall, the total healthcare cost for the treatment of FRI of the clavicle was calculated at €587.210. This corresponds to a median cost of €11.506 (P_{25}-P_{75}:

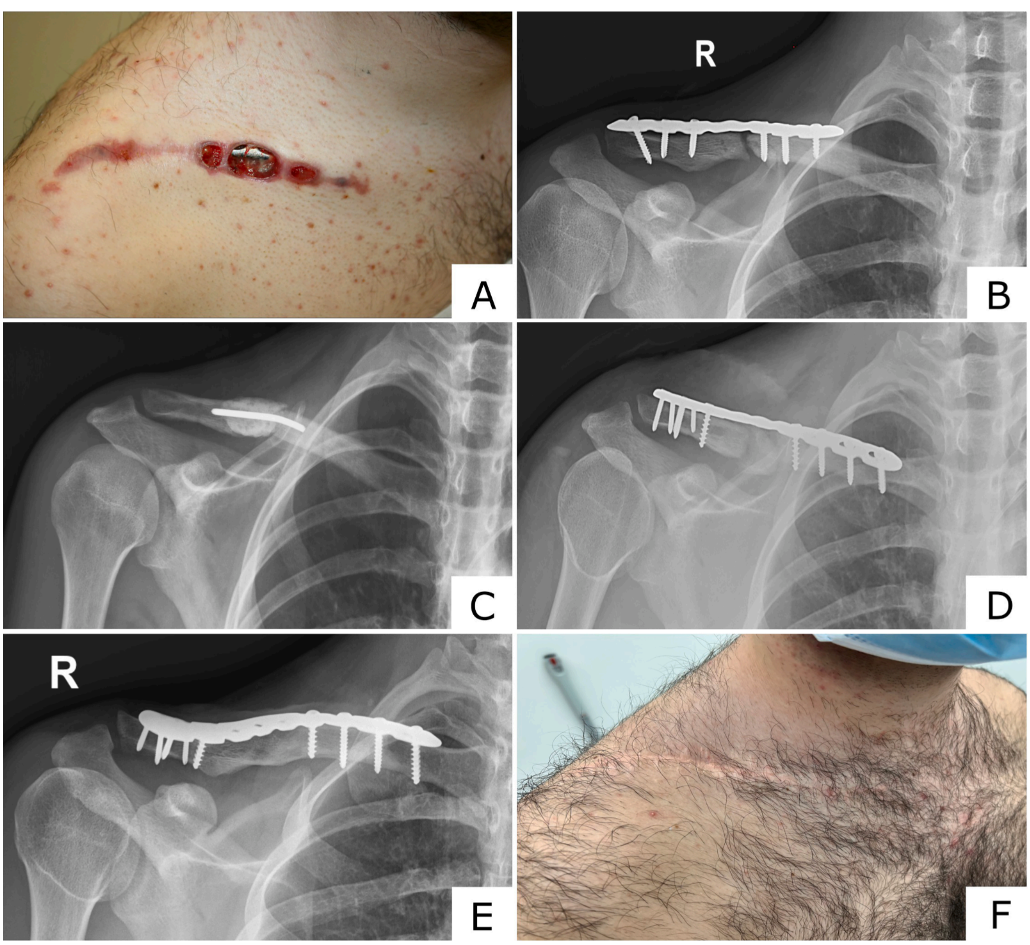

Fig. 2. A 20-year-old male suffering from a fracture-related infection of the right clavicle, treated with a two-stage surgical approach for a 3 cm bone defect. (A) The patient presented at the outpatient clinic with wound break-down, six weeks after primary fracture treatment. (B) Standard X-ray shows loosening of the medial screws six weeks after the initial fracture stabilization using plate and screw osteosynthesis (external hospital). (C) The first phase consisted of removal of all necrotic bone and hardware followed by placement of a polymethylmethacrylate (PMMA) cement spacer over a Titanium Elastic Nail (TEN). Cultures revealed the presence of *Staphylococcus epidermidis*. (D) In a second stage the cement spacer was removed and a tricortical autologous iliac crest bone graft (ICBG; 3 cm) was wedged into the remaining clavicle ends and stabilized with plate and screw osteosynthesis. (E-F) Standard X-ray revealed full consolidation of the fracture 24 months after the primary surgery, with no clinical signs of infection and a good functional outcome.

