Periprosthetic Joint Infection Increases the Risk of One-Year Mortality

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Background: Periprosthetic joint infection continues to potentially complicate an otherwise successful joint replacement. The treatment of this infection often requires multiple surgical procedures associated with increased complications and morbidity. This study examined the relationship between periprosthetic joint infection and mortality and aimed to determine the effect of periprosthetic joint infection on mortality and any predictors of mortality in patients with periprosthetic joint infection.

Methods: Four hundred and thirty-six patients with at least one surgical intervention secondary to confirmed periprosthetic joint infection were compared with 2342 patients undergoing revision arthroplasty for aseptic failure. The incidence of mortality at thirty days, ninety days, one year, two years, and five years after surgery was assessed. Multivariate analysis was used to assess periprosthetic joint infection as an independent predictor of mortality. In the periprosthetic joint infection population, variables investigated as potential risk factors for mortality were evaluated.

Results: Mortality was significantly greater (p < 0.001) in patients with periprosthetic joint infection compared with those undergoing aseptic revision arthroplasty at ninety days (3.7% versus 0.8%), one year (10.6% versus 2.0%), two years (13.6% versus 3.9%), and five years (25.9% versus 12.9%). After controlling for age, sex, ethnicity, number of procedures, involved joint, body mass index, and Charlson Comorbidity Index, revision arthroplasty for periprosthetic joint infection was associated with a fivefold increase in mortality compared with revision arthroplasty for aseptic failures. In the periprosthetic joint infection population, independent predictors of mortality included increasing age, higher Charlson Comorbidity Index, history of stroke, polymicrobial infections, and cardiac disease.

Conclusions: Although it is well known that periprosthetic joint infection is a devastating complication that severely limits joint function and is consistently difficult to eradicate, surgeons must also be cognizant of the systemic impact of periprosthetic joint infection and its major influence on fatal outcome in patients.

Level of Evidence: Prognostic Level II. See Instructions for Authors for a complete description of levels of evidence.

Total joint arthroplasty is currently one of the most frequently performed and most successful surgical procedures, greatly improving patient quality of life and functional status[1,2]. Many authors have demonstrated lower mortality rates for patients undergoing total joint arthroplasty compared with those for the general population[3-8]. Although complications following total joint arthroplasty are infrequent, their existence continues to be a cause for concern[9-12]. Periprosthetic joint infection is one particularly challenging complication of total joint arthroplasty. Substantial efforts have

A commentary by **Thomas J. Blumenfeld, MD,** is linked to the online version of this article at jbjs.org.

TABLE I Comparison of Demographics Between Patients Undergoing Treatment for Periprosthetic Joint Infection and Those Undergoing Aseptic Revision Arthroplasty

Demographics	Periprosthetic Joint Infection Group (N = 436)	Aseptic Revision Group (N = 2342)	P Value
Age* (yr)	67.0 (66.4 to 67.5)	66.2 (65.9 to 66.4)	0.22
Knee joint involved†	266 (61.0)	760 (32.5)	<0.001
No. of procedures*			
In ninety days	1.6 (1.6 to 1.6)	1.1 (1.0 to 1.1)	<0.001
In one year	2.2 (1.1 to 2.2)	1.1 (1.0 to 1.1)	<0.001
Male patients†	220 (50.5)	959 (40.9)	<0.001
Charlson Comorbidity Index†			<0.001
0	266 (61.0)	1848 (78.9)	
1	128 (29.4)	403 (17.2)	
2	27 (6.2)	75 (3.2)	
≥3	15 (3.4)	16 (0.7)	
Ethnicity†			<0.001
White	357 (81.9)	1677 (71.6)	
Black	47 (10.8)	268 (11.4)	
Other	6 (1.4)	34 (1.5)	
Missing	26 (6.0)	363 (15.5)	
BMI* (kg/m^2)	31.7 (31.3 to 32.1)	29.6 (29.4 to 29.8)	<0.001

