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Health-related quality of life and mental health in patients with major bone and joint infections

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Aims

It is well described that patients with bone and joint infections (BJIs) commonly experience significant functional impairment and disability. Published literature is lacking on the impact of BJIs on mental health. Therefore, the aim of this study was to assess health-related quality of life (HRQoL) and the impact on mental health in patients with BJIs.

Methods

The AO Trauma Infection Registry is a prospective multinational registry. In total, 229 adult patients with long-bone BJI were enrolled between 1 November 2012 and 31 August 2017 in 18 centres from ten countries. Clinical outcome data, demographic data, and details on infections and treatments were collected. Patient-reported outcomes using the 36-Item Short-Form Health Survey questionnaire (SF-36), Parker Mobility Score, and Katz Index of Independence in Activities of Daily Living were assessed at one, six, and 12 months. The SF-36 mental component subscales were analyzed and correlated with infection characteristics and clinical outcome.

Results

The SF-36 physical component summary mean at baseline was 30.9 (95% CI 29.7 to 32.0). At one month, it was unchanged (30.5; 95% CI 29.5 to 31.5; $p = 0.447$); it had improved statistically significantly at six months (35.5; 95% CI 34.2 to 36.7; $p < 0.001$) and at 12 months (37.9; 95% CI 36.4 to 39.3; $p < 0.001$). The SF-36 mental component summary mean at baseline was 42.5 (95% CI 40.8 to 44.2). At one month, it was unchanged (43.1; 95% CI 41.4 to 44.8; $p = 0.458$); it had improved statistically significantly at six months (47.1; 95% CI 45.4 to 48.7; $p < 0.001$) and at 12 months (46.7; 95% CI 45.0 to 48.5; $p < 0.001$). All mental subscales had improved by the end of the study, but mental health status remained compromised in comparison with the average USA population.

Conclusion

BJIs considerably impact HRQoL, particularly mental health. Patients suffering from BJIs reported considerable limitations in their daily and social activities due to psychological problems. Impaired mental health may be explained by the chronic nature of BJIs, and therefore the mental wellbeing of these patients should be monitored closely.

Take home message

- This study demonstrated that bone and joint infections are associated with a considerable impact on health-related quality of life, and in particular on mental health.
- Therefore, these patients would likely benefit from proactive efforts to identify and treat their mental health.

Bone & Joint Open

Introduction

Bone and joint infections (BJIs) represent a serious complication of arthroplasty or fracture surgery. Despite surgical and antibiotic treatment, BJIs are associated with high rates of complications and treatment failure.[1-3]

Both fracture-related infections (FRIs) and periprosthetic joint infections (PJIs) commonly result in significant functional impairment and considerable disability.[4,5] Several large studies have reported that patients suffer from a compromised physical outcome and health-related quality of life (HRQoL).[5-8] Recent studies highlighted the impact of FRIs and PJIs on patients' mental health. Walter et al[9] showed that after a mean of 4.2 years following successful treatment of long-bone FRI, patients reported a significantly reduced HRQoL, especially in the physical health component, compared to normative data. Additionally, they noted a moderate to severe psychological symptom burden in about 20% of their patients. The same group demonstrated in PJI patients significantly lower mental and physical quality-of-life scores compared to normative data, even following successful treatment of the infection.[10]

An epidemiological analysis on PJI in Germany from 2009 to 2019 showed that 25% of PJI patients had a secondary diagnosis regarding mental and behavioural disorders, and the number of patients with psychological comorbidities doubled over the reported decade.[11]

These studies show that BJIs affect mental health, and prompted us to examine the HRQoL, in particular the mental health of a large international patient cohort of patients treated for FRI and PJI.

Methods

The AO Trauma Infection Registry is a prospective multinational registry (registered in ClinicalTrials.gov: NCT01677000). In total, 292 adult patients with long-bone BJI were enrolled between 1 November 2012 and 31 August 2017 from 18 centres from ten countries in this registry. Study conduct, data management, patient consent (including the use of collected biomaterials for future studies), and ethical approval have been described previously.[12,13]

Baseline data were collected when patients consented to participate in the study. The follow-up period was 12 months, with planned visits at one, six, and 12 months. All patients received the standard of care treatment chosen by their treating surgeon.

