

What Are the Long-term Outcomes of Mortality, Quality of Life, and Hip Function after Prosthetic Joint Infection of the Hip? A 10-year Follow-up from Sweden

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Abstract

Background Prosthetic joint infection (PJI) is a complication after arthroplasty that negatively affects patient health. However, prior reports have not addressed the long-term consequences of hip PJI in terms of patient mortality, quality of life, and hip function.

Questions/purposes At a minimum of 10 years after PJI in patients undergoing primary THA, in the context of several large, national databases in Sweden, we asked: (1) Is mortality increased for patients with PJI after THA

compared with patients with a noninfected THA? (2) Does PJI of the hip have a negative influence on quality of life as measured by the Euro-QoL-5D-5L (EQ-5D-5L), ambulatory aids, residential status, and hip function as measured by the Oxford Hip Score (OHS)? (3) Which factors are associated with poor patient-reported outcome measures (PROMs) for patients with PJI after primary THA?

Methods This study included 442 patients with a PJI after primary THA, from a previously published

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Ethical approval for this study was obtained from the Regional Ethical Review Board of Gothenburg, Sweden (reference number 2017/329-17).

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national study, including all patients with a THA performed from 2005 to 2008 in Sweden ($n = 45,570$) recruited from the Swedish Hip Arthroplasty Registry (SHAR). Possible deep PJIs were identified in the Swedish Dispensed Drug Registry and verified by review of medical records. Mortality in patients with PJI was compared with the remaining cohort of 45,128 patients undergoing primary THA who did not have PJI. Mortality data were retrieved from the SHAR, which in turn is updated daily from the population registry. A subgroup analysis of patients who underwent primary THA in 2008 was performed to adjust for the effect of comorbidities on mortality, as American Society of Anesthesiologists (ASA) scores became available in the SHAR at that time. For the PROM analysis, we identified three controls matched by age, gender, indication for surgery, and year of operation to each living PJI patient. A questionnaire including EQ-5D-5L, ambulatory aids, residential status, and OHS was collected from patients with PJI and controls at a mean of 11 years from the primary procedure. Apart from age and gender, we analyzed reoperation data (such as number of reoperations and surgical approach) and final prosthesis in situ to explore possible factors associated with poor PROM results.

Results After controlling for differences in sex, age, and indication for surgery, we found the all-cause 10-year mortality higher for patients with PJI (45%) compared with patients undergoing THA without PJI (29%) (odds ratio 1.4 [95% CI 1.2 to 1.6]; $p < 0.001$). The questionnaire, with a minimum of 10 years of follow-up, revealed a lower EQ-5D-5L index score (0.83 versus 0.94, -0.13 [95% CI -0.18 to -0.08; $p < 0.001$]), greater proportion of assisted living (21% versus 12%, OR 2.0 [95% CI 1.2 to 3.3]; $p = 0.01$), greater need of ambulatory aids (65% versus 42%, OR 3.1 [95% CI 2.1 to 4.8]; $p < 0.001$), and a lower OHS score (36 versus 44, -5.9 [-7.7 to -4.0]; $p < 0.001$) for patients with PJI than for matched controls. Factors associated with lower OHS score for patients with PJI were three or more reoperations (-8.0 [95% CI -13.0 to -3.2]; $p = 0.01$) and a direct lateral approach used at revision surgery compared with a posterior approach (-4.3 [95% CI -7.7 to -0.9]; $p = 0.01$).

Conclusion In this study, we found that PJI after THA has a negative impact on mortality, long-term health-related quality of life, and hip function. Furthermore, the subgroup analysis showed that modifiable factors such as the number of reoperations and surgical approach are associated with poorer hip function. This emphasizes the importance of prompt, proper initial treatment to reduce repeated surgery to minimize the negative long-term effects of hip PJI.

Level of Evidence Level III, therapeutic study.

Introduction

Millions of people worldwide undergo THA every year [25]. Successful surgery provides pain relief and improves function and quality of life (QoL); research has also shown a lower mortality for patients who undergo THA compared with the general population [9]. Despite excellent long-term results that have improved over recent decades [21], severe complications can be associated with THA, including aseptic loosening of components, periprosthetic fractures, dislocations, and prosthetic joint infection (PJI) [47]. Perhaps the most devastating of these complications is PJI. Various interventions are undertaken to reduce PJI risk, including preoperative screening of patients for pertinent comorbidities [4], prophylactic administration and timing of antibiotics preoperatively [1, 12, 46], and use of laminar air flow during surgery [20]. Nevertheless, the incidence of PJI after primary THA ranges from 0.9% to 2.0% [24, 27], and all-cause mortality after PJI has been reported to be 5% after 1 year and 20% after 5 years [35]. Major healthcare costs are associated with PJI [3, 42], as are the short-term burdens of prolonged sick leave, repeated surgery [48], and pain.

However, the long-term functional outcomes of the hip and the overall health status of patients affected by PJI are unknown. Knowledge of how long-term mortality is affected by PJI and what functional limitations might be expected many years after PJI treatment would benefit patients who experience this complication and the surgeons who counsel them.

