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What can they expect? Decreased quality of life and increased postoperative complication rate in patients with a fracture-related infection

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ABSTRACT

Background: By gaining insight into the Quality of Life (QoL) status and occurrence of complications, critical facets in the care for patients with Fracture-Related Infection (FRI) can be mitigated and measures can be taken to improve their outcome. Therefore, the aims of this study were to 1) determine the QoL in FRI patients in comparison to non-FRI patients and 2) describe the occurrence of other complications in both FRI and non-FRI patients.

Methods: An ambidirectional cohort study was conducted in a level 1 trauma centre between January 1st 2016 and November 1st 2021. All patients who underwent surgical stabilisation of an isolated long bone fracture were eligible for inclusion. To avoid confounding, only patients with an Injury Severity Score (ISS) <16 were included. Data regarding patient demographics, fracture characteristics, treatment, follow-up and complications were collected of both non-FRI and FRI patients. QoL was assessed through the use of five-level EuroQol five-dimension (EQ-5D-5L) questionnaires twelve months post-injury.

Results: A total of 134 patients were included in this study, of whom 38 (28%) FRI patients and 96 (72%) non-FRI patients. In comparison to non-FRI patients, FRI patients scored significantly worse on the QoL assessment regarding the index value ($p = 0.012$) and the domains mobility ($p<0.001$), usual activities ($p = 0.010$) and pain/discomfort ($p = 0.009$). Other postoperative complications were more often reported ($p<0.001$) in FRI patients (66%, $n = 25/38$) compared to non-FRI patients (27%, $n = 26/96$). During the median follow-up of 14.5 months (interquartile range (IQR) 9.5–26.5), 25 FRI patients developed a total of 49 distinctive complications besides FRI. The complications nonunion (18%, $n = 9/49$), infection other than FRI (e.g. line infection, urinary tract infection, pneumonia) (18%, $n = 9/49$) and implant failure (14%, $n = 7/49$) were the most frequently described in the FRI group.

Conclusion: Patients who suffered from an FRI have a decreased QoL in comparison to those without an FRI. Moreover, patients with an FRI have a higher rate of additional complications. These findings can help in patient counselling regarding the potential physical and mental consequences of having a complicated course of recovery due to an infection.

Introduction

Fracture-Related Infections (FRIs) are one of the most challenging complications after fracture surgery [1]. As a result of extensive treatment and long-term consequences of the infection, FRI tend to impact the economy substantially due to high healthcare costs and increased absenteeism from work [2]. Besides these socioeconomic effects, FRI also affects the patient's daily life and functioning status [3].

Quality of Life (QoL) and mental health have become increasingly important regarding the treatment of diseases and healthcare in general. In an attempt to objectify this item, EuroQol five-dimension (EQ-5D) questionnaires are commonly used to analyse the QoL based on various subjects [4,5]. By implementing a QoL assessment, critical facets of healthcare can be improved, in particular the provision of information, choice of treatment, facilitation of communication and outpatient aftercare [6,7]. In addition, a QoL assessment could expose and prioritise underlying problems with regard to disease management strategies [7]. EQ-5D questionnaires are also used in trauma and subsequently in patients with FRI. Recent literature demonstrated a significant decrease with regard to the QoL in FRI patients [2,8,9]. These studies reported

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poorer outcomes in FRI patients concerning the physical functioning, mental health status and pain interference [2,8,10]. Unfortunately, the patient populations of these studies are either heterogenous or relatively small [2,8,10]. Hence, validation is necessary before results of QoL assessments can be implemented in FRI patient care.

In comparison with QoL, adverse outcomes after trauma- and orthopaedic surgery have been studied over a longer period of time. Several studies are available that have analysed the occurrence and consequences of complications such as nonunion, malunion, infections and pain after fracture surgery [11–13]. In addition, a lower QoL was depicted in patients who had developed either of these complications [14]. In general, auditing of postoperative complications leads to surgical quality improvement and should therefore be encouraged [15].

In order to improve future care of FRI patients, it is beneficial to get an in-depth view regarding the QoL and to gain more insight into the development of complications in this population. In current literature, there is currently no information available about the complication rate in FRI patients in particular, which leads to a knowledge gap regarding the proper provision of information towards the FRI patient. Hence, the information of our complication analysis along with the QoL results in our cohort, can be used to better counsel patients regarding the consequences of the disease in order to manage expectations and to prevent non-coherence to the treatment of FRI. Therefore, the aims of this study were to 1) determine the QoL according to the five level EQ-5D(−5L) questionnaire in FRI patients in comparison to non-FRI patients and 2) describe the occurence of additional complications in both FRI and non-FRI patients.

Methods

Study design

An ambidirectional cohort study was conducted in the University Medical Centre Utrecht (UMCU), a level 1 trauma centre in the Netherlands. A waiver was granted by the Medical Ethics Review Committee (METC-number 21/734) of the UMCU.

Patient population

Patients of at least 18 years of age with an Injury Severity Score (ISS) <16 who were treated with surgical stabilisation of a fracture of a long bone between January 1st 2016 to November 1st 2021 were eligible for inclusion in this study. Fractures of the humerus, forearm, femur, tibia or fibula were considered as long bone fractures. Exclusion criteria were, firstly, patients with an inadequate availability of data including failure to return the QoL questionnaire. Secondly, to avoid confounding, multitrauma patients with an ISS of ≥ 16 [16] and patients with a periprosthetic or pathologic fracture were excluded.

Study outcomes

The primary outcome measure of this study was the QoL as measured by using the EQ-5D-5L questionnaire in FRI patients in comparison to non-FRI patients. The secondary outcome measure was the occurence of complications in both FRI and non-FRI patients.