*The values are given as the mean, with the 95% confidence interval in parentheses. †The values are given as the number of patients, with the percentage in parentheses.

been made to prevent this complication by implementing numerous strategies that include antibiotic prophylaxis, patient risk stratification, detection and treatment of *Staphylococcus aureus* colonization, and clean operating room environment, among others[11,13,14]. Despite the introduction of these methods, the risk of infection after total joint arthroplasty remains approximately 1%[11,15-17]. In recent studies, Bozic et al. observed that infection was the third most common indication for revision hip arthroplasty (14.7% of cases) and the most common cause for failure of total knee arthroplasty (25.2% of cases)[18,19].

The risk factors for developing periprosthetic joint infection following total joint arthroplasty include male sex, advanced age, higher body mass index (BMI), and presence of comorbidities (especially cardiac conditions)[11,15,20-25]. These factors are also associated with early mortality following total joint arthroplasty[24-28], suggesting that periprosthetic joint infection would be associated with an increased risk of mortality. The disease process of periprosthetic joint infection itself may also lead to an increase in mortality, as experienced in other fields, through the potential development of fatal bacteremia[29-31]. Additionally, the need for aggressive and often multiple surgical treatments, long-term inpatient stays, and long-term use of systemic antibiotics to treat periprosthetic joint infection would be expected to alter life expectancy[32-34].

With the projected increase in the numbers of total joint arthroplasties, specifically revision arthroplasties, the burden of periprosthetic joint infection is expected to rise[15,35]. Hence, a complete understanding of the effect that this disease may have on quality and longevity of life is important. Therefore, this study aimed to determine the impact of periprosthetic joint infection on life expectancy and to identify any factors that predict increased mortality rates after treatment for periprosthetic joint infection.

Materials and Methods

After obtaining institutional review board approval, a retrospective study was undertaken. Patients undergoing revision hip or knee arthroplasty from January 2000 through March 2010 were identified utilizing the institutional database. This provided 2955 patients who underwent revision joint arthroplasty. This sample included 613 (20.7%) who were suspected of having periprosthetic joint infection. Complete data related to the workup for periprosthetic joint infection, including erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration, synovial fluid analysis and culture, tissue culture, and joint presentation, were collected. Utilizing these data, a diagnosis of periprosthetic joint infection was confirmed or was excluded on the basis of the definition of periprosthetic joint infection provided by the Musculoskeletal Infection Society[36]. As histological analysis is not performed at this institution, the definition was modified to require a sinus tract, two separate positive cultures with phenotypically identical organisms, or three of the following: elevated ESR and CRP, elevated synovial white blood cell count, elevated synovial fluid polymorphonuclear neutrophil (PMN) percentage, intra-articular purulence, and a single positive culture. The threshold was 30 mm per hour for ESR, 10 mg per liter for CRP, 3000 cells per microliter for the synovial white blood cell count, and 75% for the synovial PMN percentage[37-39]. A diagnosis of periprosthetic joint infection was confirmed in 436 patients, leaving 2342 patients in the aseptic cohort.

TABLE II Survival Over Varying Time Periods Following Initial Treatment for Periprosthetic Joint Infection Versus Aseptic Failure for Patients with Available Follow-up for the Maximum Time of the Period

Time Period (Time from Initial Treatment)	Started Period Alive		Finished Period Alive		Periprosthetic Joint Infection Survival	Aseptic Survival	Periprosthetic Joint Infection Relative Survival*	P Value
	Septic	Aseptic	Septic	Aseptic				
Time of initial treatment to thirty days	436	2342	433	2328	99.3%	99.4%	99.9%	0.82
Thirty to ninety days	433	2328	420	2322	97.0%	99.7%	97.3%	<0.001
Ninety days to one year	420	2322	390	2294	92.9%	98.8%	94.1%	<0.001
One to two years	342	2107	332	2067	97.1%	98.1%	99.0%	0.21
Two to five years	214	1407	187	1275	87.4%	90.6%	96.8%	0.14
Time of initial treatment to ninety days	436	2342	420	2322	96.3%	99.2%	97.2%	<0.001
Time of initial treatment to one year	436	2342	390	2294	89.5%	98.0%	91.5%	<0.001
Time of initial treatment to two years	384	2151	332	2067	86.5%	96.1%	90.4%	<0.001
Time of initial treatment to five years	f253	1468	187	1275	73.9%	86.9%	87.1%	<0.001