We asked the following questions in the context of several large, national databases in Sweden regarding patients with a minimum of 10 years of follow-up after PJI of the hip: (1) Is mortality increased for patients who suffer from postoperative PJI after primary THA compared with patients without PJI? (2) Does PJI of the hip have a negative influence on quality of life as measured by Euro-QoL-5D-5L (EQ-5D-5L), ambulatory aids, residential status, and hip function as measured by the Oxford Hip Score (OHS)? (3) Which factors are associated with poor patient-reported outcome measures (PROMs) for patients with PJI after primary THA?

Patients and Methods

Study Overview

We conducted a nationwide study in Sweden to determine long-term mortality, QoL, and hip function in patients who suffered from PJI within 2 years after primary THA. From a previously published nationwide study [27] that included all patients who had a THA performed between July 1, 2005 and December 31, 2008 ($n = 45,570$ patients and

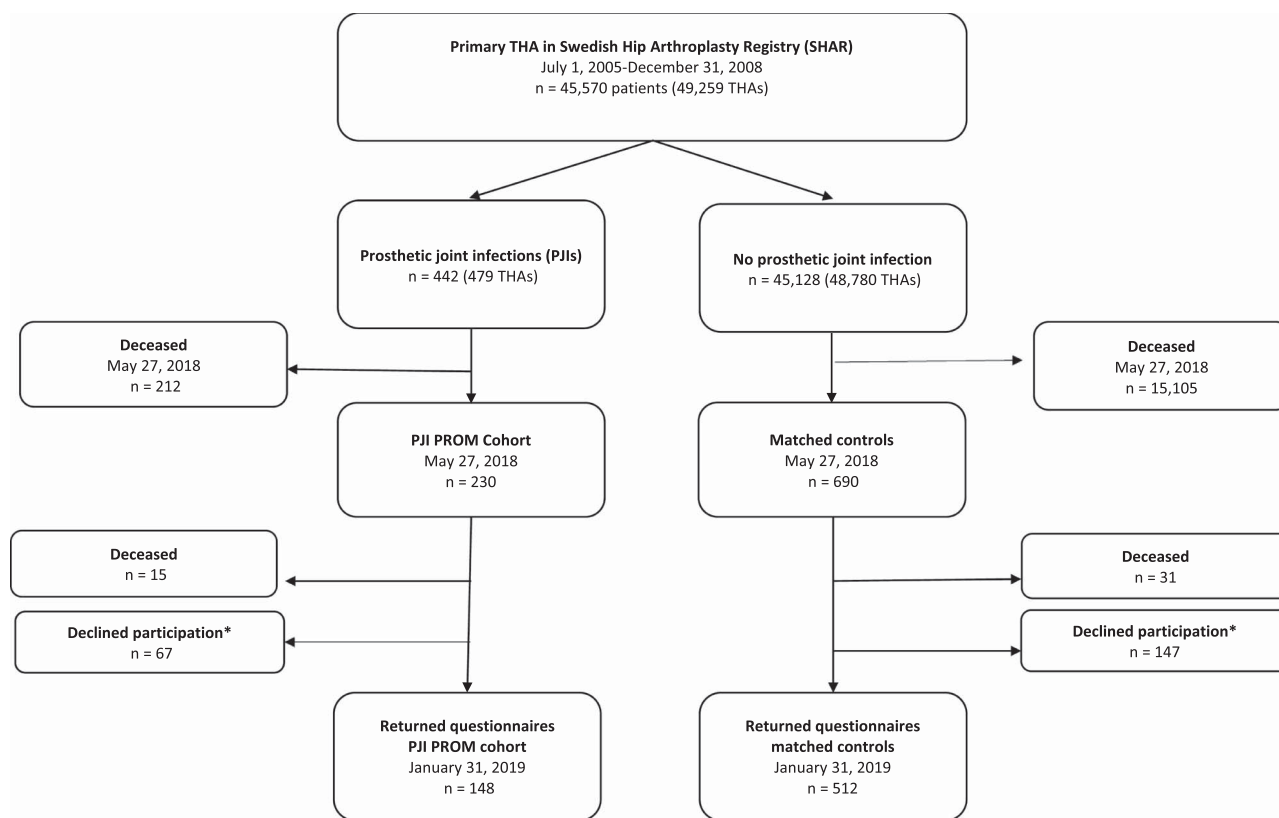


Fig. 1 This study flowchart shows patients with prosthetic joint infection and patients with hip arthroplasty and no history of infection in the Swedish Hip Arthroplasty Register who underwent primary THA between July 1, 2005 and December 31, 2008 and were included in this study. *Among patients with PJI, 59 did not return the questionnaire, four had dementia, and four declined to participate in the study. Among matched controls, 124 patients did not return the questionnaire, 15 had dementia, and eight declined to participate in the study.