Definitions

FRI was defined as the presence of at least one confirmatory FRI criterion, according to the *FRI-consensus criteria*, which are a fistula or wound break-down communicating with the bone or implant, the presence of pus, two positive microbiological cultures with the same pathogen and histological signs of infection [17]. Recurrence of FRI was deemed as the re-appearance of at least one confirmatory FRI criterion after completion of both surgical and antimicrobial treatment of the initial FRI [18]. Infection control was described as absence of 1) amputation, 2) death related to the FRI, 3) confirmatory FRI criteria and 4) ongoing antimicrobial or surgical treatment during the last follow-up consultation [18].

A complication was defined as an adverse event that had either developed during the initial admission or (outpatient) follow-up as a result of treatment of the fractured long bone, leading to a change in treatment or irreversible damage [15]. Due to the study subject being FRIs, this was exempted as a complication to draw an equivalent comparison between the FRI and non-FRI patients. The complications that were collected for this study were: nonunion, malunion, implant failure, error in technique, re-fracture, soft tissue problem, compartment syndrome, postoperative haemorrhage, deep venous thrombosis, amputation of the affected limb, persisting pain, anaemia and electrolyte disturbances, respiratory failure, infection other than FRI, Systemic Inflammatory Response Syndrome (SIRS), paralytic ileus, cardiac arrhythmia, urine retention, delirium, pressure ulcus and other not further specified complications. Delayed union was not considered as a complication. Complications were scored according to the Clavien-Dindo classification, whereas a grade I complication is a modest postoperative deviation requiring no or minor pharmacological treatment, grade II requires treatment with pharmacological drugs or interventions other than allowed for grade I complications, grade III complications need surgical intervention, grade IV is classified as organ failure and grade V as demise of the patient [19].

Regarding the complication nonunion, a comprehensive consensus definition is missing [20]. For this study, a nonunion was defined as the need for an unplanned surgical intervention after definitive wound closure or incomplete radiographic healing at one year and delayed healing defined as two consecutive clinical assessments showing no radiographic progression or incomplete radiographic healing between six months and one year [21]. Delayed union was defined as diminished radiological progression of bone-healing within the expected time frame without the need for surgical interference to ultimately achieve consolidation. These definitions were applied on follow-up x-rays of the study subjects and scored on a dichotomised scale by the three senior authors (FIJ/FH/GG), all >10 years board-certified and blinded for each other's judgement. A score of 0 was defined as normal fracture healing, 1 as delayed union and 2 as the presence of nonunion. Consensus was reached when at least two out of three senior authors assigned the same score to the follow-up x-ray or if mutual agreement occurred after careful discussion of the follow-up x-rays in cases of initial disagreement. Malunion was defined as a consolidated fracture which has healed in a non-anatomical position, thereby increasing the risk of adverse functional outcome. Error in technique was described as a surgical deficiency that had either caused malalignment, malposition or insufficient stability of the affected implant/bone in such a degree that revision surgery was indicated.

Data collection

Data from three databases was retrieved, including two prospective FRI databases, namely the Accuracy of Medical Imaging for Suspected FRI (IFI-trial) [22] database and the database of the Dutch Fracture Infection Registry (DFIR) [23], and the retrospective UMCU FRI database. Only FRI patients who had at least three deep tissue cultures taken were included in these databases. For all databases, the data capturing program Castor EDC (Castor Electronic Data Capture, v2022.5.1.0) [24] was used. In addition, a control group of consecutive non-FRI patients treated with a surgical stabilisation procedure between January 1st 2016 to November 1st 2021. All collected data used for this study was pseudonymised. Data was both prospectively and retrospectively collected, as the outcomes of the EQ-5D questionnaires were obtained prospectively, whereas demographic data was gathered retrospectively.

Data with regard to patient demographics, sex, age, Body Mass Index (BMI), substance abuse, American Society of Anaesthesiologists (ASA) classification [25] and Charlson Comorbidity Index (CCI) [26] were

collected. Fracture and trauma characteristics were identified according to the ISS [16], Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association (AO/OTA) fracture classification [27] and Gustilo-Anderson classification [28]. The follow-up and course of the disease were described according to the length-of-stay (LOS) of the initial fracture or FRI treatment, occurrence of complication(s), need for re-operation(s) and re-admission(s), and fracture consolidation. Additional data concerning the treatment and follow-up of FRI patients included time to onset of the infection, recurrence rate and infection control rate.

In order to determine the QoL of trauma patients, EQ-5D-5L questionnaires were used. The EQ-5D-5L consisted of five questions concerning the domains of mobility, self-care, usual activities, pain/discomfort and anxiety/depression, including a Visual Analogue Scale (VAS) representing the patients' general health. Patients could indicate a score on an ordinal scale of one to five with regard to the five aforementioned domains, a score of one was considered as absence of problems related to the specific domain, whilst a score of five was deemed as excessive inconvenience. In addition, the index value was calculated with the SPSS value set for the Netherlands provided by EuroQol [29]. A score of one was anchored as full health and a score of zero as a state as bad as being demised [29]. General health was assessed based on a VAS of zero to one hundred, with zero indicating the worst conceivable health and one hundred the best. In the UMCU, as standard-of-care, EQ-5D questionnaires are sent to all trauma patients admitted via the Emergency Department at a time-point of twelve months post-injury. In addition, patients seen in the outpatient clinic or admitted directly to the trauma unit without an admission via the Emergency Department, received the EQ-5D questionnaires at multiple time points post-injury as part of the IFI and DFIR trials. For this present study, the questionnaires of twelve months post-injury were collected. The transmission and collection of the QoL assessments was administered to Network Acute Care Central Netherlands (Netwerk Acute Zorg Midden-Nederland) [30] and authors of the present study. Reminders were sent within three weeks or after one month of failure to complete the EQ-5D questionnaire, respectively.