Table 3
The application of bone grafts in the treatment of patients with a fracture-related infection of the clavicle.

Sex	Age (years)	BMI (kg/ m^2)	ASA-classification	Referral	Fracture classification	Type of bone graft	Duration of follow-up (months)	Outcome	ROM
Female	17	19.46	1	Yes	15.2A	FVFG	65.9	No recurrence	Full
Male	56	30.79	2	No	15.2B	ACB	50.4	No recurrence	Full
Male	17	20.37	1	Yes	15.2A	ICBG	61.0	No recurrence	Full
Male	45	27.74	2	No	15.2A	ICBG	36.2	No recurrence	Full
Male	49	25.94	1	Yes	15.2C	ICBG	16.8	No recurrence	Full
Male	58	26.87	1	Yes	15.2C	ICBG	24.8	No recurrence	Full
Female	26	25.18	2	Yes	15.2A	FVFG	27.8	No recurrence	Full
Male	50	22.30	1	Yes	15.2A	FVFG	18.0	No recurrence	Full
Male	45	26.19	2	Yes	15.2B	FVFG	12.0	No recurrence	Full
Male	49	31.19	2	Yes	15.2C	ICBG	12.9	No recurrence	Full
Male	49	27.41	2	Yes	15.2A	ICBG	13.9	No recurrence	Full
Female	37	28.72	1	No	15.2A	FVFG	24.8	No recurrence*	Anteflexion: full; abduction: 160°

BMI: body mass index (kg/m^2); ASA classification: American society of anesthesiologists; ROM: range of motion; FVFG: free vascularized fibular bone graft; ACB: autologous cancellous bone graft; ICBG: tricortical autologous iliac crest bone graft. *Recovery was complicated by ankle instability which required fixation with a syndesmosis screw.