49,259 THAs) in the Swedish Hip Arthroplasty Registry (SHAR), we identified 2217 possible deep PJIs in the Swedish Dispensed Drug Registry. After a review of these medical records, we determined that 442 patients had a verified PJI according to the Musculoskeletal Infection Society criteria [37]. Some limitations inherent to the SHAR prompted a unique methodologic approach for this study. Because PROMs were not routinely collected during this period and the American Society of Anesthesiologists (ASA) class as a measure of comorbidities was not collected until 2008, different methodologic approaches and databases were required to answer our three questions.

Primary Endpoint of Mortality

To answer our first research question on mortality, we used the SHAR database, which is updated daily from the population registry [29]. The databases are matched by each patient’s Personal Identification Number (PIN) [30]. Mortality data were compared between the 442 patients with

PJI and the remaining cohort of 45,128 patients without infection who were registered in the SHAR for primary THA during the same period. All-cause mortality was determined at the time of patient selection on May 27, 2018 (Fig. 1). We used a Cox proportional hazards regression model adjusted for age, sex, and indication for primary THA to calculate the hazard ratio for the PJI group compared with the noninfected THA group. Because the ASA class as a measure of comorbidities was not collected in the SHAR until 2008, we performed a subgroup analysis to better understand the effect of comorbidities using this measure for 2008 alone, stratifying comorbidities as ASA class 1 to 2 and 3 to 4.

Secondary Endpoint of Patient-reported Outcome Scores

To investigate our second research question on the effect of PJI on PROMs, a control group of patients who did not undergo reoperation and who did not have PJI were selected from the SHAR using propensity score matching [6]. The model included age, gender, indication for surgery, and year

Table 1. Characteristics of patients with PJI within 2 years of primary THA and matched controls who responded to the patient-reported outcome questionnaire

	PJI (n = 148)	Control (n = 512)	p value
Mean age at primary surgery, years \pm SD	65.3 \pm 10.1	65.3 \pm 10.1	> 0.99
Mean age at follow-up, years \pm SD	76.4 \pm 10.0	76.4 \pm 10.0	
Female sex	53 (78)	48 (247)	0.35
Indication for operation			
Primary OA	86 (128)	87 (444)	0.94
Acute trauma, hip fracture	2 (3)	4 (19)	0.44
Complication trauma	1 (1)	1 (3)	> 0.99
Secondary OA	0 (0)	0 (0)	
Sequelae of childhood hip disease ^a	4 (6)	3 (14)	0.41
Femoral head necrosis	5 (7)	4 (22)	0.82
Inflammatory joint disease	1 (2)	2 (10)	> 0.99
Other	1 (1)	0 (0)	0.22
Surgical approach ^a			
Direct lateral	56 (83)	40 (207)	0.001
Posterior	41 (61)	59 (300)	< 0.001
Minimally invasive hip replacement surgery	3 (4)	1 (4)	
Implant fixation ^a			
Cemented	66 (98)	71 (364)	0.25
Uncemented	21 (31)	16 (81)	0.14
Hybrid	2 (3)	1 (4)	0.19
Reversed hybrid	9 (13)	9 (48)	0.83
Resurfacing	1 (2)	3 (13)	0.39
Mean follow-up time, years \pm SD	11 \pm 12	11 \pm 12	0.89
Mean year of operation \pm SD	2007 \pm 0.99	2007 \pm 0.88	0.10

Data presented as % (n) unless otherwise indicated; OA, osteoarthritis; PJI, prosthetic joint infection.

^aNumbers may not add up to total patients due to missing data.

of operation (see Supplementary Table 1; Supplemental Digital Content 1, <http://links.lww.com/CORR/A576>). Propensity scores were estimated using logistic regression with greedy nearest-neighbor matching and no caliper. The patients in the control group were selected without replacement. A ratio of 1:3 was chosen to improve the precision, while maintaining similar standardized mean differences among the covariates as with a 1:1 match (see Supplementary Table 1; Supplemental Digital Content 1, <http://links.lww.com/CORR/A576>). A questionnaire comprising PROMs, including the Swedish versions of the EQ-5D-5L [19], residential status, need of ambulatory aids, and OHS [10], was administered to living patients who had a PJI (n = 215) and the respective patients in the control group (n = 659) (Fig. 1) to assess health-related QoL and hip function. Questionnaires were mailed in June 2018 with up to two reminders if there was no response. If the questionnaire was not returned before the end of the study period (January 31, 2019), the patient was considered a

nonresponder. The response proportions for the questionnaire were 69% (148 of 215) for patients with PJI and 78% (512 of 659) for matched controls (Fig. 1). The characteristics of respondents and nonrespondents to the PROM questionnaire were assessed. There were no differences in patient characteristics for respondents (Table 1, except for surgical approach). Ninety-four percent (139 of 148) of patients with PJI underwent a reoperation as part of the PJI treatment, and 95% (132 of 139) had the same surgical approach used in the primary surgery (Table 2). The surgical treatment for 68% (101 of 148) of the patients consisted of debridement, antibiotics, and implant retention (DAIR) and for 25% (37 of 148) a one- or two-stage revision was performed; 6% (9 of 148) had nonsurgical treatment with antibiotics only. One percent (2 of 139) of patients treated with surgery and 22% (2 of 9) of nonoperatively treated patients with PJI still had suppressive antibiotic treatment at follow-up. A hybrid time tradeoff value set was used to calculate the EQ-5D-5L index value