The study was approved by our Institutional Review Board (IRB) and at each site's local IRB or ethics committee. Written informed consent was obtained from all individual participants who were included in the study. The AO Foundation and AO Trauma Clinical Priority Programme on Bone Infection funded the original study.[13]

Inclusion and exclusion criteria

Adult patients (aged 18 years or older) with confirmed *Staphylococcus aureus* (either methicillin resistant or sensitive) infection involving a long bone (femur, tibia, fibula, humerus, radius, ulna, or clavicle) due to FRI or PJI were eligible, regardless of the stage of infection or prior treatment history. *S. aureus* infection was confirmed by positive deep cultures from baseline examinations or by a definitive diagnosis of active *S. aureus* infection (from the surgical site by the treating surgeon). Prisoners, pregnant patients, and those unable to either give consent or attend the follow-up visits were excluded.[12,13]

Outcome measures

Patient attributes, medical history, comorbidities (Charlson Comorbidity Index),[14] treatment approaches, and complications were recorded.

The patients' physical and mental health, functional status, and degree of independence were assessed at baseline and at all follow-up visits using the following instruments: the 36-item Short Form Health Survey questionnaire version 2 (SF-36 v2),[15] Parker Mobility Score (PMS),[16] and Katz Index of Independence in Activities of Daily Living (Katz ADL).[17] Healing status was recorded at each follow-up as "cured", "healing", or "other" by the individual investigational sites according to their standard of care.[12,13,16–18]

The SF-36 questionnaire consists of 36 questions assessing both physical and mental health status. The SF-36 Mental Component Summary (MCS) subscales are: Vitality Scale (VS), Social Functioning Scale (SFS), Role Emotional Scale (RES), and Mental Health Scale (MHS). To calculate a score from the different items of the SF-36 questionnaire, a raw score was calculated for each of the subscales while weighting the items. The raw scores were subsequently transformed to a standardized scale ranging from 0 to 100 according to the 1998 general USA population using a *z*-score standardization. Higher scores represent better health status.[19] Afterwards, a norm-based transformation was applied in order to yield scales with a mean of 50 and a SD of 10.[13]

Statistical analysis

Unadjusted mixed-effects models for repeated measures (MMRMs) were used to estimate the outcomes at each follow-up and compare their changes over the course of follow-up with baseline. These models were used for group comparisons between subgroups (PJI vs FRI; methicillin-resistant *S. aureus* (MRSA) vs methicillin-sensitive *S. aureus* (MSSA)) at each follow-up visit. The models included a fixed, categorical effect for visit and an unstructured covariance on patient level, and were fitted using restricted maximum likelihood estimation (REML). Significance tests for change over follow-up were based on least-squares means. For outcomes with a serious violation of the normality assumption, simple summary statistics on the outcomes were produced by follow-up visit. Change from baseline was analyzed using the Wilcoxon signed-rank test. Independent-samples *t*-test was applied to analyze difference in SF-36 scores according to healing status (cured vs healing/other) at 12 months.

Additionally, the correlation between the SF-36 scores and the Katz ADL sum score, and the Parker Mobility score, was assessed using the Spearman correlation. Complications were reported by category at the patient level, while multiple events of the same type were combined for each patient and the worst severity or outcome for each event type was presented for analysis. Event rates were calculated with the denominator defined as the total population size, irrespective of dropouts during follow-up. The 95% Clopper-Pearson CIs were provided for calculated event rates. Sensitivity analyses were restricted to patients for whom an in-hospital complication form was completed.

Table I. 36-Item Short-Form Health Survey questionnaire mental subscales and Mental Component Summary over one-year follow-up — results from mixed models for repeated measures.