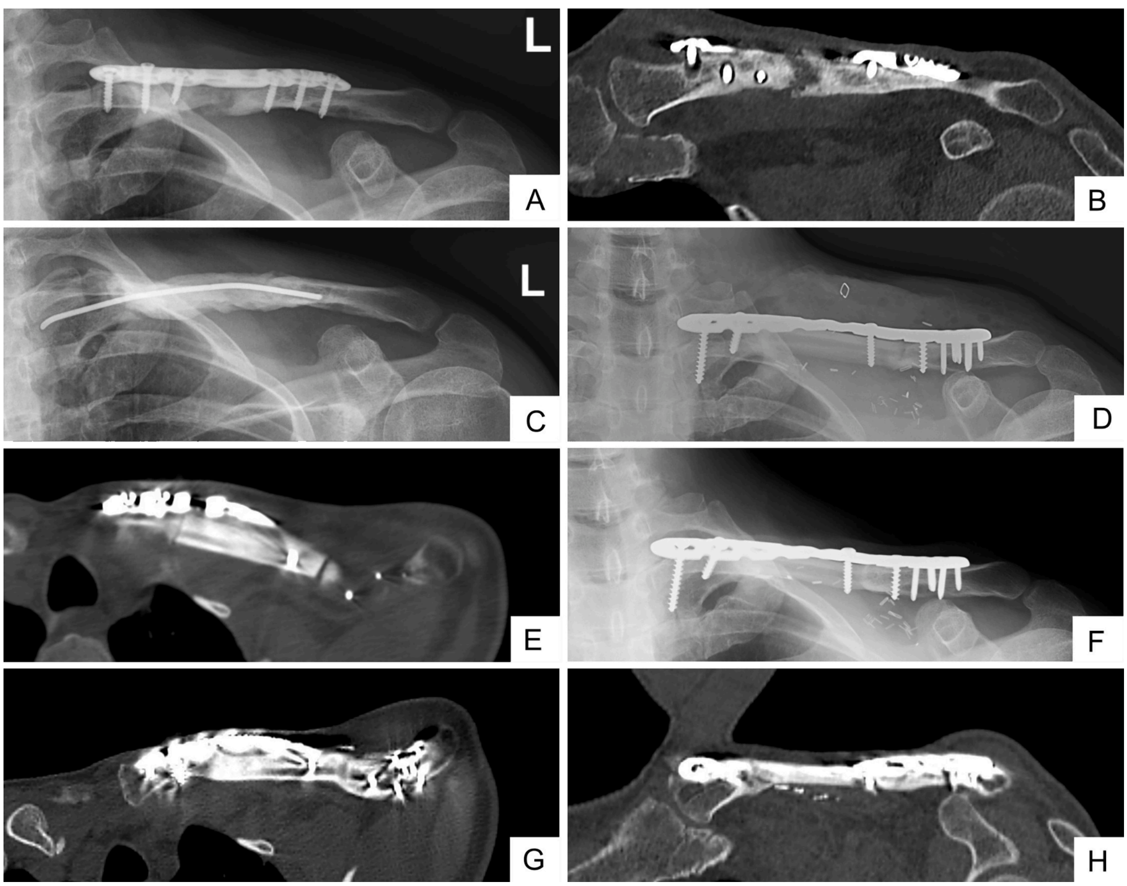

Fig. 3. A 50-year-old male suffering a fracture-related infection of the left clavicle, treated with a two-stage surgical approach for a 7 cm bone defect. The patient underwent two surgical revisions for infection after the primary fracture fixation at different external hospitals. (A) Standard X-ray and (B) coronal computed tomography (CT) scan demonstrate loosening of the medial screws, 29 months after the initial fracture stabilization using plate and screw osteosynthesis. (C) Standard X-ray demonstrates the polymethylmethacrylate (PMMA) cement spacer which was moulded over a Titanium Elastic Nail (TEN) and placed after removal of all necrotic bone and hardware during the first stage. Cultures revealed the presence of *Staphylococcus epidermidis*. In a second stage the cement spacer was removed, and a free vascularized fibular bone graft (FVFG) was wedged into the remaining clavicle ends and stabilized with plate and screw osteosynthesis. (D) Standard X-ray and (E) coronal CT scan show the FVFG during the first postoperative week. (F) Standard X-ray, (G) axial and (H) coronal CT scan images demonstrate full incorporation of the FVFG approximately two years after implantation.

€7.953–23.798) per patient. The distribution of costs over the four cost categories is displayed in Table 4.

Discussion

With an increase in the number of operatively treated clavicle fractures, related complications like FRI are encountered more frequently. FRI of the clavicle is a challenging complication that requires

Fig. 4. A 50-year-old male suffering a fracture-related infection of the left clavicle, treated with a two-stage surgical approach for a 7 cm bone defect using a free vascularized fibular bone graft (Fig. 2). (A-D) Approximately two years postoperatively, the skin island has integrated completely, and the patient remained infection-free with a good functional outcome.

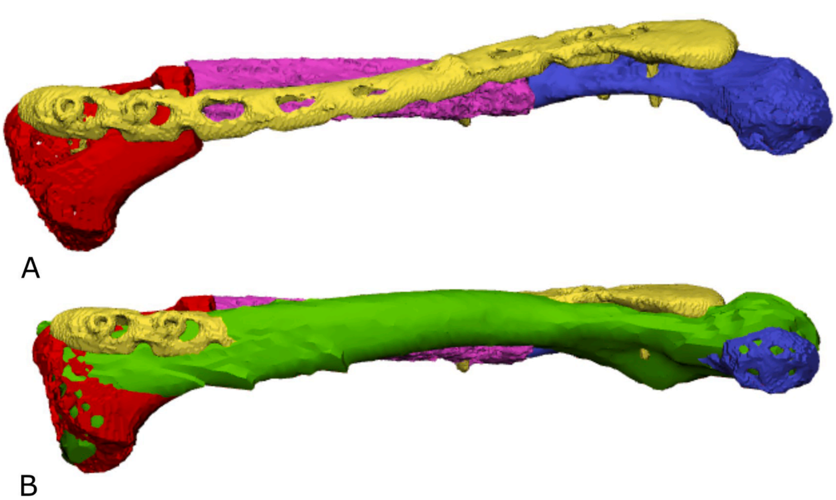

Fig. 5. A 50-year-old male suffering a fracture-related infection of the left clavicle, treated with a two-stage surgical approach for a 7 cm bone defect using a free vascularized fibular bone graft (Fig. 2,3). (A-B) An anteroposterior view of a 3D-reconstructed computed tomography (CT) image of both clavicles. These 3-dimensional images illustrate the left clavicle (red-blue) that was operatively treated with a vascularized fibular bone graft (FVFG) (purple) (A), as well as the mirrored contralateral clavicle (green) (B). The plate (yellow) position is added for demonstrational purposes. Note the importance of correcting the length of the clavicle. The images were segmented and aligned in Mimics innovation suite 20.0 (materialise, Leuven, Belgium).