[28]. The range of EQ-5D-5L index was -0.661 to 1, anchored at 0 for death and 1 being full health. EQ-VAS has a range from 0 to 100, anchored at 100 for best imaginable health [13]. The nonPJI group reported fewer problems in each of the EQ-5D-5L dimensions compared with the PJI group (see Supplementary Table 2; Supplemental Digital Content 2, <http://links.lww.com/CORR/A577>); to statistically examine this, we dichotomized as either no or minor problems (score of 1 or 2) or major problems (score of 3-5). Assisted living was defined as one of the following: home care, serviced apartment, nursing home, or equivalent. Ambulatory aid was defined as the use of a cane or crutches, walker, or wheelchair. The range of OHS was 0 to 48, with 48 being the best outcome [33]. Density plots were used to describe the distribution of the OHS.

Nonrespondents had no differences in patient characteristics (see Supplementary Table 3; Supplemental Digital Content 3, <http://links.lww.com/CORR/A578>).

Secondary Endpoint Regarding Factors Associated with Poor PROMs

To answer our third research question on factors associated with poor patient-reported outcomes, data including age, gender, implant fixation, and diagnosis of patients with PJI who responded to the questionnaire were extracted from the SHAR (Table 1). Data regarding revision surgery, such as surgical intervention for PJI, total number of reoperations, surgical approach at reoperation, and prosthesis in situ at follow-up were extracted from medical records for the first 2 years, and then from the SHAR during the following years (Table 2).

To assess the influence of factors possibly associated with inferior functional outcome for patients with PJI, we performed a univariate analysis. Factors with $p < 0.10$ were entered into a multiple linear regression model including gender, age, total number of reoperations, surgical approach at reoperation, and prosthesis status at follow-up.

Ethical Approval

This study was approved by the Regional Ethical Review Board of Gothenburg, Sweden (reference number 2017/329-17).

Statistical Analysis

We used a Kaplan-Meier survival curve to visualize the unadjusted mortality in patients with PJI after THA and those without infection (Fig. 2). A log-rank test was used to

Table 2. Surgical details for the patients with prosthetic joint infection (PJI), 10 to 14 years' follow-up

Surgical details	Patients with PJI
Surgical intervention for PJI (n = 148)	
No reoperation	6 (9)
DAIR	68 (101)
One-stage revision ^a	3 (4)
Two-stage revision ^a	22 (33)
Resection arthroplasty ^a	1 (1)
Surgical approaches at reoperation (n = 148)	
Direct lateral	47 (69)
Posterior	41 (60)
Other ^b	7 (10)
No reoperation	6 (9)
Prosthesis in situ at follow-up (n = 148)	
Original prosthesis ^c	67 (99)
Exchanged prosthesis ^d	32 (48)
Resection arthroplasty	1 (1)
Total number of reoperations (n = 148)	
≤ 1	53 (78)
2	21 (31)
≥ 3	26 (39)
Total number of reoperations, indication ^e (n = 293)	
Prosthetic joint infection	90 (265)
Aseptic loosening	2 (7)
Fracture	1 (4)
Dislocation	3 (9)
Other ^f	3 (8)

Data presented as (n).

^aIncluding DAIR.

^bMinimally invasive surgery—anterior, mixed approaches, trochanteric osteotomy.

^cChange of mobile components (head or liner) were not considered as exchanged prosthesis.

^dRevision of acetabular, femoral, or both components.

^eIndications for reoperations during follow-up for the PJI cohort.

^fTechnical reasons, pain, implant failure, or multiple reasons; DAIR = debridement, antibiotic and implant retention.

compare survival distributions of the two groups. We used a Cox proportional hazards regression model adjusted for age, sex, and indication for primary surgery to calculate the hazard ratio for the PJI group compared with the THA group without infection. The proportional hazards assumption was tested using Cox time-dependent variables.

Regarding PROM analysis continuous variables have been expressed as medians or means. Dependent variables were analyzed using frequency histograms and were assessed for normal distribution. EQ-5D-5L and OHS data were

