Managing more than bones: the psychological impact of a recurrent fracture-related infection

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Aims

Fracture-related infections (FRIs) are a devastating complication of fracture management. However, the impact of FRIs on mental health remains understudied. The aim of this study was a longitudinal evaluation of patients' psychological state, and expectations for recovery comparing patients with recurrent FRI to those with primary FRI.

Methods

A prospective longitudinal study was conducted at a level 1 trauma centre from January 2020 to December 2022. In total, 56 patients treated for FRI were enrolled. The ICD-10 symptom rating (ISR) and an expectation questionnaire were assessed at five timepoints: preoperatively, one month postoperatively, and at three, six, and 12 months.

Results

Recurrent FRI cases consistently exceeded the symptom burden threshold (0.60) in ISR scores at all assessment points. The difference between preoperative-assessed total ISR scores and the 12-month follow-up was not significant in either group, with 0.04 for primary FRI ($p = 0.807$) and 0.01 for recurrent FRI ($p = 0.768$). While primary FRI patients showed decreased depression scores post surgery, recurrent FRI cases experienced an increase, reaching a peak at 12 months (1.92 vs 0.94; $p < 0.001$). Anxiety scores rose for both groups after surgery, notably higher in recurrent FRI cases (1.39 vs 1.02; $p < 0.001$). Moreover, patients with primary FRI reported lower expectations of returning to normal health at three (1.99 vs 1.11; $p < 0.001$) and 12 months (2.01 vs 1.33; $p = 0.006$).

Conclusion

The findings demonstrate the significant psychological burden experienced by individuals undergoing treatment for FRI, which is more severe in recurrent FRI. Understanding the psychological dimensions of recurrent FRIs is crucial for comprehensive patient care, and underscores the importance of integrating psychological support into the treatment paradigm for such cases.

Take home message

- This study highlights the significant psychological impact of fracture-related infections (FRIs), particularly recurrent FRIs, on patients.
- It demonstrates that patients with recurrent FRIs experience higher levels of depression and anxiety over time compared to those with primary FRIs.
- The findings emphasize the necessity of incorporating psychological support into the treatment plans for patients dealing with recurrent FRIs to ensure comprehensive care.

Introduction

Orthopaedic and trauma surgery is perpetually challenged by the complexities of bone and joint infections (BJIs), giving rise to multifaceted implications for patients, their families, and healthcare systems alike. These infections encompass a spectrum

of conditions, including fracture-related infections (FRIs).[1] FRIs present a devastating array of complications that demand intricate management strategies.[2] The anticipated increase in long bone fractures, particularly within the elderly population, underscores the seriousness of this concern.[3] The risk of post-traumatic infection is nuanced, ranging from 1% to 2% for closed fractures, and escalating up to 30% for Gustilo-Anderson type III open tibia fractures.[4] The achievement of infection eradication boasts variable success rates, with reported recurrence rates between 13% and 21%.[5-7]

The aftermath of FRIs encompasses a spectrum of challenges, including immobility, potential fear of amputations, extended hospital stays, multiple surgeries, and the socioeconomic implications of income loss.[8,9] The financial burden is substantial, with direct healthcare costs estimated to be six to eight times higher than in noninfected cases, largely attributed to extended hospitalization.[10,11] Recent consensus regarding the definition of FRI offers clarity, yet effective management remains intricate, necessitating interdisciplinary collaboration and comprehensive guidelines.[12] Surgical objectives encompass infection eradication and restoration of bone integrity and stability, often entailing multistage interventions.[13] Moreover, the recurrence of FRI presents a particularly concerning scenario, potentially leading to greater morbidity, prolonged treatment courses, and heightened psychological distress.[14] Notably, a nationwide analysis conducted in Germany revealed that over 25% of all FRIs (1,893 out of 7,158 individuals) had a pre-existing secondary psychological comorbidity according to diagnoses of the International Classification of Diseases (ICD)-10 chapter F.[15] Further, it was observed that the number of patients with psychological comorbidities had increased by 24% over the past decade.[16]

However, despite the prevailing emphasis on surgical evaluation, research focusing on patient-reported outcomes remains limited. Notably, the profound impact of FRI on mental health, the intricate psychological adaptation to the trauma, and the occurrence of FRI as a consequential secondary sequela have been relatively underexplored. These crucial facets deserve meticulous attention in order to comprehensively understand the holistic implications of FRI beyond the physical realm.