Table 4
Healthcare costs for patients with a fracture-related infection of the clavicle (N = 28).

Category	Per patient	Total	Relative share
Honoraria	€1.985 (370 – 3.839)	€153.011	26%
Materials (implants & screws)	€1.264 (999 – 1.769)	€41.263	7%
Hospitalization	€4.213 (1.284 – 16.126)	€347.992	59%
Pharmaceuticals	€717 (492 – 1.147)	€44.944	8%
Total	**€11.506 (7.953 – 23.798)**	**€587.210**	**100%**

The per patient costs show the median followed by P_{25}-P_{75}.

debridement of all non-viable tissues, which may result in an osseous defect that requires a complex surgical reconstruction. The main objectives of this study were to evaluate the clinical outcome and healthcare costs for patients treated for FRI of the clavicle and propose a standardized treatment algorithm.

In our cohort of 630 clavicular fractures, we observed a total of 28 FRIs. Eighteen (2.9%) of these patients were from our hospital, and ten (1.5%) were referred from other hospitals with an infection. The prevalence of infection is in line with a study by Wolf et al. who observed an infection rate of 3.1% (21/672) [16], but higher than the 0.4% (1/251) observed by Shen et al. [17]. However, neither of these studies used a validated definition to define infection. In the study by Shen et al. an additional four patients were diagnosed with a 'superficial infection'. Furthermore, the incidence in our study might be higher than may be expected as our hospital is a level-1 trauma center that receives many complex referral cases.

Clinical and functional outcome

Out of the eight patients who had their implant removed, none experienced a recurrence of infection. Among the five patients who were treated with a DAIR approach, all underwent their FRI surgery within seven weeks after initial fracture fixation. One of these patients, treated with a DAIR approach at three weeks, was diagnosed with a recurrence of infection. Three patients received a one-stage approach for FRI, with one of them receiving ACBG. None of these patients experienced a recurrence of infection. Seven patients underwent a two-stage revision surgery, with six receiving ICBG and one receiving FVFG, all without recurrence of infection. Of the five patients who needed multiple revisions, four were successfully treated with FVFG, and one patient had a recurrence after the use of a massive allograft. Overall, two patients (7.1%) suffered a recurrence of infection. Both were treated for the recurrent infection and remained infection-free ever since (follow-up > 3 years).

The functional outcome in our cohort was satisfactory. Only two patients had minor limitations in their range of motion. Fracture consolidation was achieved in 96% of the patients. The relatively low recurrence rate, good functional outcome and high consolidation rate in our patient cohort underline the importance of a multidisciplinary team approach. In case of complex reconstructions (e.g., FVFG), treating physicians should strongly consider referring these patients to specialized centers.

Healthcare costs

The median healthcare costs per patient, following treatment of an FRI of the clavicle (€11.506; P_{25}-P_{75}:(€7.953 – €23.798)) were 3.5 times higher compared to non-infected operatively (€3.296; P_{25}-P_{75}:(€2.857 – €4.025)) treated clavicle fractures [24]. It is likely that the actual number is even greater, as the healthcare costs incurred by patients before they were referred to our hospital were not considered in this study. The main cost driver in our study was length-of- stay. In comparison, healthcare costs for the treatment of FRI of the patella and tibia in our center were approximately 3 and 4 times more, respectively [22, 25]. Nevertheless, the relative share of the different cost categories was rather similar, with hospitalization as the main cost driver [22,25]. The current study differs from both the patella and tibia FRI study in that the