Statistical analysis

All data analyses were conducted in Statistical Package for the Social Sciences (SPSS®) statistics (version 26.0, Armonk, NY, USA: IBM Corp.). Data was presented as dichotomised and ordinal variables in counts and percentages (n (%)), or as continuous variables in median and interquartile range (IQR) or in mean and standard deviation (SD) according to the normality distribution of the variable. Regarding the baseline characteristics and QoL analyses, FRI patients and patients with complications were compared to a control group. In case of dichotomised variables, Chi-Squared tests or Fisher's exact tests were performed depending on the estimated cell size. Independent *t*-tests or Mann-Whitney U tests were performed for continuous variables, based on the normality test of the variable. The level of statistical significance was set at $p < 0.05$.

Results

Baseline characteristics

In total, 513 unique patients were identified who were eligible for inclusion in this present study. Ultimately 134 patients were included, of whom 38 (28%) FRI patients and a control group of 96 (72%) non-FRI patients. The majority of patients (63%, $n = 325/513$) were excluded as a result of failure to complete the EQ-5D questionnaire, herewith a response rate of 37% was reported. The baseline characteristics of the respondents who were included in this study and a group of non-respondents who met all inclusion criteria and did not meet exclusion criteria, are presented in Appendix 1. Non-respondents were significantly younger and healthier, had a lower ISS, less open fractures and shorter duration of admission compared to respondents. Besides, FRI was more often reported amongst the respondents. A synopsis of the complete in- and exclusion process is available in Fig. 1.

An overview of the baseline characteristics of the patients in this cohort is available in Table 1. The cohort consisted of predominantly males (62%, $n = 83$), with a median age of 52.0 years (IQR 32.0–63.0). Majority of the patients were classified as ASA 1 (46%, $n = 61$) along with a median CCI index of 1.0 (IQR 0.0–3.0). Most injuries were caused by low energy trauma's (58%, $n = 78$), with a corresponding median ISS of 9.0 (IQR 4.8–10.0). Fractures were most often located at the tibia/fibula (57%, $n = 76$) and a third of the patients had an open fracture (31%, $n = 42$), which demonstrated to be more prevalent in FRI patients contrary to non-FRI patients (61%, $n = 23/38$ vs. 20%, $n = 19/96$). In particular, Gustilo-Anderson grade III fractures were more common in the FRI group versus the control group of non-FRI patients (32%, $n = 12/38$ vs. 9% $n = 9/96$). The median follow-up duration was 14.5 months (IQR 9.5–26.5), FRI patients had a significantly longer follow-up (22.7 (IQR 13.3–30.5)) as opposed to non-FRI patients (12.6 (IQR 8.1–22.4)). During this follow-up, 53 (40%) patients were re-admitted and 66 (49%) patients were re-operated after the initial fracture fixation operation. Higher re-admission (95%, $n = 36/38$ vs. 18%, $n = 17/96$) and re-operation (97%, $n = 37/38$ vs. 30%, $n = 29/96$) rates were reported amongst FRI patients compared to non-FRI patients. In 60% ($n = 61/102$) of patients, complete fracture consolidation was achieved after one year, with complete consolidation in 30% of FRI patients ($n = 10/33$) and in 74% of non-FRI patients ($n = 51/69$).

A more in-depth view of FRI patients is presented in Table 2. The average onset of FRI was 17.5 days (IQR 11.0–41.8). During follow-up, recurrence of FRI occurred in 26% ($n = 10$) and overall infection control was achieved in 92% ($n = 35$) of cases.

QoL assessment (EQ-5D-5L questionnaires)

The QoL of FRI and non-FRI patients was assessed based on general health indicated by a VAS score, the EuroQol index value and the five domains of the EQ-5D questionnaire, namely: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. In comparison to non-FRI patients, FRI patients had a significantly worse EuroQol index value ($p = 0.012$, 0.8 (0.7–0.9) vs 0.7 (0.5–0.9)) and scored inferior regarding the domains mobility ($p<0.001$), usual activities ($p = 0.010$) and pain/discomfort ($p = 0.009$), and the EuroQol index value (Table 3). In the domain mobility, 24% of FRI patients indicated that they experienced severe problems compared to 1% of the non-FRI patients. Other differences were observed in the domains daily activities, as 16% of FRI patients experienced severe problems vs. 2% of non-FRI patients, and in the domain pain and discomfort, as 34% of FRI patients described moderate pain compared to 14% of non-FRI patients. The domains self-care ($p = 0.064$) and anxiety/depression ($p = 0.24$), including the VAS score ($p = 0.31$), were unsignificant components of the QoL analysis.

Occurrence of complications

In this cohort, 50 patients (37%) developed at least one other complication besides FRI, during the admission or follow-up due to treatment of a fractured long bone (Table 4). These 50 patients developed, apart from FRI, a total of 80 other complications. The complications infection other than FRI (e.g. line infection, urinary tract infection, pneumonia) (16%, $n = 13/80$), nonunion (15%, $n = 12/80$) and implant failure (13%, $n = 10/80$) were the most frequently described in the total study cohort. Most (44%, $n = 35/80$) complications were scored as grade III according to the Clavien-Dindo classification, requiring a re-operation to treat the complication.

In the FRI group, 49 complications were reported in 25 FRI patients, with a median of 1.0 (IQR 0.0–2.0) other complication per patient and a corresponding complication rate of 66% ($n = 25/38$). The complications