Therefore, the aim of this study was a longitudinal assessment of psychological symptom burden and expectations of recovery in patients with recurrent FRI in comparison to those with primary FRI. By exploring the nuances of these psychological dimensions in the context of reinfection cases, this research seeks to contribute to a more comprehensive understanding of the psychological impact of FRI and to inform strategies for improved patient care and outcomes.

Methods

Design, setting, and participants

A prospective, longitudinal study of patients treated for FRI was conducted in a Level 1 trauma centre in Germany. The inclusion period was defined from January 2020 to December 2022. A FRI was verified in all cases according to the consensus definition.[17] FRI was verified through the fulfilment of at least one of the subsequent confirmatory criteria: 1) the presence of fistula, sinus tract, or wound breakdown; 2) observation of purulent drainage or pus during the surgical procedure; 3) identification of phenotypically indistinguishable microorganisms through culture in at least two distinct deep-tissue/implant samples (inclusive of sonication fluid); and 4) histopathological discoveries such as microorganism presence in deep-tissue samples or the identification of more than five polymorphonuclear neutrophils (PMNs) per high-power field (HPF).[18] To ensure comparability between cases with primary FRI and recurrent FRI, it was verified that both groups remained infection free during the 12-month follow-up period. In the event that a patient exhibited confirmatory symptoms of FRI requiring additional treatment within that timeframe, the follow-up period was reset to the initial point.

The exclusion criteria included patients with multiple fractures, pathological fractures, a known comorbid psychological disorder according to chapter F of the ICD-10,[15] malignancy, or antibiotic therapy due to any other infectious disease. Additionally, to address missing values, only patients who had completed all questionnaires in full were considered. Eligible patients aged 18 years or older were consecutively enrolled. Patients were enrolled regardless of whether they presented with primary infection or reinfection and whether the initial fracture was open or closed.

Informed consent was obtained from all individual participants included. The study was approved by the institutional ethics committee of the University Clinic of Regensburg according to the Declaration of Helsinki (file number 20-1680-101).[19] This study was registered at the German Clinical Trials Register (DRKS; file number: 00025492).

In total, 56 patients were included in the study. Out of these, 16 (28.6%) presented with a recurrent FRI. Overall, more patients were male than female in both groups (58.7% vs 28.3%, and 68.8% vs 31.2%; p = 0.930). The distribution of sex among the patients showed no significant difference between the two groups (p = 0.930). The mean age of patients with and without reinfection was 56.2 years (standard deviation (SD) 15.2) and 57.1 years (SD 14.5), respectively. This difference was not statistically significant (p = 0.839) (Table I).

Outcome measures

The following patient-reported outcome measures (PROMs) were assessed at five different timepoints, specifically one week preoperatively, one month postoperatively, and after three, six, and 12 months. The questionnaires were administered by the study team in person during inpatient treatment and ambulatory visits. Additionally, at each timepoint clinical data were collected including site of infection, radiographs, and treatment procedure. Open fractures were classified according to the Gustilo-Anderson classification.[20] Revision rates were defined as required surgeries between infection occurrence and infection eradication. Achieved bone consolidation was determined with an evaluated RUST score > 10.[21]

The ICD-10 sympton rating (ISR) is an inventory for symptom rating based on the ICD-10 classification system. It serves as a licence-free alternative to the well-known international SCL90 (Symptom Checklist 90).[22] In a comparative study, the total scales of ISR and SCL-90 showed a strong correlation of $r = 0.833$.[23] The ISR comprises 29 items, and respondents rate each item on a five-point scale. The inventory assesses various factors, including depression, anxiety, obsession, somatic symptoms, eating disorders, as

Table I. Patient characteristics.

Characteristic	FRI without reinfection (n = 40)	Reinfection FRI (n = 16)	p-value*
Sex, n (%)			0.930
Male	27 (58.7)	11 (68.8)	
Female	13 (28.3)	5 (31.2)	
Mean age, yrs (SD)	56.2 (15.2)	57.1 (14.5)	0.839
Open fractures, n (%)	16 (40.0)	4 (25.0)	0.045
GA II	6	1	
GA IIIa	5	0	
GA IIIb	3	2	
GA IIIc	2	1	
Anatomical localization, n (%)			0.597
Humerus	2 (5.0)	1 (6.3)	
Femur	4 (10.0)	3 (18.8)	
Tibia	23 (57.5)	7 (43.8)	
Ankle	6 (15.0)	3 (18.8)	
Foot	5 (12.5)	2 (12.1)	
Mean time from injury to symptom onset, days (SD)	83.1 (11.2)	84.7 (14.3)	0.987
Mean revision rate (range)	2.1 (1 to 4)	2.1 (1 to 5)	0.920
Surgical procedure, n (%)			0.802
DAIR	2 (5.0)	1 (6.3)	
External fixation	6 (15.0)	2 (12.5)	
One-stage exchange	17 (42.4)	2 (12.5)	
Two-stage exchange	11 (27.5)	7 (43.8)	
Arthodesis	2 (5.0)	3 (18.8)	
Amputation	2 (5.0)	1 (6.3)	