*The relative survival for periprosthetic joint infection, the survival attributable to the periprosthetic joint infection diagnosis (after adjusting for the aseptic control), decreases over time, with the most significant decreases occurring in the first year.

To ascertain the deceased patients in this cohort, a Social Security number or other identifiers were used to search the Social Security Death Index. If the patient had died, the date of death was recorded. Mortality incidence within thirty days, ninety days, one year, two years, and five years of admission was calculated. The time until death was calculated as the amount of time elapsing from the initial surgical intervention for joint failure (revision) to the date of death. For calculating mortality at thirty days, ninety days, and one year, the entire cohort was utilized, as the minimum time frame from admission to the mortality search was eighteen months. To maintain a minimum buffer of six months between the desired follow-up length and the mortality search, the cohort was limited to all patients with an initial arthroplasty date prior to April 1, 2009, when calculating the two-year death incidence; this provided a minimum of thirty months between mortality search and admission. Similarly, the cohort was limited to admissions prior to April 1, 2006, when calculating the five-year death incidence. Patients undergoing aseptic revision were used as a control group. If an association between periprosthetic joint infection and mortality was observed, attempts to further quantify this risk were made

TABLE III Multivariate Logistic Regression Comparing Mortality and Variables for Four Models

Variables	Model 1* (N = 2778)		Model 2† (N = 2778)		Model 3‡ (N = 2778)		Model 4§ (N = 2375)	
	Odds Ratio#	P Value**	Odds Ratio#	P Value**	Odds Ratio#	P Value**	Odds Ratio#	P Value**
Periprosthetic joint infection diagnosis	5.6 (3.7-8.6)	<0.001	6.0 (3.9-9.2)	<0.001	5.6 (3.4-9.2)	<0.001	5.9 (3.5-10.2)	<0.001
Age			1.1 (1.1-1.1)	<0.001	1.1 (1.1-1.1)	<0.001	1.1 (1.1-1.1)	<0.001
Male sex					1.7 (1.1-2.7)	0.02	1.6 (1.0-2.6)	0.06
Charlson Comorbidity Index					1.7 (1.4-2.0)	<0.001	1.7 (1.4-2.0)	<0.001
Knee joint involved					0.9 (0.6-1.5)	0.69	0.8 (0.5-1.4)	0.43
Procedures in ninety days					0.8 (0.5-1.1)	0.17	0.8 (0.5-1.2)	0.32
Ethnicity					NA††	0.84	NA††	0.82
Black (versus white)					1.0 (0.5-2.3)	0.96	0.8 (0.4-2.1)	0.76
Other (versus white)					0.3 (0.0-6.5)	0.48	0.4 (0.0-7.6)	0.56
Unknown (versus white)					1.2 (0.6-2.3)	0.59	1.3 (0.6-2.7)	0.51
BMI							1.0 (1.0-1.1)	0.20

*Model 1 compared mortality with periprosthetic joint infection alone. †Model 2 compared mortality with periprosthetic joint infection adjusted for age. ‡Model 3 compared mortality with periprosthetic joint infection adjusted for age, sex, Charlson Comorbidity Index, ethnicity, number of procedures within ninety days of the original procedure, and knee joint involved. §Model 4 compared mortality with periprosthetic joint infection adjusted for all variables. #The values are given as the odds ratios, with the 95% confidence intervals in parentheses. **A periprosthetic joint infection diagnosis, age, male sex, and Charlson Comorbidity Index were found to be significant predictors in the model predicting one-year mortality. ††NA = not applicable.