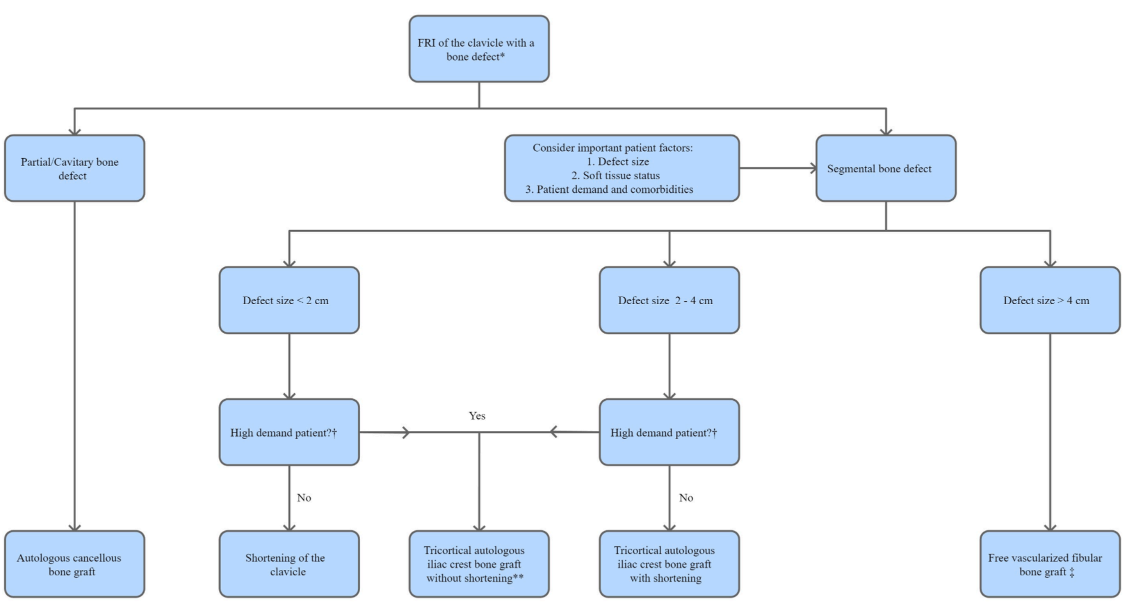

Fig. 6. Standardized treatment protocol for the treatment of fracture-related infection of the clavicle with a bone defect. The subdivision in centimetres is arbitrary, but it should help the surgeon plan the procedure. One of the most important aspects is the stability of the construct using an implant with a sufficient length. * Patients with an FRI without a bone defect should be treated according to the general FRI treatment principles [21]. ✝ Patient demand should be based on age, level of preoperative physical activity, job demands, and demands in daily living. ** In most healthy adult patients, harvesting tricortical autologous iliac crest bone grafts of up to 3 cm can be performed safely. When larger grafts are required, there is a risk of avulsion of the anterior superior iliac spine. ‡ Alternatives to a vascularized fibular bone graft, such as the Masquelet technique, should be discussed with the patient if they are unfit to undergo the procedure due to comorbidities or if they are unwilling to undergo the procedure. It should be stated that in larger bone defects these alternatives probably have a lower success rate.

patient cohort was larger (28 vs. respectively 10 and 12 patients) and the total costs per patient were distributed less equally. Moreover, the median hospitalization cost (i.e., length-of-stay) was more than five times lower after FRI of the clavicle. There are some possible explanations for the lower hospitalization costs or shorter length-of-stay for patients with an FRI of the clavicle. One being that multiple revision surgeries (and hospitalizations) in cases of bone transport of the tibia for example, are not necessary for the clavicle.

Treatment strategies

For the treatment of FRI of the clavicle *without* a bone defect we recommend following the general FRI treatment principles [26]. For patients *with* an infection and an osseous defect we advocate for a standardized treatment protocol based on the defect size, quality of surrounding soft tissues, and patient's needs. The treatment algorithm applied in this study is based on expert opinion and is shown in Fig. 6. As mentioned in previous publications, time from fracture fixation is not the only factor that should be considered in treatment planning of FRI [27]. Other factors such as fracture stability, dead space management and adequate soft tissue coverage are also essential for successful treatment of FRI [18]. Fracture (construct) stability is of great importance to prevent and/or eradicate infection [28] and this is in our opinion especially true in case of clavicle fractures. As structural bone grafts provide more stability than cancellous bone grafts, we recommend using structural bone grafts in segmental defects. Partial osseous defects may be treated with ACBG as the remaining part of the clavicle may function as a container for the ACBG and provide stability. While some studies have reported positive results using ACBG in revision surgery for aseptic non-union, to the best of our knowledge, there are currently no studies specifically examining the use of ACBG for treating FRI of the clavicle [29–31]. The Masquelet technique to treat larger segmental defects of the clavicle resulting from FRI, is not our preferred treatment option since it does not provide adequate stability. The only publication that reported the use of the Masquelet technique for treating segmental clavicular defects in adults was a case report, which showed that the technique was successful in treating an aseptic non-union with a four-centimeter segmental defect [32].