Outcome	n	Mean (95% CI)	Change (95% CI)	p-value
Norm-based SF-36 Vitality Scale				
Baseline	279	44.0 (42.6 to 45.4)		
1 mth	255	44.6 (43.2 to 46.1)	0.6 (-0.7 to 1.9)	0.364
6 mths	212	48.5 (47.1 to 50.0)	4.5 (3.1 to 5.9)	< 0.001
12 mths	193	48.1 (46.5 to 49.7)	4.1 (2.5 to 5.6)	< 0.001
Norm-based SF-36 Social Functioning Scale				
Baseline	281	35.4 (33.7 to 37.0)		
1 mth	258	33.8 (32.1 to 35.5)	-1.6 (-3.3 to 0.1)	0.065
6 mths	212	40.8 (39.1 to 42.5)	5.5 (3.7 to 7.3)	< 0.001
12 mths	193	42.9 (41.1 to 44.6)	7.5 (5.6 to 9.4)	< 0.001
Norm-based SF-36 Role Emotional Scale				
Baseline	273	33.4 (31.5 to 35.2)		
1 mth	256	32.5 (30.5 to 34.5)	-0.9 (-2.7 to 1.0)	0.351
6 mths	212	38.0 (36.0 to 40.0)	4.6 (2.4 to 6.8)	< 0.001
12 mths	192	38.8 (36.7 to 40.8)	5.4 (3.3 to 7.4)	< 0.001
Norm-based SF-36 Mental Health Scale				
Baseline	279	41.0 (39.6 to 42.5)		
1 mth	255	42.8 (41.3 to 44.2)	1.7 (0.4 to 3.0)	0.009
6 mths	212	45.9 (44.5 to 47.3)	4.8 (3.5 to 6.2)	< 0.001
12 mths	192	46.1 (44.5 to 47.7)	5.0 (3.4 to 6.6)	< 0.001
SF-36 MCS				
Baseline	271	42.5 (40.8 to 44.2)		
1 mth	253	43.1 (41.4 to 44.8)	0.6 (-1.0 to 2.1)	0.458
6 mths	210	47.1 (45.4 to 48.7)	4.5 (2.9 to 6.2)	< 0.001
12 mths	191	46.7 (45.0 to 48.5)	4.2 (2.5 to 6.0)	< 0.001

MCS, Mental Component Summary; SF-36, 36-Item Short-Form Health Survey questionnaire.

Within a further sensitivity analysis, the risk for any (re)hospitalization due to infection was estimated. This analysis was restricted to patients who completed the one-year follow-up or experienced a rehospitalization/reoperation. The 95% CIs were provided for event rates. Descriptive summary tables comparing SF-36 mental subscales and MCS at 12 months according to occurrence of any in-hospital complications, or complications leading to hospitalization or prolongation of such, were produced while using Mann-Whitney U tests. Unadjusted MMRMs were used to compare changes in the outcomes between baseline and the course of follow-up within patients with and without any (re)hospitalization due to infection and for group comparisons at each follow-up.

Results

Overview

In total, 292 patients met the inclusion criteria, gave written consent, and entered the study; 14 patients (4.8%) died during the follow-up period, and 82 (28.1%) dropped out due to loss to follow-up (n = 62; 75.6%), consent withdrawal (n = 9; 11.0%), or other reasons (n = 11; 13.4%).[13] Patient characteristics, infection details, hospitalization, and treatment specifics, as well as complications, are summarized in Supplementary Table i and in the previous publication.[13]

General and physical outcomes

At one-, six-, and 12-month follow-up, a cure rate of 4.5% (12/265), 36.8% (78/212), and 62.1% (118/190), respectively, was recorded. At one year, in 72 cases (37.9%) the status was "healing" or "other".[13]

Results from the mixed-effects models indicate that at one month, the SF-36 mean PCS score (30.5 (95% CI 29.5 to 31.5)) was comparable to the baseline score (30.9 (95% CI 29.7 to 32.0; p = 0.447)). At six and 12 months the improvements from baseline were statistically significant, with a mean PCS score of 35.5 (95% CI 34.2 to 36.7) (p < 0.001) and 37.9 (95% CI 36.4 to 39.3; p < 0.001), respectively. However, the PCS mean score at 12 months was lower than the USA population norm (50).

Table II. Difference in 36-Item Short-Form Health Survey questionnaire mental subscales, Mental Component Summary scale, and Physical Component Summary scale according to healing status at 12 months.