*Independent-samples *t*-test.
DAIR, debridement, antibiotics and implant retention; GA, Gustilo-Anderson; SD, standard deviation.

well as additional supplementary factors related to suicide, sleep problems, memory issues, sexuality, and traumatic experiences.[24] The overall internal consistency of the ISR is high, with a Cronbach's α of 0.92 for the total score, and the syndrome scales also show good internal consistency, ranging between 0.78 and 0.86.[25]

To assess patients' expectations, the German version of the HSS expectation questionnaire, originally developed for hip arthroplasty, was used.[26,27] The instrument consists of 18 items assessing the four dimensions "everyday activity", "pain relief and functional improvement", "medication and social participation", and "gait improvement". The items are rated on a four-point Likert scale ranging from "back to normal state or complete improvement" to "not back to normal state, but a slight improvement". The internal consistency was determined with a Cronbach's α of 0.89.[26]

Statistical analysis

Data analysis was conducted using SPSS Statistics v. 28.0 (IBM, USA). Descriptive measures were calculated for all the variables. Mean and SD were used to express continuous variables. To compare continuous variables between the two groups, independent-samples *t*-tests were used, following confirmation of suitable distribution for parametric testing through Levene's test. To compare continuous variables within one group assessed at longitudinal timepoints, a repeated measures analysis of variance (ANOVA) with a Bonferroni-adjusted post-hoc analysis to control for inflated type I errors was calculated, following confirmation of suitable distribution for parametric testing through Levene's test. There were no violations of the assumption of homogeneity of variances. Significance was set at $p < 0.05$.

Results

In cases without reinfection, 16 patients (40.0%) had open fractures, compared to four patients (25%) in the reinfection group ($p = 0.045$, independent-samples *t*-test). In both groups, the majority of infections were anatomically localized at the tibia. The mean revision rate was similar for both cases without reinfection and reinfection cases, with values of 2.1 ($p = 0.920$, independent-samples *t*-test) (Table I). All patients remained infection-free in the 12 months' follow-up interval, and bone consolidation was achieved in 51 (91.1%) patients. Three patients underwent an amputation and two patients required a total knee arthroplasty in the follow-up time due to severe gonarthritis.

Comparing participants with primary infection and cases with recurrent FRI, significant differences were observed in the trajectories of their psychological scores over different time intervals (Figure 1). Preoperatively, the ISR total score for primary infection cases was 0.77, while for cases with recurrent FRI the score was 0.60. This difference was statistically significant ($p = 0.022$). The difference was even more pronounced at one month's follow-up (0.94 vs 0.46; $p \leq 0.001$). There was no statistically significant difference three months postoperatively. However, at the six-month assessment, primary infection cases had an ISR total score of 0.74, while recurrent FRI cases had a score of 0.520, showing a statistically significant difference ($p = 0.002$). After 12 months, primary infection cases reached an ISR total score of 0.81, whereas recurrent FRI cases had a score of 0.59 ($p = 0.016$). Notably, the clinically relevant threshold for symptom burden, set at 0.60, was exceeded by the group of recurrent FRI cases at each timepoint of assessment. However, the difference between preoperative-assessed total ISR scores and the 12 months' follow-up was not significant in both groups, with 0.04 for primary FRI ($p = 0.807$) and 0.01 for recurrent FRI ($p = 0.768$).