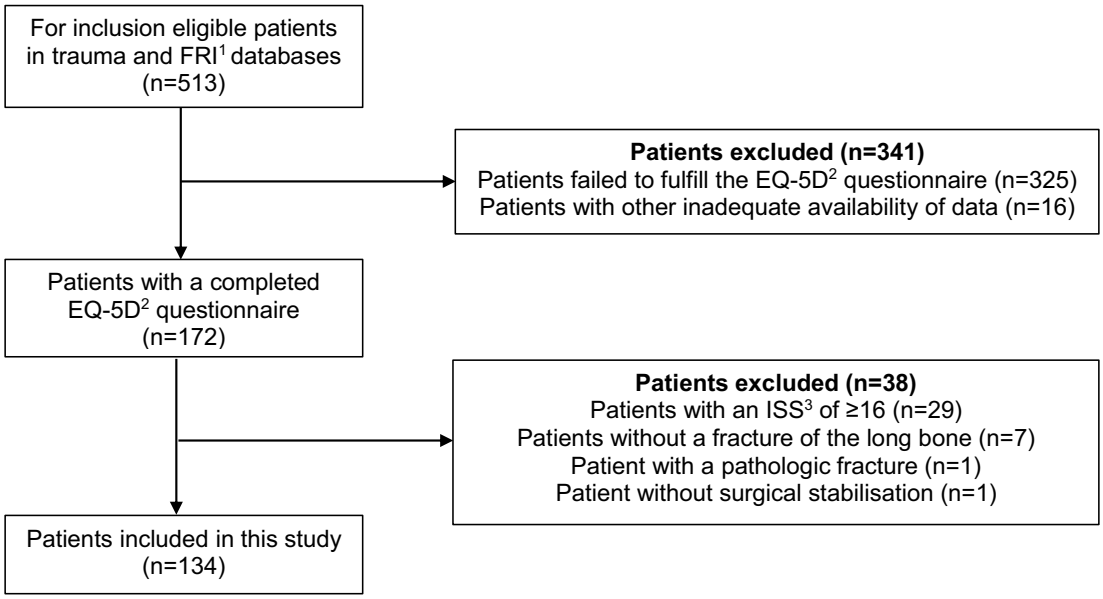

Fig. 1. Flow diagram of patient in- and exclusion.
[1] Fracture-Related Infection.
[2] EuroQol five-dimension.
[3] Injury Severity Score.

nonunion (18%, $n = 9/49$), infection other than FRI (18%, $n = 9/49$) and implant failure (14%, $n = 7/49$) were most often reported among FRI patients. Almost half of the complications (41%, $n = 20/49$) were scored as a grade III complication as per the Clavien-Dindo classification. Moreover, out of the 21 non fracture-related complications in FRI patients, 9 (43%) complications occurred before and 12 (57%) complications after onset of the FRI.

Non-FRI patients developed complications in 26% ($n = 25/96$) of cases, with a total of 31 complications in 96 patients. The median of other complications per non-FRI patient was 0.0 (IQR 0.0–1.0). The most common complications in non-FRI patients were error in technique (19%, $n = 6/31$), infection other than FRI (13%, $n = 4/31$) and nonunion, malunion and implant failure (10%, $n = 3/31$). Half of the complications (52%, $n = 16/31$) were assessed as grade III according to the Clavien-Dindo classification.

Discussion

This study describes the QoL and the occurrence of postoperative complications in FRI patients in an attempt to quantify the impact of FRI in a variety of long bone fractures on daily life. The QoL of FRI patients was determined to be significantly worse regarding the domains mobility, usual activities and pain/discomfort compared to patients without an FRI. In addition, a high burden of postoperative complications was demonstrated. In the group of 38 FRI patients, 25 patients had a complicated postoperative course and developed a total of 49 complications besides FRI, with an accompanying complication rate of 66% ($n = 25/38$). The most reported complications in FRI patients were nonunion, infection other than FRI (e.g. line infection, urinary tract infection, pneumonia) and implant failure, respectively. The personal impact of FRI and possible implications for daily practice will be discussed in the following sections.

First, the decreased QoL in FRI patients with a long bone fracture is in accordance with the results of previously conducted studies [2,8,31]. However, due to the use of different outcome measurement systems in these studies, namely PROMs (Patient Reported Outcomes Measurement System) with focus on several domains [2] and the (German) Short Form 36 (SF-36) [8], it can be difficult to compare the results in an unequivocal approach. Besides, dissimilar time-points regarding the collection of the QoL assessment were reported and, most importantly, different control groups were used, such as non-FRI patients with a long bone fracture [2], normative health data of the general national population [8,31] and complicated vs. uncomplicated osteomyelitis [31]. In addition, the scored domains are not equally affected in each study. Iliaens et al. reported a significantly worse physical functioning and pain interference [2], Walter et al. demonstrated substandard scores regarding physical, mental and general health [8], and Hotchen et al. reported an overall inferior QoL in patients with complicated osteomyelitis [31], whereas the present study demonstrated worse scores with regard to mobility, usual activities and pain/discomfort. Besides studies that affirmed our findings, one recently published article could not confirm a decreased QoL in patients with FRI, which might be related to a different composition and size of the studied groups, as only patients with osteomyelitis who encountered treatment failure were included [32].

Second, this present study demonstrated a complication rate of 37% in the total cohort. Infection other than FRI (10%, $n = 13/134$), nonunion (9%, $n = 12/134$) and implant failure (7%, $n = 10/134$) were the most common complications. These results are inconsistent with the reported outcomes of Meeuwis et al. [33]. Their study described a complication rate of 19.8% and wound infections (4.2%), loss of reduction or fixation (3.7%) and error in osteosynthesis (1.8%) as the most frequently disclosed complications in a general fracture population [33]. Nonunion was present in only 1% of their cases, this considerable difference might be explained due to the use of different definitions regarding nonunion, as no definition was elaborated in their study. Additionally, there were substantial differences in the composition of both study populations, such as the inclusion period, the number of open fractures and the large group of FRI patients included in our cohort [33,34]. The large number of FRI patients in our cohort could be an explanation for the high number of reported complications in our study (37%), as FRI patients require re-admissions and re-operations to adequately treat the infection, both of which can lead to an increased risk of the development of complications. Other studies analysed specific fracture sites, such as the hip [35], tibia plateau [13] and ankle [36]. These studies reported acute urinary retention, reduction of knee motion and postoperative wound problems as relatively common complications [13,35,36]. Besides reduction of motion at the affected fractured site,

Table 1
Baseline characteristics.