Variable	Visit	Cured		Healing/other		Difference between treatment groups, mean (95% CI)	p-value*
		n	Mean (95% CI)	n	Mean (95% CI)		
Norm-based SF-36 Vitality Scale	12 mths	117	50.7 (48.4 to 52.9)	70	46.3 (43.4 to 49.1)	4.4 (0.8 to 8.0)	0.017
Norm-based SF-36 Social Functioning Scale	12 mths	117	45.9 (43.8 to 48.1)	70	38.0 (34.6 to 41.4)	7.9 (3.9 to 11.9)	< 0.001
Norm-based SF-36 Role Emotional Scale	12 mths	117	42.9 (40.3 to 45.5)	69	32.7 (29.1 to 36.3)	10.2 (5.9 to 14.6)	< 0.001
Norm-based SF-36 Mental Health Scale	12 mths	117	47.9 (45.7 to 50.1)	69	43.9 (40.9 to 47.0)	4.0 (0.3 to 7.7)	0.034
SF-36 MCS	12 mths	117	49.2 (46.9 to 51.5)	68	44.1 (40.7 to 47.6)	5.0 (1.0 to 9.0)	0.014
SF-36 PCS	12 mths	117	41.4 (39.4 to 43.4)	68	32.8 (30.5 to 35.0)	8.6 (5.5 to 11.7)	< 0.001

*Independent-samples *t*-test.
MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, 36-Item Short-Form Health Survey questionnaire.

Table III. Descriptive summary of 36-Item Short-Form Health Survey questionnaire mental subscales and Mental Component Summary scale at 12 months according to occurrence of any in-hospital complications, or complications leading to hospitalization or prolonged hospital stay.

Variable	Complications		p-value*
	No (n = 173)	Yes (n = 20)	
Norm-based SF-36 Vitality Scale			0.097
n	173	20	
Mean (SD, range)	49.5 (12.3, 20.9 to 70.8)	45.2 (9.4, 27.1 to 64.6)	
Median (IQR)	49.0 (39.6 to 58.3)	44.3 (39.6 to 50.5)	
Norm-based SF-36 Social Functioning Scale			0.005
n	173	20	
Mean (SD, range)	44.1 (13.1, 13.2 to 56.8)	36.1 (12.5, 13.2 to 56.8)	
Median (IQR)	45.9 (35.0 to 56.8)	35.0 (32.3 to 45.9)	
Norm-based SF-36 Role Emotional Scale			0.044
n	172	20	
Mean (SD, range)	39.9 (15.3, 9.2 to 55.9)	33.5 (15.0, 9.2 to 55.9)	
Median (IQR)	42.3 (30.6 to 55.9)	32.6 (26.7 to 46.2)	
Norm-based SF-36 Mental Health Scale			0.060
n	172	20	
Mean (SD, range)	47.0 (12.6, 7.8 to 64.1)	43.8 (8.3, 30.3 to 64.1)	
Median (IQR)	50.0 (38.7 to 55.6)	44.4 (37.3 to 48.6)	
SF-36 MCS			0.167
n	171	20	
Mean (SD, range)	47.9 (13.5, 5.4 to 69.0)	44.6 (12.4, 24.0 to 67.4)	
Median (IQR)	50.4 (38.9 to 58.5)	42.7 (36.0 to 55.6)	

*Mann-Whitney U test.
MCS, Mental Component Summary; SF-36, 36-Item Short-Form Health Survey questionnaire.

Table IV. Results from mixed models for repeated measures comparing 36-Item Short-Form Health Survey questionnaire mental subscales and Mental Component Summary scale to (re)hospitalization due to infection.

Variable	Visit	Any (re)hospitalization due to infection*		Difference between groups (Yes vs No (re)hospitalization), mean (95% CI)	p-value†
		No, mean (95% CI)	Yes, mean (95% CI)		
Norm-based SF-36 Vitality Scale	12 mths	47.5 (45.2 to 49.9)	48.5 (46.4 to 50.7)	1.0 (-2.2 to 4.2)	0.552
Norm-based SF-36 Social Functioning Scale	12 mths	43.4 (40.9 to 46.0)	42.4 (40.0 to 44.8)	-1.0 (-4.5 to 2.5)	0.563
Norm-based SF-36 Role Emotional Scale	12 mths	39.9 (36.9 to 42.9)	37.8 (35.0 to 40.5)	-2.1 (-6.2 to 1.9)	0.300
Norm-based SF-36 Mental Health Scale	12 mths	45.0 (42.6 to 47.4)	47.0 (44.8 to 49.2)	2.0 (-1.2 to 5.3)	0.221
SF-36 MCS	12 mths	46.2 (43.6 to 48.7)	47.2 (44.8 to 49.6)	1.0 (-2.5 to 4.6)	0.558

Results from mixed models for repeated measures with an unstructured covariance (patient level), including the respective outcome at all visits as outcome. Presented values are least-square (LS) means and difference in LS means.
*Hospitalization at baseline not taken into account.
†p-value for comparison of mean value between groups at 12 months follow-up.
MCS, Mental Component Summary; SF-36, 36-Item Short-Form Health Survey questionnaire.