Regarding the depression subscales, no difference was observed in the preoperatively evaluated scores. Patients with a primary FRI exhibited decreased depression scores after the surgery, while the scores went up for recurrent FRI cases (1.59 vs 0.87 at one month; $p < 0.001$). For primary FRI cases the scores remained relatively stable, while the recurrent FRI group displayed a considerable increase reaching a peak of 1.92 at 12 months ($p < 0.001$). Also, here, the threshold for symptom burden (1.0) was crossed at each evaluation timepoint for the reinfection group. A longitudinal comparison of the

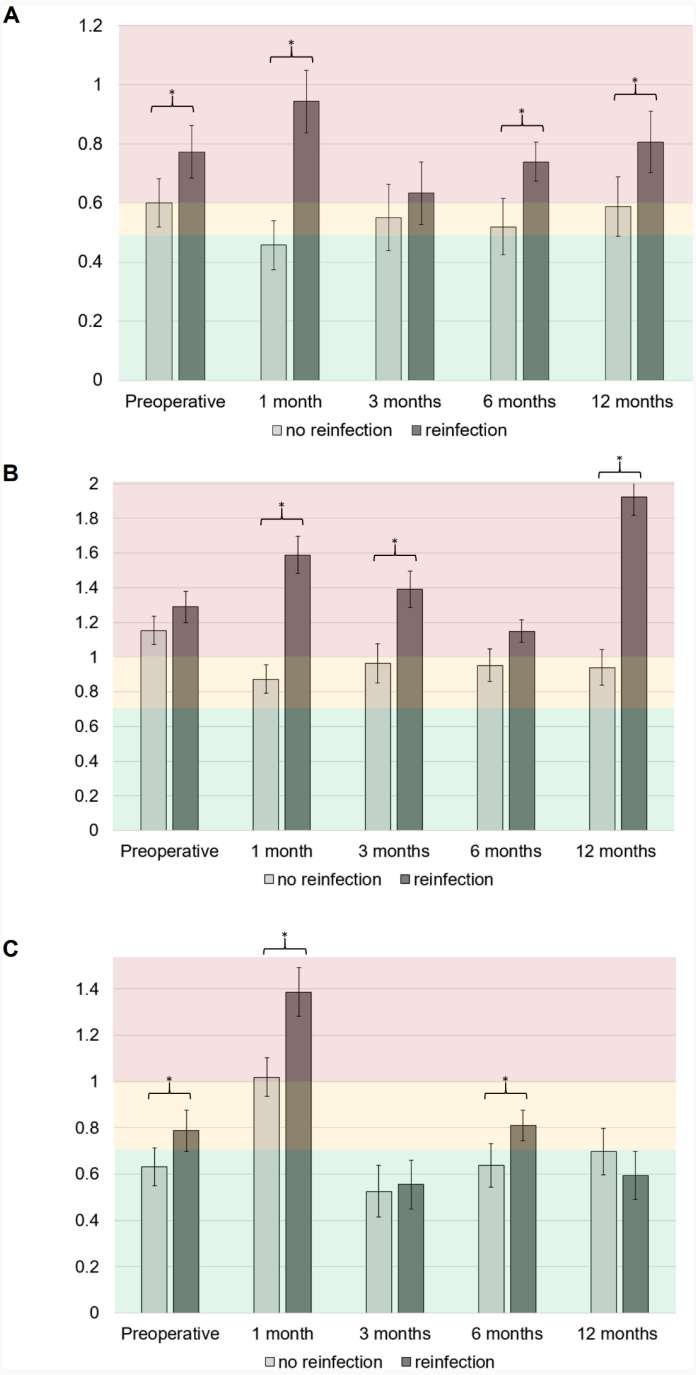

Fig. 1

Mean values of the International Classification of Diseases-10 symptom rating (ISR) responses shown for a) the total score, b) the subscale depression, and c) the subscale anxiety. Higher scores stand for higher symptom burden. Scores in the green area are defined as no symptom burden and the yellow area codes for suspected symptom burden. The red area shows the threshold for clinically relevant symptom burden, which is 0.6 for the total score, and 1.0 for depression and anxiety, respectively. *p ≤ 0.05, independent-samples *t*-test.

depression scores assessed preoperatively and at 12 months revealed a statistically significant increase for the reinfected FRI cohort (1.29 vs 1.92; p = 0.001), while the scores decreased significantly in the primary FRI cohort (1.15 vs 0.94; p = 0.015). Analyzing the anxiety subscale scores showed that before the surgical intervention, primary infection cases displayed an anxiety subscale score of 0.63, while cases with recurrent FRI had a higher score of 0.79 (p = 0.005). For both groups, the anxiety level increased after the surgery, which was higher for the recurrent FRI group (1.39 vs 1.02; p < 0.001). The defined threshold for symptom burden of 1.0 was surpassed by both cohorts at one month. Comparing the preoperative anxiety scores with those at the final follow-up revealed a decrease in the recurrent FRI group (0.79 vs 0.59; p = 0.024), while the scores in the primary FRI group did not change significantly.