TABLE IV Bivariate Analysis of Potential Predictors of Mortality in the First Year After Treatment for Periprosthetic Joint Infection			
Variable	First-Year Mortality (N = 46)	First-Year Survival (N = 390)	Bivariate P Value
Age* (yr)	73.2 (71.7 to 74.7)	66.2 (65.6 to 66.8)	<0.001
Male sex†	27 (58.7)	193 (49.5)	0.24
Knee joint involved†	28 (60.9)	238 (61.0)	0.98
No. of procedures*			
In ninety days	1.5 (1.3 to 1.6)	1.6 (1.6 to 1.7)	0.26
In one year	1.6 (1.4 to 1.8)	2.2 (2.2 to 2.3)	<0.001
Charlson Comorbidity Index†			<0.001
0	16 (34.8)	250 (64.1)	
1	16 (34.8)	112 (28.7)	
2	8 (17.4)	19 (4.9)	
≥3	6 (13.0)	9 (2.3)	
Ethnicity†			0.46
White	36 (78.3)	321 (82.3)	
Black	4 (8.7)	43 (11.0)	
Other	1 (2.2)	5 (12.8)	
Unknown	5 (10.9)	21 (5.4)	
Specific comorbidities†			
Diabetes	12 (26.1)	90 (23.1)	0.65
Cardiac disease	25 (54.3)	115 (29.5)	<0.001
Chronic obstructive pulmonary disease	12 (26.1)	46 (11.8)	0.09
Gastrointestinal disorders	4 (8.7)	8 (2.1)	0.03
History of cerebrovascular accident	9 (19.6)	16 (4.1)	<0.001
Renal disease	0 (0)	1 (0.3)	0.11
BMI* (kg/m²)	30.0 (27.2 to 32.8)	31.9 (31.1 to 32.8)	0.16

*The values are given as the mean, with the 95% confidence interval in parentheses. †The values are given as the number of patients, with the percentage in parentheses.

by controlling for other potential predictors of mortality. These predictors included sex, age, ethnicity, number of joint-related procedures, BMI, and Charlson Comorbidity Index. The Charlson Comorbidity Index provides a method of quantifying overall health and is predictive of mortality[40]. For this analysis, the Dartmouth-Manitoba adaptation was used to calculate the Charlson Comorbidity Index and was not adjusted for age[41]. The number of joint-related procedures was gathered from the institutional database and was limited to the total number of procedures performed on a lower-extremity joint within one year of the initial treatment. The null hypothesis was that periprosthetic joint infection would not impact mortality in this cohort.

Another goal of this study was to identify any factors that predicted one-year mortality in patients with periprosthetic joint infection. Factors investigated included age, sex, ethnicity, number of procedures, Charlson Comorbidity Index, specific comorbidities, and infecting organism. Specific comorbidities were related to cardiac disorder, respiratory disorder, gastrointestinal disorder, neurologic disorder, or diabetes[42]. Infecting organisms were assessed for each periprosthetic joint infection admission and were aggregated taxonomically. The null hypothesis was that none of the tested variables would predict mortality in the cohort treated for periprosthetic joint infection.

To test the null hypotheses, bivariate analysis was performed. This consisted of the Student t test for continuous variables and the chi-square test (number of events greater than ten) or Fisher exact test (lower event size) for

categorical variables. Multivariate analysis was then performed to ascertain independent predictors of the studied outcome if a sufficient event size existed. Multivariable analysis for the entire cohort was performed with a logistic regression, including all potential variables in a pseudo-stepwise manner: first including only periprosthetic joint infection, then including periprosthetic joint infection and age, then including all variables except BMI, and finally including all potential predictors of mortality. BMI was excluded in the third model, as this variable was only available in 2375 (85.5%) of the 2778 cases. Subsequently, multivariable analysis was performed on the periprosthetic joint infection cohort to determine independent predictors of mortality in this cohort.