Table V. Spearman correlation between duration of hospital stay at baseline and 36-Item Short-Form Health Survey questionnaire mental subscales and Mental Component Summary at 12 months' visit.

Variable	12-month visit		
	n	r_s	p-value
Norm-based SF-36 Vitality Scale	193	-0.009	0.904
Norm-based SF-36 Social Functioning Scale	193	0.006	0.936
Norm-based SF-36 Role Emotional Scale	192	-0.044	0.540
Norm-based SF-36 Mental Health Scale	192	-0.102	0.157
SF-36 MCS	191	-0.017	0.817

Interpretation for correlation coefficient (absolute value): 0.0 to < 0.2: very weak, 0.2 to < 0.4: weak, 0.4 to < 0.6: moderate, 0.6 to < 0.8: strong, 0.8 to 1.0: very strong.
Duration of hospitalization is only available for hospital stay at time of inclusion, not for any re-hospitalizations.
MCS, Mental Component Summary; SF-36, 36-Item Short-Form Health Survey questionnaire.

Results from the mixed-effects models indicate that the mean PMS score at one month with 4.2 (95% CI 3.9 to 4.6) was lower compared to baseline with 4.8 (95% CI 4.4 to 5.1; p = 0.002). At six and 12 months the improvements from baseline were statistically significant, with a mean PMS score of 6.2 (95% CI 5.9 to 6.6; p < 0.001) and 6.9 (95% CI 6.6 to 7.2; p < 0.001), respectively.

The mean Katz ADL score at one month (4.4 (SD 2.0)) was comparable to baseline (4.7 (SD 1.9); p = 0.070)) and increased significantly at six months' (5.3 (SD 1.5); p < 0.001) and 12 months' follow-up (5.5 (SD 1.2); p < 0.001). Approximately half of the patients maintained their independence level at each follow-up visit, and almost 40% became more independent at six and 12 months compared to baseline (n = 76 (38.4%) and n = 71 (39.4%), respectively). Approximately 10% became more dependent compared to baseline (n = 20 (10.1%) at six months and n = 15 (8.3%) at 12 months).[13]

Mental quality of life

Results from the mixed-effects models indicate that at one month, the SF-36 mean MCS score (43.1 (95% CI 41.4 to 44.8)) was comparable to the baseline score (42.5 (95% CI 40.8 to 44.2); p = 0.458). At six and 12 months, the improvements from baseline were statistically significant, with a mean MCS score of 47.1 (95% CI 45.4 to 48.7) (p < 0.001) and 46.7 (95% CI 45.0 to 48.5) (p < 0.001), respectively (Table I). At baseline, mean mental subscales were: VS 44.0 (95% CI 42.6 to 45.4); SFS 35.4 (95% CI 33.7 to 37.0); RES 33.4 (95% CI 31.5 to 35.2); and MHS 41.0 (95% CI 39.6 to 42.5). At one month, all mean mental subscales were comparable to baseline values. At six- and 12-month follow-up visits, all four subscales showed a significant increase (p < 0.001) (Table I), which was confirmed by the unadjusted MMRMs (Supplementary Table i). At final follow-up, mean mental subscales were: VS 48.1 (95% CI 46.5 to 49.7); SFS 42.9 (95% CI 41.1 to 44.6); RES 38.8 (95% CI 36.7 to 40.8); and MHS 46.1 (95% CI 44.5 to 47.7).

Comparing mental health according to the type of infection, the VS and SFS were significantly lower in PJI patients compared to the FRI cohort, both at baseline and final follow-up. The MCS as well as the RES and MHS were comparable in PJI and FRI patients (Supplementary Table ii). Comparing SF-36 mental subscales and MCS according to antibiotic resistance, MRSA infections were not associated with worse mental health when compared to MSSA infections. Only the VS and SFS were lower at baseline in more resistant infections (Supplementary Table iii). The SFS was also lower at the later follow-up visits in MRSA than in MSSA infections.