	All patients (*n* = 134)	No FRI [1] (*n* = 96)	FRI [1] (*n* = 38)	p-value
Patient characteristics				
Sex (male)	83 (62%)	60 (63%)	23 (61%)	0.85
Age (years)	52.0 (32.0–63.0)	49.5 (31.3–63.5)	56.0 (36.5–63.0)	0.26
Body Mass Index (kg/m²) (n = 126)	24.8 (23.0–27.5)	25.1 (23.0–27.6)	24.6 (23.0–27.5)	0.93
Substance abuse				
Nicotine (n = 114)	38 (33%)	30 (40%)	8 (21%)	0.059
Drugs (n = 112)	10 (9%)	8 (11%)	2 (5%)	0.49
ASA classification [2]				0.40
ASA 1	61 (46%)	40 (42%)	21 (55%)	
ASA 2	57 (43%)	44 (46%)	13 (34%)	
ASA 3	16 (12%)	12 (13%)	4 (11%)	
Charlson Comorbidity Index	1.0 (0.0–3.0)	1.0 (0.0–3.0)	1.0 (0.0–2.0)	0.51
Fracture and trauma characteristics				
Injury Severity Score	9.0 (4.8–10.0)	9.0 (4.0–10.0)	9.0 (5.0–11.5)	0.24
High-energy trauma	56 (42%)	37 (39%)	19 (50%)	0.25
Crush injury	10 (7%)	5 (5%)	5 (13%)	0.15
(Additional) injuries				0.008
One fracture one extremity	64 (48%)	51 (53%)	13 (34%)	
Multiple fractures same extremity	6 (5%)	6 (6%)	0 (0%)	
Multiple fracture different extremities	13 (10%)	5 (5%)	8 (21%)	
Other [3]	51 (38%)	34 (35%)	17 (45%)	
Fracture location				0.097
Humerus	7 (5%)	6 (6%)	1 (3%)	
Forearm	18 (13%)	14 (15%)	4 (11%)	
Femur	33 (25%)	28 (29%)	5 (13%)	
Tibia/fibula	76 (57%)	48 (50%)	28 (74%)	
Open fracture	42 (31%)	19 (20%)	23 (61%)	<0.001
Gustilo-Anderson classification (n = 42)				1.00
Type I	10 (24%)	5 (26%)	5 (22%)	
Type II	10 (24%)	5 (26%)	5 (22%)	
Type III	21 (50%)	9 (47%)	12 (52%)	
Type unknown	1 (2%)	0 (0%)	1 (4%)	
Implant used at index operation				0.083
G-nail, PFNA [4] *or similar*	8 (6%)	6 (6%)	2 (5%)	
Intramedullary nail	47 (35%)	39 (41%)	8 (21%)	
Plate	72 (54%)	46 (48%)	26 (68%)	
Screws or k-wires	4 (3%)	3 (3%)	1 (3%)	
External fixation	3 (2%)	2 (2%)	1 (3%)	
Disease course and follow-up				
Length-of-stay (days) (n = 130)	7.5 (4.8–13.3)	6.5 (4.0–11.0)	15.0 (5.8–38.0)	0.001
Need for re-operations [5]	66 (49%)	29 (30%)	37 (97%)	<0.001
Need for re-admissions [5]	53 (40%)	17 (18%)	36 (95%)	<0.001
Follow-up duration (months)	14.5 (9.5–26.5)	12.6 (8.1–22.4)	22.7 (13.3–30.5)	0.002
Fracture consolidation (n = 102)	61 (60%)	51 (74%)	10 (30%)	<0.001
Dichotomised variables: n (%)				
Continuous variables: median (IQR [6]*)*				
Calculation of p-values for dichotomised variables: Chi-squared test and Fisher's exact test				
Calculation of p-values for continuous variables: Mann-Whitney U test				

[1] Fracture-Related Infection.
[2] American Society of Anaesthesiologists.
[3] All other additional injuries that could not be specified to one of the previously stated categories.
[4] Proximal Femoral Nail Antirotation.
[5] Including Fracture-Related Infection re-operations and re-admissions, excluding planned removal of implant(s) only.
[6] Interquartile range.

Table 2
Characteristics of FRI [1] patients.

	FRI [1] (*n* = 38)
Time to onset of infection (days)	17.5 (11.0–41.8)
Follow-up duration (months)	22.7 (13.3–30.5)
Average number of re-operations	3.0 (2.0–6.0)
Average number of re-admissions	2.0 (1.0–3.3)
Recurrence of FRI [1]	10 (26%)
Infection control at last follow-up visit	35 (92%)
Dichotomised variables: n (%)	
Continuous variables: median (IQR [2]*)*	

[1] Fracture-Related Infection.
[2] Interquartile range.

the aforementioned complications were also demonstrated in this present cohort, although in a different frequency.

In addition to the general complication analysis, the subgroup of FRI patients was analysed separately. To our knowledge, the occurrence of other complications in FRI patients in particular has not been studied before, hence these results can be interpreted as new data. Apart from the FRI, a complication rate of 66% was reported in the subgroup of FRI patients. The most prevalent other complications in FRI patients were nonunion (18%), infection other than FRI (18%) and implant failure (14%).

Additional findings of this study were an increased LOS, a higher number of re-admissions and more re-operations in the subgroup of FRI patients. These outcomes can be explained due to the extensive treatment, most often involving new operations and subsequent intravenous administration of antibiotics, which is needed to control the FRI [3]. The increased LOS is likely influenced by the difference in reported data between both groups, as LOS of initial fracture fixation was reported for non-FRI patients and LOS of the initial FRI treatment was reported for FRI patients.