Participants' expectations of returning to a state of normal health exhibited fluctuations over the study period. While there was no difference in the scores preoperatively, patients with a primary FRI had significantly lower expectations at three months (1.99 vs 1.11; p < 0.001), as well as at 12 months (2.01 vs 1.33; p = 0.006) (Figure 2). The Pearson

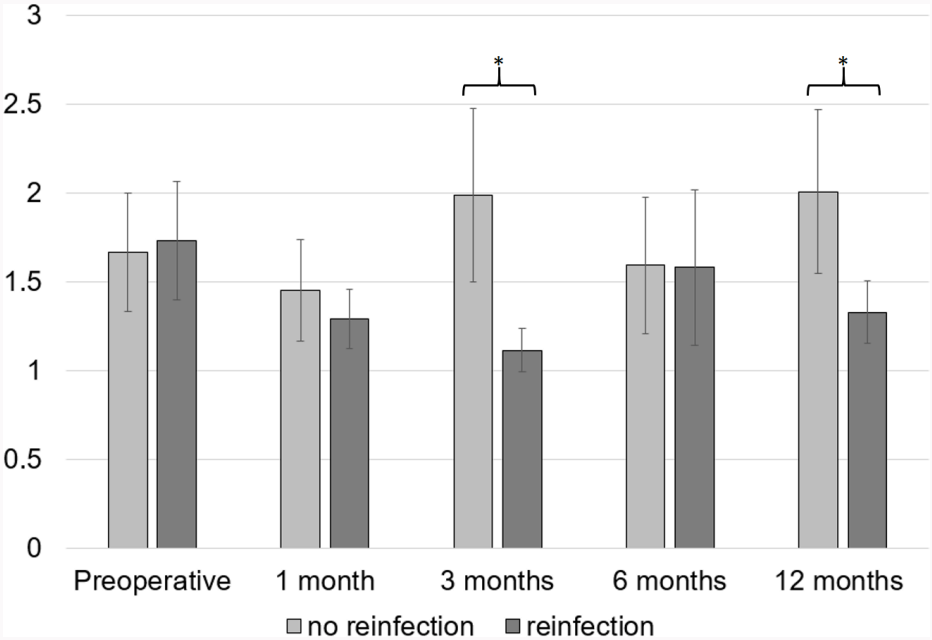

Fig. 2
Mean expectation scores. Higher scores depict lower expectation to return to a state of normal health. *p ≤ 0.05, independent-samples *t*-test.

correlation did not reveal any statistically significant association between the ISR and the expectation scores.

Discussion

This longitudinal study aimed to investigate the psychological impact of recurrent FRI in comparison to primary FRI. The main findings demonstrated that patients with primary FRI exhibited lower total ISR scores, as well as lower depression scores, at all timepoints of assessment compared to the preoperative scores, while only anxiety scores were elevated one month postoperatively. In comparison, patients with recurrent FRI exhibited a higher psychological symptom burden. Notably, the total ISR scores and the depression scores exceeded the clinically relevant threshold for symptom burden at all timepoints of assessment. In both groups, a longitudinal comparison of the ISR total scores assessed preoperatively and at the 12-month follow-up did not reveal significant changes. However, the depression subscores increased for the reinfected FRI cohort (1.29 vs 1.92; p = 0.001), while the scores decreased in the primary FRI cohort (1.15 vs 0.94; p = 0.015). Interestingly, the anxiety subscores were found to be significantly decreased after 12 months in patients with recurrent FRI. A comparable study conducted with periprosthetic joint infection patients has shown that in the ISR, total scores were statistically significantly higher at a 12-month follow-up compared to preoperatively assessed scores (0.55 vs 0.87; p = 0.002). Additionally, depression and anxiety scores increased with time and peaked at six months (1.6; p = 0.005) and 12 months (1.12; p = 0.001), respectively.[28]