Association between mental health and healing status

At final follow-up, the mean MCS and all mean mental subscales were significantly higher in patients with cured BJI (n = 117; 49.2%) compared to patients with not cured BJI or ongoing healing status (n = 68; 44.1%) (p = 0.014, independent-samples *t*-test) (Table II). During the follow-up period, a higher Katz ADL score and a higher PMS score were associated with increased MCS and increased mental subscales (Supplementary Tables iv and v). At one year, physical outcome was also significantly better in cured patients, with a mean PCS of 41.4 (95% CI 39.4 to 43.4) (p < 0.001, independent-samples *t*-test; Table II).

Effect of complications on mental health

In total, 41 patients experienced complications that required prolonged hospitalization or readmission and ten patients died during readmission. Based on the sensitivity analysis (i.e. analysis including only patients who either completed the one-year follow-up or experienced at least one in-hospital complication), the risk of in-hospital complication was 18.9% (95% CI 13.9 to 24.7). The rehospitalization risk during the study was 63.4% (95% CI 57.1 to 69.4). Patients were rehospitalized due to infection a median of 1.0 (IQR 0.0 to 1.0) times during the study period and received surgical treatment at a median of 1.0 (IQR 0.0 to 3.0) times.

The occurrence of complications had a significant negative effect on social functioning and the emotional role. Patients with any in-hospital complication or complications leading to hospitalization or a prolonged hospital stay had a SFS of 36.1 and RES of 33.5 at final follow-up, which were significantly lower than in uncomplicated courses with a SFS of 44.1 (p = 0.005, Mann-Whitney U test) and RES of 39.9 (p = 0.044, Mann-Whitney U test). The overall MCS, the MHS, and the VS were lower in patients who suffered complications; however, the difference was not significant (Table III). Interestingly, rehospitalization was not associated with a worse mental outcome (Table IV), and the duration of the initial hospital stay had no impact on mental health at 12 months' follow-up (Table V).

Discussion

The AO Trauma Bone Infection Registry patient cohort of major BJIs was not only associated with a compromised physical outcome and limited cure rate of 62%,[13] but also demonstrated substantial impairment of mental health. Although patients' mental states generally improved by the end of the study based on the SF-36 MCS and all mental subscales, their mental health status remained compromised in comparison with the average member of the USA population.

At baseline, the social functioning and the emotional roles were severely compromised, with a mean SFS of 35.4 and a mean RES of 33.4, compared to average values of the norm population at 50. At final follow-up, both scales remained compromised (RES 38.8; SFS 42.9). The RES captures the extent to which psychological problems interfere with work or other daily activities.[19] A lower RES suggests that patients are able to spend less time on activities or are able to work less. The SFS describes the experienced extent to which physical health or psychological problems interfere with normal social activities.[20] Thus, patients with a major BJI experience considerable limitations in their daily and social activities due to psychological issues. Their vitality and mental health were compromised at baseline, with a VS of 44.0 and a MHS of 41.0. However, the limitations were not as pronounced as role function and social function. At final follow-up, the values increased to a VS of 48.1 and a MHS of 46.1. The VS captures the energy level – feeling tired and worn out versus feeling drive and energy. Overall mental health expressed by the MHS extends from constant feelings of nervousness and depression to permanent sensations of happiness, peacefulness, and calm.

A possible explanation for this long-lasting impact on the patients' mental health may be the chronicity of BJIs and the high rate of unexpected complications.