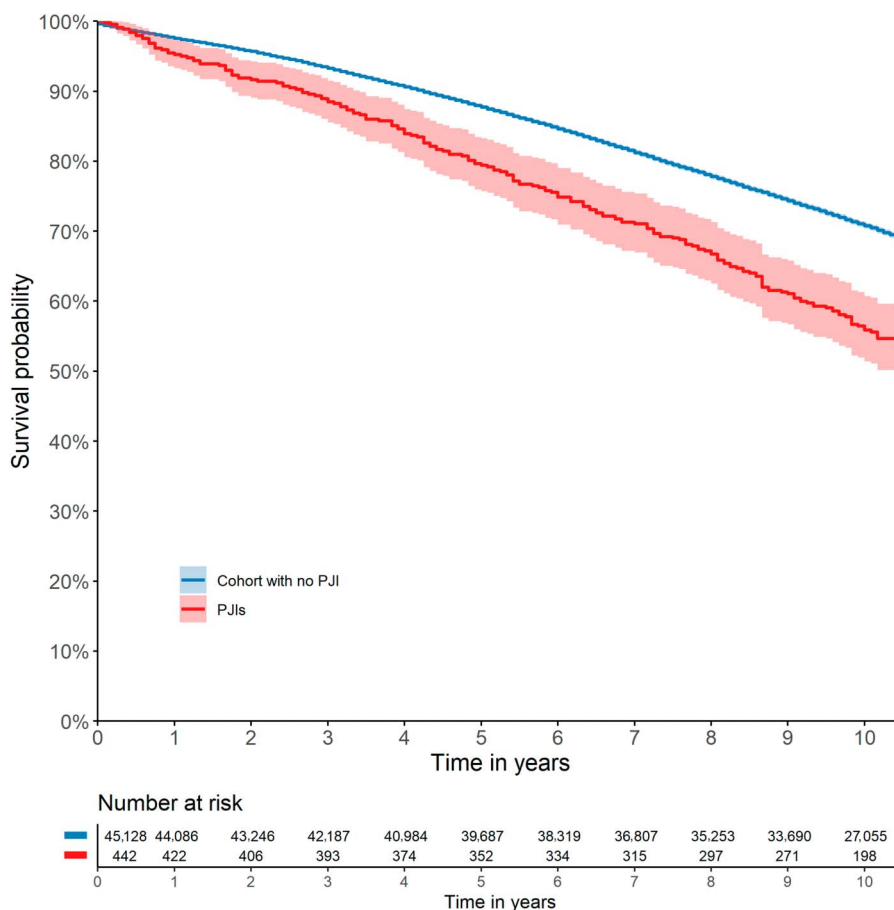


Fig. 2 This Kaplan-Meier survival curve has 95% CIs. All-cause mortality is shown for patients with prosthetic joint infection (PJI) who underwent THA and patients who underwent THA and had no history of infection. Data were extracted from the Swedish Hip Arthroplasty Register. All patients underwent THA in Sweden between July 1, 2005 and December 31, 2008.

skewed toward higher values. The chi-square test or the Fisher exact test was used to compare categorical data between patients with PJI and controls. The Mann-Whitney U test or t-test was used to evaluate between-group differences in continuous variables depending on distribution, such as, EQ-5D-5L index score, EQ-VAS score, and OHS. Categorical data were entered into a multiple logistic regression model to adjust for gender and age as potential confounders. Continuous data were also entered into a multiple linear regression model; a normal P-P plot for EQ-VAS, EQ-5D-5L, and OHS residuals were evaluated in the model.

Tests were two-tailed, and statistical significance was defined as a p value < 0.05 or 95% CI for estimate from the linear regression analysis, and for odds ratios or HRs not equal to 1.00. For continuous variables, statistical significance was defined as a p value < 0.05 or 95% CI excluding 1.00. Statistical analyses were performed using SPSS version 25 (IBM Corp).

Results

Mortality

After controlling for differences in age, indication for surgery, and sex, we found that all-cause mortality was higher in the PJI group than in those without infection. The 10-year all-cause mortality rate was 45% (197 of 442) for patients with PJI and 29% (13,098 of 45,128) for the non-PJI THA group (OR 1.4 [95% CI 1.2 to 1.6]; $p < 0.001$) (Fig. 2).

In the subgroup analysis of 12,946 patients who underwent surgery in 2008, when the ASA score became available, a Cox regression model adjusted for age, sex, and indication for THA was performed and revealed no difference in mortality risk for patients with PJI compared with the non-PJI group for those with ASA class 3 or 4 (HR 1.1 [95% CI 0.8 to 1.4]; $p = 0.23$). However, patients who

Table 3. Patient-reported outcome measures in patients with prosthetic joint infection and controls

	PJI (n = 148)	Control (n = 512)	OR or multiple regression estimates	
			(95% CI)	p value
EQ-VAS, median (IQR)	65 (30)	80 (30)	-9.9 (-13.7 to 6.1) ^b	< 0.001
EQ-5D-index, median (IQR)	0.83 (0.37)	0.94 (0.21)	-0.13 (-0.18 to 0.08) ^b	< 0.001
EQ-5D-5L ^c , % (n/N major problems)				
Mobility	50 (74 of 147)	24 (118 of 498)	3.4 (2.3 to 5.0) ^a	< 0.001
Self-care	22 (32 of 147)	12 (59 of 498)	2.1 (1.3 to 3.4) ^a	0.003
Usual activities	43 (63 of 147)	24 (119 of 498)	2.4 (1.6 to 3.6) ^a	< 0.001
Pain/discomfort	37 (55 of 147)	24 (119 of 498)	1.9 (1.3 to 2.8) ^a	0.001
Anxiety/depression	16 (23 of 147)	10 (50 of 498)	1.7 (1.0 to 2.8) ^a	0.06
Ambulatory aid ^d	65 (96 of 147)	41 (211 of 509)	3.1 (2.1 to 4.8) ^a	< 0.001
Assisted living ^e	21 (31 of 148)	12 (62 of 510)	2.0 (1.2 to 3.3) ^a	0.01
OHS, median (IQR)	36 (19)	44 (13)	-5.9 (-7.7 to 4.0) ^b	< 0.001

Data presented as % (n) unless otherwise indicated.