This ambidirectional study is subject to certain limitations. Firstly, since questionnaires were used, the results of this assessment could be influenced by response and non-response bias, respectively. With the use of the standardised EQ-5D questionnaire and the subsequent utilisation of reminders, the likelihood of these forms of bias were reduced. However, significant differences between respondents and non-respondents were reported in this cohort, especially concerning the age, ASA classification and severity of the trauma. This corresponds with previously conducted QoL assessments in trauma patients [37,38]. As a consequence of this considerable bias, this study is not generalisable to the entire fracture population and more research is needed to validate these findings in a prospective cohort with the possibility of sending subsequent reminders to avoid non-response bias. Compared to studies of both Gunning et al. and van der Vliet et al., originating from the same institute, our reported response rate is significantly lower (37% vs. 59% and 77%, respectively) [39,40]. This difference could be explained due to the composition of population [39] and the use of reminders by telephone in their study [40]. Secondly, due to the retrospective review of the severity of complications, the assessment might be subject to misclassification bias. However, due to the strict use of definitions and the double and blind assessment of the researchers, this bias is thought to be limited. Thirdly, as a result of the retrospective nature of this study, it was not possible to extract all data regarding both physical and psychological comorbidities that could have affected the QoL and hence outcomes of this study. Lastly, as a result of the relatively small size of the cohort, it was not possible to correct for potential confounders that might have influenced the QoL.

In conclusion, patients who suffered from an FRI have a decreased

Table 3
Quality of Life assessment in patients with or without a Fracture-Related Infection.

	All patients (*n* = 134)	No FRI [1] (*n* = 96)	FRI [1] (*n* = 38)	p-value
Mobility				<0.001
1 – No problems	49 (37%)	39 (41%)	10 (26%)	
2 – Mild problems	50 (37%)	40 (42%)	10 (26%)	
3 – Moderate problems	22 (16%)	15 (16%)	7 (18%)	
4 – Severe problems	10 (8%)	1 (1%)	9 (24%)	
5 – Extreme problems	3 (2%)	1 (1%)	2 (5%)	
Self-care (n = 133)				0.064
1 – No problems	98 (74%)	75 (79%)	23 (61%)	
2 – Mild problems	23 (17%)	14 (15%)	9 (24%)	
3 – Moderate problems	7 (5%)	4 (4%)	3 (8%)	
4 – Severe problems	4 (3%)	1 (1%)	3 (8%)	
5 – Extreme problems	1 (1%)	1 (1%)	0 (0%)	
Daily activities (n = 133)				0.010
1 – No problems	43 (32%)	34 (36%)	9 (24%)	
2 – Mild problems	57 (43%)	44 (46%)	13 (34%)	
3 – Moderate problems	22 (17%)	14 (15%)	8 (21%)	
4 – Severe problems	8 (6%)	2 (2%)	6 (16%)	
5 – Extreme problems	3 (2%)	1 (1%)	2 (5%)	
Pain and discomfort (n = 133)				0.009
1 – No pain	34 (26%)	27 (28%)	7 (18%)	
2 – Mild pain	65 (49%)	51 (54%)	14 (37%)	
3 – Moderate pain	26 (20%)	13 (14%)	13 (34%)	
4 – Severe pain	6 (5%)	2 (2%)	4 (11%)	
5 – Extreme pain	2 (2%)	2 (2%)	0 (0%)	
Anxiety and depression (n = 133)				0.24
1 – No symptoms	88 (66%)	64 (67%)	24 (63%)	
2 – Mild symptoms	37 (28%)	25 (26%)	12 (32%)	
3 – Moderate symptoms	5 (4%)	5 (5%)	0 (0%)	
4 – Severe symptoms	2 (2%)	1 (1%)	1 (3%)	
5 – Extreme symptoms	1 (1%)	0 (0%)	1 (3%)	
Index value (n = 131)	0.8 (0.7–0.9)	0.8 (0.7–0.9)	0.7 (0.5–0.9)	0.012
General health (n = 133)	75.0 (61.0–85.0)	75.0 (65.0–85.0)	75.0 (57.5–80.0)	0.31
Dichotomised or ordinal variables: n (%)				
Continuous variables: median (IQR [2])				
Calculation of p-values for dichotomised variables: Fisher's exact test				
Calculation of p-values for continuous variables: Mann-Whitney U test				

[1] Fracture-Related Infection.
[2] Interquartile range.

QoL in comparison to those without an FRI. Moreover, this is the first study that has provided information regarding the complication rate in FRI patients, clarifying that patients with an FRI have a higher risk of developing additional complications. Both these findings can help in patient counselling regarding the potential physical and mental consequences of having a complicated course of recovery due to an FRI after fracture surgery.

Table 4
Occurrence of complications [1].

	All patients (*n* = 134)	No FRI [2] (*n* = 96)	FRI [2] (*n* = 38)	p-value
Total number of complications	80	31	49	
Patients who developed complication(s)	50 (37%)	25 (26%)	25 (66%)	<0.001
Average number of complications per patient	0.0 (0.0–1.0)	0.0 (0.0–1.0)	1.0 (0.0–2.0)	<0.001
Type of complications (n = 80)				0.18
Nonunion	12 (15%)	3 (10%)	9 (18%)	
Malunion	4 (5%)	3 (10%)	1 (2%)	
Implant failure	10 (13%)	3 (10%)	7 (14%)	
Error in technique	7 (9%)	6 (19%)	1 (2%)	
Re-fracture	1 (1%)	0 (0%)	1 (2%)	
Soft tissue problem	3 (4%)	2 (6%)	1 (2%)	
Compartment syndrome	1 (1%)	0 (0%)	1 (2%)	
Postoperative haemorrhage	4 (5%)	2 (6%)	2 (4%)	
Deep venous thrombosis	2 (3%)	0 (0%)	2 (4%)	
Amputation	1 (1%)	0 (0%)	1 (2%)	
Persisting pain	6 (8%)	2 (6%)	4 (8%)	
Anaemia and electrolyte disturbances	3 (4%)	2 (6%)	1 (2%)	
Respiratory failure	1 (1%)	0 (0%)	1 (2%)	
Infection [3]	13 (16%)	4 (13%)	9 (18%)	
SIRS [4]	1 (1%)	0 (0%)	1 (2%)	
Paralytic ileus	1 (1%)	0 (0%)	1 (2%)	
Cardiac arrhythmia	1 (1%)	0 (0%)	1 (2%)	
Urine retention	5 (6%)	1 (3%)	4 (8%)	
Delirium	1 (1%)	0 (0%)	1 (2%)	
Pressure ulcer	1 (1%)	1 (3%)	0 (0%)	
Other [5]	2 (3%)	2 (6%)	0 (0%)	
Clavien-Dindo classification (n = 80)				0.45
Grade I	26 (32%)	11 (36%)	15 (31%)	
Grade II	15 (19%)	5 (16%)	10 (20%)	
Grade III	35 (44%)	15 (48%)	20 (41%)	
Grade IV	4 (5%)	0 (0%)	4 (8%)	
Grade V	0 (0%)	0 (0%)	0 (0%)	
Dichotomised variables: n (%)				
Continuous variables: median (IQR [6])				
Calculation of p-values for dichotomised variables: Chi-squared test and Fisher's exact test				
Calculation of p-values for continuous variables: Mann-Whitney U test				