Source of Funding

Results

In this cohort, the incidence of mortality for all patients was 0.6% (seventeen of 2778) within thirty days, 1.3% (thirty-six of 2778) within ninety days, 3.4% (ninety-four of 2778) within one year, 5.4% (136 of 2535) within two years, and 15.0% (259 of 1721) within five years. Patients with periprosthetic joint
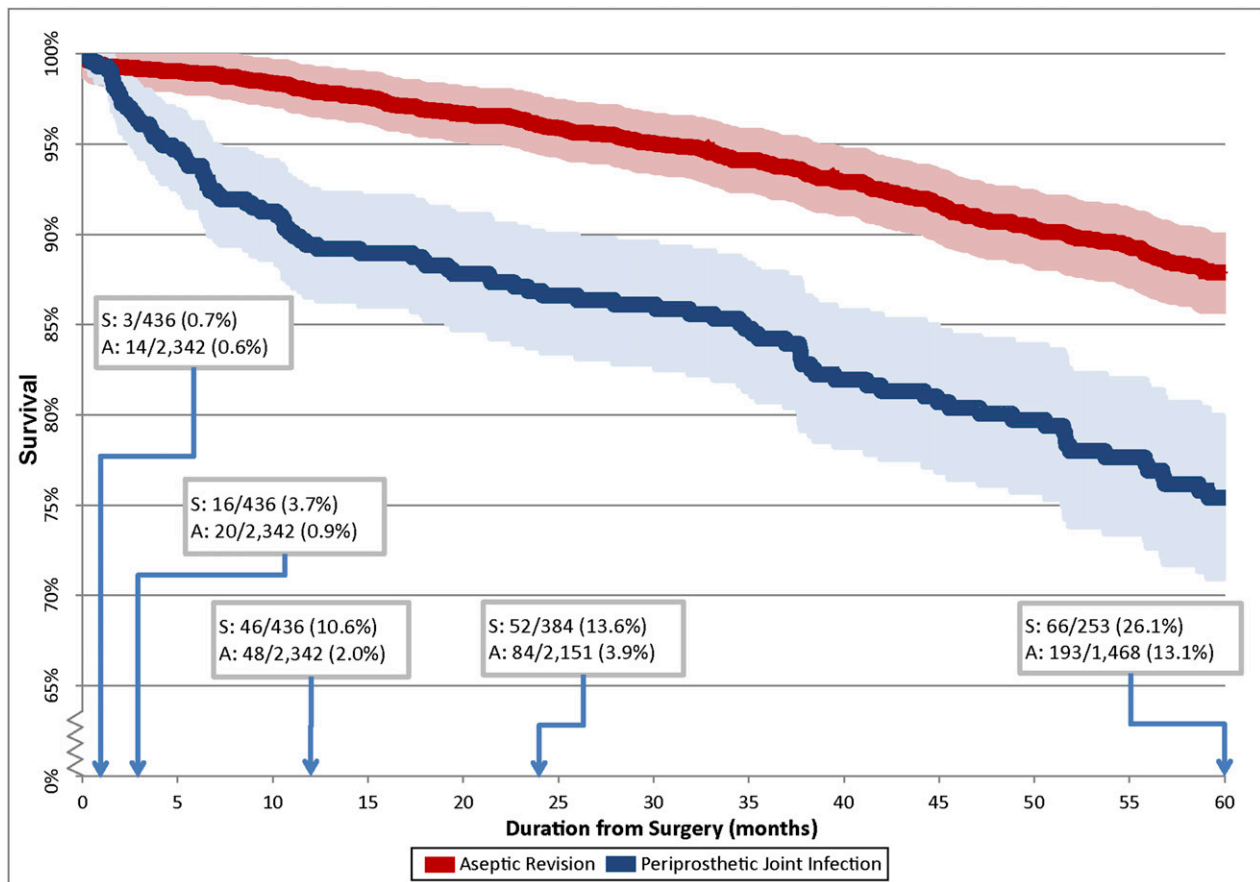
Fig. 1