^aEQ-5D dimensions, ambulatory aid, and assisted living were entered into a multiple logistic regression model with adjustments for sex and age.

^bEQ VAS, EQ-5D index, and OHS were entered into a multiple linear regression model with adjustments for sex and age.

^cComplete response chart for EQ-5D-5L dimensions is available (see Supplementary Table 3; Supplemental Digital Content 3, <http://links.lww.com/CORR/A578>).

^dUse of a cane or crutches, walker, or wheelchair.

^eHome care, serviced apartment, nursing home, or equivalent; EQ = European Quality of Life; OHS = Oxford Hip Score; PJI = prosthetic joint infection.

had PJI and ASA class 1 or 2 displayed an increased mortality risk (HR 1.4 [95% CI 1.0 to 2.0]; $p < 0.05$) compared with controls.

Patient-reported Outcome Scores

After controlling for sex and age, we found that QoL was worse for the PJI group than for the non-PJI group (Table 3). The estimates from the multiple linear regression model showed that PJI was associated with a lower EQ-VAS score (-9.9 [95% CI -13.7 to -6.1]; $p < 0.001$) and EQ-5D-5L index score (-0.13 [95% CI -0.18 to -0.08]; $p < 0.001$). The multiple linear regression model also revealed a higher risk of major problems in all EQ-5D-5L dimensions except for the anxiety and depression dimension for patients with PJI (OR 1.7 [95% CI 1.0 to 2.8]; $p = 0.06$), with PJI having the greatest impact on mobility (OR 3.4 [95% CI 2.3 to 5.0]; $p < 0.001$) (Table 3).

We found that more patients with PJI were in assisted living and used more ambulatory aids; the multiple logistic regression model showed that PJI was associated with more patients needing help in their own homes or living in an institution (21% versus 12%, OR 2.0 [95% CI 1.2 to 3.3]; $p = 0.01$) and requiring ambulatory aids (65% versus 42%, OR 3.1 [95% CI 2.1 to 4.8]; $p < 0.001$).

Patients with PJI experienced worse hip function than patients in the control group (Table 3). The median OHS

was 36 (IQR 19) for the PJI group and 44 (IQR 13) for controls. Patients with PJI had lower median scores than the control group for all 12 items on the OHS questionnaire (data not shown). Estimates from the multiple linear regression model showed that PJI was associated with lower OHS (-5.9 [95% CI -7.7 to -4.0]; $p < 0.001$). The distribution of the summarized OHS showed a markedly worse pattern for patients with PJI than for controls (Fig. 3).

Factors Associated with Poor PROMs Among Patients with PJI

After controlling for potentially confounding variables such as age, gender, surgical intervention for PJI, total number of reoperations, and surgical approach at revision, being female was the only factor we found that was associated with lower EQ-5D-5L index scores (OR -0.14 [95% CI -0.23 to -0.05]; $p = 0.01$). Older age (OR -0.5 [95% CI -0.83 to 0.1]; $p = 0.03$), gender (women: OR 21.3 [95% CI -14.0 to -6.7]; $p < 0.001$), and three or more reoperations (OR -10.8 [95% CI -21.5 to -6.7]) were associated with lower EQ-VAS scores.

Estimates from the multiple linear regression showed that reoperation using the direct lateral approach (OR -4.3 [95% CI -7.7 to -0.9]; $p = 0.01$), being female (OR -4.1 [95% CI -7.7 to 4.0]; $p = 0.01$), and three or more