[1] Complications that had either developed during the initial admission or (outpatient) follow-up excluding Fracture-Related Infection.
[2] Fracture-Related Infection.
[3] All infections other than Fracture-Related Infection.
[4] Systemic Inflammatory Response Syndrome.
[5] Other complications that could not be further specified, namely: cessation of the operation due to unforeseen logistic circumstances and delay in diagnosis.
[6] Interquartile range.

Declaration of competing interest

The authors declare that they have no financial interests or personal relationships that could have influenced the outcomes of this study. The authors declare that they did not receive funding for this study.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.injury.2024.111425.

References

[1] Metsemakers W-J, Morgenstern M, Senneville E, Borens O, Govaert GAM, Onsea J, et al. General treatment principles for fracture-related infection: recommendations from an international expert group. Arch Orthop Trauma Surg 2020;140:1013–27.

[2] Iliaens J, Onsea J, Hoekstra H, Nijs S, Peetermans WE, Metsemakers W-J. Fracture-related infection in long bone fractures: a comprehensive analysis of the economic impact and influence on quality of life. Injury 2021;52:3344–9. https://doi.org/10.1016/j.injury.2021.08.023.

[3] Moriarty TF, Metsemakers W-J, Morgenstern M, Hofstee MI, Vallejo Diaz A, Cassat JE, et al. Fracture-related infection. Nat Rev Dis Primers 2022;8:67. https://doi.org/10.1038/s41572-022-00396-0.

[4] Balestroni G, Bertolotti G. EuroQol-5D (EQ-5D): an instrument for measuring quality of life. Monaldi Arch Chest Dis 2015;78. https://doi.org/10.4081/monaldi.2012.121.

[5] Dakin H. Review of studies mapping from quality of life or clinical measures to EQ-5D: an online database. Health Qual Life Outcomes 2013;11:151. https://doi.org/10.1186/1477-7525-11-151.

[6] the LIVSFORSK network, Haraldstad K, Wahl A, Andenæs R, Andersen JR, Andersen MH, et al. A systematic review of quality of life research in medicine and health sciences. Qual Life Res 2019;28:2641–50. https://doi.org/10.1007/s11136-019-02214-9.

[7] Higginson IJ. Measuring quality of life: using quality of life measures in the clinical setting. BMJ 2001;322:1297–300. https://doi.org/10.1136/bmj.322.7297.1297.

[8] Walter N, Rupp M, Hierl K, Pfeifer C, Kerschbaum M, Hinterberger T, et al. Long-term patient-related quality of life after fracture-related infections of the long bones. Bone Joint Res 2021;10:321–7. https://doi.org/10.1302/2046-3758.105.BJR-2020-0532.

[9] Govaert GAM, Termaat MF, Glaudemans AWJM, Geurts J aP, de Jong T, de Jong VM, et al. [Diagnosis and treatment of fracture-related infections]. Ned Tijdschr Geneeskd 2019;163.

[10] Ziegler P, Schlemer D, Flesch I, Bahrs S, Stoeckle U, Werner S, et al. Quality of life and clinical-radiological long-term results after implant-associated infections in patients with ankle fracture: a retrospective matched-pair study. J Orthop Surg Res 2017;12:114. https://doi.org/10.1186/s13018-017-0608-x.

[11] Ekegren C, Edwards E, de Steiger R, Incidence Gabbe B. Costs and predictors of non-union, delayed union and mal-union following long bone fracture. IJERPH 2018;15:2845. https://doi.org/10.3390/ijerph15122845.

[12] Mavrogenis AF, Panagopoulos GN, Megaloikonomos PD, Igoumenou VG, Galanopoulos I, Vottis CT, et al. Complications after hip nailing for fractures. Orthopedics 2016;39. https://doi.org/10.3928/01477447-20151222-11.

[13] Papagelopoulos PJ, Partsinevelos AA, Themistocleous GS, Mavrogenis AF, Korres DS, Soucacos PN. Complications after tibia plateau fracture surgery. Injury 2006;37:475–84. https://doi.org/10.1016/j.injury.2005.06.035.

[14] Gitajn IL, Titus AJ, Tosteson AN, Sprague S, Jeray K, Petrisor B, et al. Deficits in preference-based health-related quality of life after complications associated with tibial fracture. Bone Joint J 2018;100-B:1227–33. https://doi.org/10.1302/0301-620X.100B9.BJJ-2017-1488.R1.

[15] Veen EJ, Janssen-Heijnen MLG, Leenen LPH, Roukema JA. The registration of complications in surgery: a learning curve. World J Surg 2005;29:402–9. https://doi.org/10.1007/s00268-004-7358-8.