In total, 19% of the study population suffered from a severe complication that required prolonged hospitalization or readmission. The surgical and antibiotic treatment used to treat BJIs is often associated with complications requiring rehospitalization or revision surgery.[21] Even though the standard duration for systemic antibiotic therapy is six to 12 weeks, severe complications affecting the renal, hepatic, or haematopoietic system may have a long-term effect and affect mental wellbeing after one year. In addition, complex revision surgeries to treat BJIs are also associated with frequent adverse events.[1,21,22]

The most common major complications after PJI revision arthroplasty are dislocation, loosening, and reinfection. Septic revision arthroplasty is associated with a high rate of reinfection (up to 5%).[23,24] In our study population, the occurrence of any in-hospital complication, rehospitalization, or prolongation of inpatient stay had a negative effect on patients' mental health, which persisted at final follow-up. Social interaction (SFS) and daily activities (RES) were significantly affected by complications (Table III). The study design captured the long-term effect of complications on mental health and not the immediate impact, since patient-reported outcome measures (PROMs) were collected only at defined timepoints and not with each hospitalization. The duration of the initial hospitalization had no long-term impact on mental health at 12-month follow-up (Table V). It is plausible that a prolongation of the primary hospitalization in a chronic disease with complications and rehospitalization has no significant impact on the long-term outcome. However, without PROM collection immediately after the hospital stay, we do not know if the length of hospitalization had an immediate effect on patients' mental health.

Interestingly, any rehospitalization due to infection was not associated with a worse mental outcome at final follow-up. The treatment of BJIs commonly includes staged procedures which require a planned rehospitalization, for example in a two-stage arthroplasty exchange procedure for PJI performed as a scheduled rehospitalization. Unfortunately, we were not able to discriminate between planned and unplanned rehospitalizations. A planned rehospitalization may not affect patients' mental health significantly, whereas unexpected complications may negatively impact mental health. Consequently, unexpected rehospitalizations due to the reported complications may have an effect on the patients' psychological wellbeing.

This study has limitations. The general limitations of the AO Trauma Bone Infection Registry have been discussed

in previous publications.[12,13] The most important limitations of the registry are: 1) the baseline status of the patient population was heterogeneous with regard to the chronicity and progression of the infection; 2) the study patient population was heterogeneous and not evenly distributed among the geographical locations, with under-represented regions (e.g. South America) or regions that were not represented at all (e.g. Africa); 3) BJIs associated with pathogens other than *S. aureus* were not included in this registry; 4) the reporting of revision surgeries may not have been consistent; 5) this registry suffered from a high dropout rate; 6) information on the cause of rehospitalization was not documented; 7) HRQoL may also be affected by the initial trauma or index surgery; and 8) SF-36 scores of the international cohort were compared with the USA norm population.[12,13] Additionally, a true comparison of the cure rate with literature data is not possible because there is no universally accepted definition of 'cure'.[13]

One important issue limiting the generalizability of the results is that estimates on minimal clinically important improvement or difference (MCII/MCID) in SF-36 mental scales are not well established in orthopaedic patients. To the best of our knowledge, these estimates are not available for patients with BJIs and it is difficult to generalize estimates of MCIIs across diseases and treatments, since different diseases may impact different aspects of mental health.[25] Therefore, comparing our results of BJIs with other orthopaedic disease entities is difficult. Ogura et al[26] found in patients with musculoskeletal tumours a MCID of five points for both the PCS and the MCS subscales. Translating this to our cohort, only social and emotional functioning showed a clinically important improvement from baseline to one-year follow-up.

In this registry, the SF-36 questionnaire was used to capture a general overview of the patients' mental and physical status. More specific questionnaires for mental health may have offered a more in-depth analysis on the patients' psychological wellbeing such as anxiety, depression, and coping with diseases.[27]

This study demonstrated that BJIs are associated with a considerable impact on HRQoL and in particular on mental health. At one year, patients still reported reduced mental health. Patients experienced considerable limitations in their daily and social activities due to psychological problems during the one-year follow-up period. Treatment complications were associated with a significant impact on patients' mental health, persisting to the final follow-up visit.

Because patients with BJIs experience significant mental health impairment, they would likely benefit from proactive efforts to identify and treat their mental health.

Supplementary material

Tables detailing 36-Item Short-Form Health Survey questionnaire (SF-36) mental subscales and Mental Component Summary (MCS), comparison of SF-36 mental subscales and Mental Component Scales according to origin of infection, comparison of SF-36 mental subscales and MCS according to methicillin-resistant *Staphylococcus aureus* versus methicillin-sensitive *Staphylococcus aureus* infection, Katz activities of daily living sums score and its correlation with SF-36 mental subscales and MCS, and correlation of Parker Mobility Score with SF-36 mental subscales and MCS.

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