Several studies have focused on the reconstruction of segmental osseous defects using ICBG or FVFG after non-union of the clavicle [11, 33-40]. Most of these were case reports or case series [33–40] and only one of the studies had FRI as their main focus area [11]. The use of ICBG showed a good outcome with union rates ranging from 75% to 100%, with a significant improvement in shoulder function and pain reduction after surgery [35–39]. Four case reports describing the use of FVFG in nine patients demonstrated good results, with fracture union in eight out of the nine patients, with osseous defect sizes ranging from four centimeters up to twelve centimeters [11,33,34,40].

The use of other free vascularized grafts for defect management has also been described. Vascularized medial femoral condyle corticoperiosteal bone grafts were successfully used to treat defects up to five centimeters [41,42]. We have no experience with this technique and prefer bone grafts with an anatomical shape that closely resembles that of the clavicle, as changes in clavicular curvature and/or length can result in scapular dyskinesis [39,43].

Shortening of 10% or more already significantly affects the scapular kinematics [44]. Therefore, to optimize the chance to return to FROM, shortening (or lengthening) of the clavicle should be prevented, especially in highly demanding patients. In our center 3D planning is therefore a critical step in the management of these cases (Fig. 5) [11]. Patient demands and other patient specific factors should be considered when evaluating the options for bone grafting. One of these factors is the soft tissue envelope overlying the infection site. A good soft tissue envelope forms a physical barrier for new microorganisms to contaminate the wound and plays a role in delivery of host immunity and antibiotics [45]. Virtually no data exists on the utilization of vascularized bone grafts in clavicular fractures. In case of infection with poor surrounding soft tissues, a vascularized graft is considered to be superior to non-vascularized grafts as it induces angiogenesis which aids in fighting of the infection and contributes to fracture healing due to its osteogenic properties [46]. Moreover, a skin island can significantly improve soft tissue healing. Therefore, in our opinion, there should be a low threshold for choosing a vascularized bone graft including a skin island in case of poor soft tissue coverage (Figs. 3 and 4). Patients should be involved in the decision making and they should be clearly informed about possible complications. For example, using large ICBG can cause wound healing problems and pain at the donor site. Additionally, there is a risk of avulsion of the anterior superior iliac spine postoperatively [36,47]. Similarly, using an FVFG can also result in donor site morbidity, including problems with wound healing or changes in gait [48]. In our cohort one patient who was treated with an FVFG, suffered postoperative ankle instability that required fixation with a syndesmosis screw.

Limitations

This study is subject to some limitations. First, due to the retrospective nature of this study, no exact measures of the defect sizes could be calculated. Measuring the size of the defect is challenging due to the inaccuracy of postoperative x-rays. Even with CT scans, it is difficult to measure the defect size accurately since pre-fracture CT images are not always available, and comparing the length based on the contralateral side can be challenging and is sometimes not accurate. Second, clinical outcome was based only on physician assessment. Patient reported outcome measures such as the Constant-Murley score (CMS) would have been a good tool to assess shoulder function. However, interpretation of the CMS would have been difficult in this cohort as this was a retrospective study, and prospective administration of the questionnaires would mean that all patients would have to fill out the questionnaire at different timepoints in their follow-up. Lastly, for the ten patients who were referred to our hospital after being treated elsewhere, it was not possible to calculate the costs incurred in the hospital where the patient was initially treated. This led to an underestimation of healthcare costs of referral patients.

Conclusion

FRI is a serious complication that can occur after the surgical treatment of clavicle fractures. In our opinion, when treated adequately using a multidisciplinary patient-specific approach, the outcome of patients with an FRI of the clavicle is good. The median healthcare costs of these patients are up to 3.5 times higher compared to non-infected operatively treated clavicle fractures. Although not studied individually, we consider factors such as the size of the bone defect, condition of the soft tissue, and patient demand important when it comes to guiding our surgical decision making in cases of osseous defects.

Declaration of Competing Interest

All authors declare no conflict of interest with respect to the preparation and writing of this article.

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