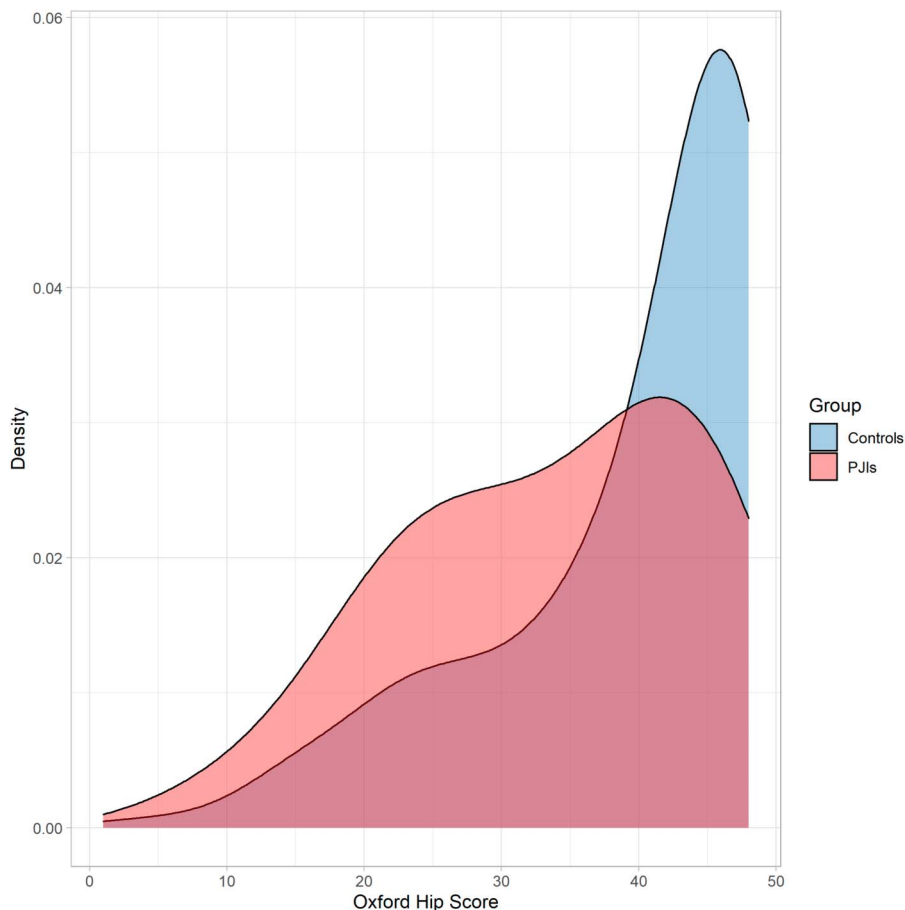


Fig. 3. The distribution of the OHS for patients with PJI and propensity score-matched controls is shown in this density plot. The range of the OHS is 0 to 48. Density is shown as the percentage of patients in the PJI and control groups.

reoperations (OR -8.0 [95% CI -13.0 to -3.2]; $p = 0.01$) were associated with a lower OHS score.

Discussion

PJI is a severe complication of THA that is associated with prolonged hospitalization, repeat surgery, and high healthcare costs [48]. Despite extensive research in the field of PJI, there is limited knowledge about its long-term consequences in terms of mortality, QoL, or hip function. We investigated the association between PJI and mortality in a nationwide cohort of patients who underwent primary THA between 2005 and 2008 and compared the PROMs of patients with PJI and matched controls during a follow-up period of 10 to 14 years. We also examined the influence of surgical factors on PROMs. We found that patients with PJI who underwent THA had higher mortality, reduced QoL, and worse hip function in the long term.

Limitations

As in many other epidemiologic long-term follow-up studies, there are limitations to the present work. We were unable to adjust for all possible risk factors associated with increased mortality and poor functional outcome. Additionally, there were no data on BMI for our cohort, and because obesity is a known risk factor for both infection and early death and is associated with worse patient-reported outcomes after hip arthroplasty [15], this may have introduced selection bias. In this study, we were limited to the data in the SHAR database—introduced in 2008—in which ASA class is the only comorbidity score; this may limit more granular analysis of PJI and mortality. However, the association between comorbidities and long-term mortality after THA has been questioned [8]. There is a risk of immortal time bias regarding PJI patients, but the magnitude of this considering the 10-year follow-up is likely very small as 90% of the PJIs were diagnosed within 90 days. The potential impact of immortal time bias in the PJI group would be an underestimation of the

mortality rate. The results from this study are generalizable as it is a true national patient cohort with a complete follow-up of all patients with a PJI in Sweden during a 3.5-year period. A limitation regarding PROMs is that we did not have pre-operative PROMs for this group, so it is difficult to gauge a change in patient status. However, we had a good overall propensity score matching for the characteristics of the study population, thus reducing potential bias and confounding effects, and we had a high response rate given the long-term follow-up. The PJI cohort in this study consisted of a high percentage of patients with only DAIR procedures (likely explained by the large number of PJIs with early detection), which could reduce the generalizability to centers with different treatment protocols (such as, higher proportions of one- or two-stage revisions). We have not been able to analyze our PROM findings based on validated minimum clinically important difference (MCID) for PJIs of the hip, but we could interpret our findings in previous research on the EQ-5D-5L and OHS [5, 18]. Regarding factors that influence PROMs in patients with PJI, we explored the confounding effects of surgical factors, but we acknowledge that several other factors could have influenced the outcome, including time to diagnosis, time to infection control, and socioeconomic factors.