[16] Baker SP, O'neill B, Haddon WJ, Long WB. The Injury Severity Score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma Acute Care Surg 1974;14:187–96.

[17] McNally M, Govaert G, Dudareva M, Morgenstern M, Metsemakers W-J. Definition and diagnosis of fracture-related infection. EFORT Open Rev 2020;5:614–9. https://doi.org/10.1302/2058-5241.5.190072.

[18] Buijs MAS, van den Kieboom J, Sliepen J, Wever KLH, van Breugel JM, Hietbrink F, et al. Outcome and risk factors for recurrence of early onset fracture-related infections treated with debridement, antibiotics and implant retention: results of a large retrospective multicentre cohort study. Injury 2022;53:3930–7. https://doi.org/10.1016/j.injury.2022.10.017.

[19] Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187–96. https://doi.org/10.1097/SLA.0b013e3181b13ca2.

[20] Wittauer M, Burch M-A, McNally M, Vandendriessche T, Clauss M, Della Rocca GJ, et al. Definition of long-bone nonunion: a scoping review of prospective clinical trials to evaluate current practice. Injury 2021;52:3200–5. https://doi.org/10.1016/j.injury.2021.09.008.

[21] Westgeest J, Weber D, Dulai SK, Bergman JW, Buckley R, Beaupre LA. Factors associated with development of nonunion or delayed healing after an open long bone fracture: a prospective cohort study of 736 subjects. J Orthop Trauma 2016;30:149–55. https://doi.org/10.1097/BOT.0000000000000488.

[22] Govaert G, Hobbelink M, Reininga I, Bosch P, Kwee T, de Jong P, et al. The accuracy of diagnostic Imaging techniques in patients with a suspected Fracture-related Infection (IFI) trial: study protocol for a prospective multicenter cohort study. BMJ Open 2019;9:e027772.

[23] Govaert GAM. Dutch fracture infection registry. ICTRP Trial Reg 2020. https://trialsearch.who.int/Trial2.aspx?TrialID=NL8647. accessed January 7, 2023.

[24] Castor E.D.C. (2019). Castor electronic data capture. [online] Available at: https://castoredc.com. n.d.

[25] ASA physical status classification system | American Society of Anesthesiologists (ASA) n.d. https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system (accessed February 21, 2021).

[26] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83. https://doi.org/10.1016/0021-9681(87)90171-8.

[27] Meinberg E, Agel J, Roberts C, Karam M, Kellam J. Fracture and dislocation classification compendium—2018. J Orthop Trauma 2018;32:S1–10. https://doi.org/10.1097/BOT.0000000000001063.

[28] Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg 1976;58:453–8.

[29] van Reenen M., Janssen B., Elly Stolk, Secnik Boye K., Herdman M., Kennedy-Martin M., et al. EQ-5D-5L User Guide Version 3.0 2018.

[30] Netwerk Acute Zorg Midden-Nederland n.d. https://www.netwerkacutezorgmn.nl/(accessed January 10, 2023).

[31] Hotchen AJ, Dudareva M, Corrigan RA, Ferguson JY, McNally MA. Can we predict outcome after treatment of long bone osteomyelitis?: a study of patient-reported quality of life stratified with the BACH classification. Bone Joint J 2020;102-B:1587–96. https://doi.org/10.1302/0301-620X.102B11.BJJ-2020-0284.R1.

[32] Zayzan K, Yusof N, Sulong A, Zakaria Z, Ab Rahman J. Functional outcome and quality of life following treatment for post-traumatic osteomyelitis of long bones. Smedj 2022;63:251–5. https://doi.org/10.11622/smedj.2020164.

[33] Meeuwis MA, de Jongh MAC, Roukema JA, van der Heijden FHWM, Verhofstad MHJ. Technical errors and complications in orthopaedic trauma surgery. Arch Orthop Trauma Surg 2016;136:185–93. https://doi.org/10.1007/s00402-015-2377-5.

[34] Hackl S, Keppler L, von Rüden C, Friederichs J, Perl M, Hierholzer C. The role of low-grade infection in the pathogenesis of apparently aseptic tibial shaft nonunion. Injury 2021;52:3498–504. https://doi.org/10.1016/j.injury.2021.08.014.

[35] Poh KS, Lingaraj K. Complications and their risk factors following hip fracture surgery. J Orthop Surg (Hong Kong) 2013;21:154–7. https://doi.org/10.1177/230949901302100207.

[36] Ovaska M. Complications in ankle fracture surgery. Acta Orthop 2015;86:1–35. https://doi.org/10.3109/17453674.2014.1002273.

[37] van der Vliet QMJ, Bhashyam AR, Hietbrink F, Houwert RM, Öner FC, Leenen LPH. Routine incorporation of longer-term patient-reported outcomes into a Dutch trauma registry. Qual Life Res 2019;28:2731–9. https://doi.org/10.1007/s11136-019-02211-y.

[38] Gabbe BJ, Cameron PA, Hannaford AP, Sutherland AM, McNeil JJ. Routine follow up of major trauma patients from trauma registries: what are the outcomes? J Trauma: Injury, Infect Crit Care 2006;61:1393–9. https://doi.org/10.1097/01.ta.0000225926.34180.47.

[39] Gunning A, van Heijl M, van Wessem K, Leenen L. The association of patient and trauma characteristics with the health-related quality of life in a Dutch trauma population. Scand J Trauma Resusc Emerg Med 2017;25:41. https://doi.org/10.1186/s13049-017-0375-z.

[40] van der Vliet QMJ, Sweet AAR, Bhashyam AR, Ferree S, van Heijl M, Houwert RM, et al. Polytrauma and high-energy injury mechanisms are associated with worse patient-reported outcomes after distal radius fractures. Clin Orthop Relat Res 2019;477:2267–75. https://doi.org/10.1097/CORR.0000000000000757.