The psychological burden of patients dealing with FRI has not received substantial attention. Failing to acknowledge the significance of these challenging circumstances might have repercussions on resource distribution and the ranking of preventative actions, and could even hinder the incorporation of counselling as an essential element within trauma surgery standard care. As such, this finding underscores the necessity of directing future research endeavours towards comprehending the psychological needs of orthopaedic patient cohorts.[29] Aligned with the presented results, it has been demonstrated that FRI patients report significantly lower quality of life in comparison to normative data. In that cohort, 32.4% of the patients (12/37) surpassed the clinically significant threshold for the burden of depression symptoms evaluated with the ISR even after a mean of 4.2 years after successful treatment with achieved infection eradication and bone consolidation.[30] A recent qualitative study additionally revealed clear indications from FRI patients about their need for psychological support. The patients reported that meditation and yoga practices served as valuable tools for them to maintain a positive outlook during recovery.[14] While the efficacy of such supplementary therapeutic approaches in FRI patients awaits validation, their incorporation into clinical practice could be a practical and cost-effective measure. In addition, it is well established that patients benefit from the incorporation of multidisciplinary teams,[12,31] and the results of this study emphasize the potential of and rationale for including a psychologist as a vital member of the treatment team. The presented data indicate a notable divergence in psychological scores during the treatment period, particularly evident at one month postoperatively. This introduces a critical dimension to our understanding of patient recovery following surgical interventions for FRI, suggesting that the immediate postoperative phase may be particularly challenging for patients. This calls attention to the vulnerability of patients during the initial stages of recovery, prompting consideration for proactive and targeted psychological interventions in the early postoperative period. Furthermore, the persistence of psychological impairment with regard to depression at later timepoints of assessment in cases of recurrent FRI emphasizes the need for sustained psychological support throughout the recovery trajectory in this patient group.

The findings of this study demonstrated that patients with a primary FRI had significantly lower expectations of returning to a state of normal health compared to recurrent FRI patients at three months and 12 months. One possible interpretation of this is that patients with recurrent FRI may have developed a more optimistic outlook on their recovery expectations due to their prior experience with the complication. Patients who have faced a similar treatment before may have learned to adapt to the challenges of recovery, cope with pain, and set more realistic recovery goals. Such familiarity with the recovery process might result in a more positive outlook, leading them to anticipate a higher likelihood of returning to normal health. Moreover, patients with recurrent FRI might have benefited from improved social support networks and rehabilitation strategies built from their earlier experiences, further enhancing their optimism regarding recovery. In the recurrent FRI group, expectations increased longitudinally until the six-month follow-up when the trend reversed. This observation aligns with the possibility that as time passed and their initial improvements became less pronounced, they may have experienced a decline in their perceived prospects for recovery. The same potential explanation may apply for the observation that expectations decreased at three months in the primary FRI groups. The patients may have received more intensive medical care and rehabilitation immediately following their injury, leading to substantial initial progress in their recovery. As a result, at the three-month assessment, they may have experienced a decline in the rate of improvement, which could lead to lower expectations. These patients may have expected their recovery to continue at the same pace as the initial stages but found that it was slowing down, causing them to rate their expectations lower on the HSS.

Numerous limitations necessitate careful consideration when interpreting the outcomes of this study. First, its sample size and exclusive focus on a single centre may restrict the extent to which the findings can be generalized beyond this specific context. Furthermore, the relatively modest cohort size precludes the ability to conduct subgroup analyses for distinct fracture localizations and to compare different treatment approaches. In addition, the longitudinal nature of the study, while valuable for capturing temporal changes, does not establish definitive causality and cannot fully address potential fluctuations in patients' psychological wellbeing that might be attributed to factors unrelated to FRI treatment. In addition, only patients who completed all questionnaires were included in the analysis, potentially introducing bias if those who dropped out had different psychological experiences. Finally, it is essential to note that the reliance on PROMs introduces the potential for response bias and subjective interpretation, which could influence the accuracy of the collected data.

The findings demonstrate the significant psychological burden experienced by individuals undergoing treatment for FRI, which is more severe in recurrent FRI. Understanding the psychological dimensions of recurrent FRIs is crucial for comprehensive patient care, and underscores the importance of integrating psychological support into the treatment paradigm for such cases.

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T. Loew: Conceptualization, Methodology, Resources, Writing – review & editing.
T. Hinterberger: Conceptualization, Methodology, Supervision, Writing – review & editing.
V. Alt: Conceptualization, Methodology, Resources, Writing – review & editing.
M. Rupp: Conceptualization, Data curation, Methodology, Supervision, Validation, Writing – review & editing.

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Data sharing

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Ethical review statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. This study protocol was reviewed and approved by the institutional ethics committee of University Hospital Regensburg (file number 20-1680-101). Written informed consent was obtained from participants to participate in the study.

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Trial registration number

This study was registered at the German Clinical Trials Register (DRKS, file number: 00025492).