Mortality

In the present study, the long-term mortality was higher in patients with PJI undergoing THA than in those without infection: 48% versus 34% at 10 years. This is in agreement with the findings of a previous study that reported 1- and 5-year weighted mortality rates of 4% and 21%, respectively [35], which are comparable to the rates of 5% and 21% (Fig. 2), respectively, in our PJI cohort. Elective THA is associated with a lower mortality risk than in the general population [9]. This has been attributed to the selection of healthier patients for surgery. Many factors contribute to increased mortality, including age, male sex, malignancies, cardiovascular disease, diabetes, and other comorbidities [51]. Many of these risk factors also apply to PJI [48], which has been linked to higher rates of short-term mortality [17]. The ASA class was used to indicate comorbidities; however, it affected only the mortality risk for those with scores of 1 or 2. A previous study explains that chronic disease influences mortality to a greater extent in previously healthy individuals [32] than in those who already have significant preexisting comorbidities and ASA scores of 3 or 4. Decreased mobility and hip function may increase the risk of chronic diseases because of decreased physical activity in the long term [7]. This may lead us to consider PJI as a chronic disease even when the infection is cured. Moreover, the 10-year mortality rate for PJI is higher than the pooled 10-year mortality rate for all cancers in the United States (44% versus 39%) [34], emphasizing the dire nature of PJI after THA.

Patient-reported Outcome Scores

Although patients with PJI had lower scores in all dimensions of the EQ-5D-5L, the greatest difference relative to the control group was in mobility, with 50% of patients reporting major problems (versus 24% for controls) (Table 3). Anxiety and depression showed the least difference between groups, with a relatively low incidence of 16% in patients with PJI and 10% in controls. This might be explained by the fact that the psychological impact of PJI is transient and may be overcome through long-term adaptation [31]. The positive effects of primary THA on PROMs have been shown to persist over time [6]. However, two studies showed that PROMs after revision arthroplasty deteriorated more rapidly after medium-term follow-up [40, 44], which could be attributed to repeat surgery in combination with advancing age and perhaps obesity [15]. In the present study, we investigated only long-term outcomes; therefore, it is unclear whether the effects of PJI on PROMs occur early or increase over time. One factor that may contribute to lower QoL is the loss of independence in the living situation and the need for ambulatory aids, both of which were more common in patients with PJI than in patients in the control group. The absence of physical exercise can lead to a loss of independence in daily living, which is associated with increased costs [14] and lower QoL [43]. A previous study in Denmark investigating PROMs in patients with chronic PJI of the hip reported a mean EQ-5D index score of 0.71 for patients with PJI and 0.86 for the general population [41], which is comparable to our results. The difference in group level between patients with PJI and patients in the control group may be clinically relevant as it is greater than the suggested MCID for the EQ-5D-5L index score [18]. Our study also showed that patients who experienced PJI had worse hip function than those without infection. This explains the greater need for support in daily living in the former group and their more frequent use of ambulatory aids. A mobile lifestyle and maintenance of physical activity is generally conducive to good QoL, especially in the elderly population [2].

Patients with PJI experienced worse hip function than controls based on OHS scores, which may be clinically relevant considering the MCID (Fig. 3). A meta-analysis showed that postoperative PROM scores were slightly worse after revision surgery than after primary THA in both the short and long term [45]. These findings suggest that repeat surgery negatively affects outcomes. In our study, 94% of patients with PJI (Table 2) and none of the patients in the control group underwent a reoperation. Repeat revision surgery for PJI is common and includes DAIR [48]; one- or two-stage exchange procedures; and in some cases, permanent resection arthroplasty [48]. Our data indicate that the number of surgical procedures of the hip contributes to worse hip function; however, there were no differences in PROMs depending on whether the prosthesis itself was original or revised. A possible explanation is that the negative effect of repeated soft tissue injury may be more

important than the retention of prosthetic components, although the number of patients in these groups were too limited to analyze more fully. It is important to perform meticulous debridement to minimize the risk of further surgery [22]; however, a more radical one- or two-stage exchange procedure is advocated if there are associated factors such as chronic infection or if a DAIR procedure fails to eradicate the infection [16, 49, 50, 52]. The direct lateral approach for THA due to osteoarthritis or hip fracture is associated with an inferior postoperative score compared with a posterior approach [23]. A recent study has also shown that the direct lateral approach is associated with inferior postoperative PROMs if used in a single DAIR procedure compared with the posterior approach [39]. However, the negative effect is transient or small, and long-term follow-up data are lacking [26, 36, 39]. In our study, the difference in OHS from the multiple regression model was 4.3 between patients reoperated via the direct lateral approach compared with the posterior approach, which could reflect a clinically relevant difference as the MCID for the OHS has been reported to be between 2 and 5 [5, 33, 36]. Because approximately 90% of patients underwent a reoperation with the same approach used in the primary surgery (Table 2) and most had a diagnosis of PJI within 3 months of surgery [27], repeated damage to the gluteus medius [11] or gluteal superior nerve [38] may explain the long-term pain, discomfort, and impaired hip function in patients undergoing surgery using the direct lateral approach.

Conclusion

We found that hip PJI has considerable long-term negative effects on mortality, health-related QoL, and hip function. Multiple reoperations of the hip consequently contribute to persisting poor hip function even in the long term, but using a posterior approach for a reoperation rather than the direct lateral approach may help preserve function. These findings emphasize the importance of prompt and proper early surgical intervention and correct antibiotic treatment to reduce repeat surgery to minimize the negative effects of hip PJI.

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