Kaplan-Meier survival curve with 95% confidence intervals for five years from first admission for patients undergoing revision arthroplasty. The analysis is separated into patients undergoing treatment for periprosthetic joint infection or aseptic failure. Vertical marks indicate censoring. At established time points (thirty days, ninety days, one year, two years, and five years), the mortality incidence in all patients available for analysis at that time point is displayed. A = patients undergoing aseptic revision, and S = patients undergoing septic revision.

infection had similar age, but were more likely male, had elevated age-unadjusted Charlson Comorbidity Index, were more likely undergoing knee revision arthroplasty, and had a greater number of joint-related procedures compared with patients undergoing aseptic revision surgery (Table I). Mortality was significantly greater ($p < 0.001$) in patients with periprosthetic joint infection than in patients undergoing aseptic revision at the ninety-day, one-year, two-year, and five-year time points (Fig. 1). When assessing each individual time period, the mortality incidence was significantly greater ($p < 0.001$) in patients with periprosthetic joint infection from thirty to ninety days and from ninety days to one year (Table II). Also, the relative five-year survival rate in patients with periprosthetic joint infection was 87.3%. Furthermore, periprosthetic joint infection was a predictor of one-year mortality when adjusting only for age; when adjusting for ethnicity, age, sex, number of procedures within ninety days, joint, and Charlson Comorbidity Index; and when adjusting for all variables (Table III), including BMI, rejecting the null hypothesis.

Advanced age ($p < 0.001$), increased Charlson Comorbidity Index ($p < 0.001$), cardiac disease ($p < 0.001$), gastro-intestinal disorders ($p = 0.03$), and history of cerebrovascular accident ($p < 0.001$) were significant predictors of mortality in patients with periprosthetic joint infection in bivariate analysis (Table IV). No significant difference in mortality was observed between patients with hip infections and those with knee infections. Infections caused by gram-negative organisms resulted in a one-year mortality rate of 19.3% (eleven of fifty-seven) compared with 9.2% (thirty-five of 379) in periprosthetic joint infection cases without gram-negative organisms ($p = 0.02$) (see Appendix). For major taxonomic groups, multiple trends were evident, including significantly increased mortality ($p = 0.08$) in patients who had periprosthetic joint infection due to methicillin-resistant *S. aureus* (MRSA) (15.9% [thirteen of eighty-two]) compared with patients who had periprosthetic joint infection due to methicillin-sensitive *S. aureus* (MSSA) (7.4% [seven of ninety-five]). When performing multivariate analysis, age, number of surgical procedures in the first year, Charlson Comorbidity Index, cardiac disease, history of stroke, and polymicrobial infections were independent predictors of one-year mortality in patients with periprosthetic joint infection (Table V).

TABLE V Multivariate Analysis of Potential Predictors of Mortality in the First Year After Treatment for Periprosthetic Joint Infection

Variable	Odds Ratio*	P Value
Age	1.1 (1.0 to 1.1)	0.001
Male sex	2.3 (1.0 to 5.3)	0.05
Knee joint involved	1.5 (0.6 to 3.6)	0.35
No. of procedures		
In ninety days	2.5 (0.9 to 7.0)	0.09
In one year	0.3 (0.1 to 0.8)	0.01
Charlson Comorbidity Index	1.6 (1.2 to 2.1)	0.001
Ethnicity		
Black (versus white)	1.5 (0.4 to 6.4)	0.56
Other (versus white)	0.6 (0.0 to 14.6)	0.74
Unknown (versus white)	2.2 (0.5 to 9.2)	0.27
Comorbidities		
Diabetes	0.5 (0.2 to 1.3)	0.15
Cardiac disease	2.7 (1.1 to 6.3)	0.03
Chronic obstructive pulmonary disease	2.5 (0.9 to 7.0)	0.09
Gastrointestinal disorders	2.8 (0.5 to 15.3)	0.23
History of cerebrovascular accident	3.6 (1.0 to 12.7)	0.05
Renal disease	0.0 (0.0 to 0.0)	1.0
BMI	1.0 (1.0 to 1.1)	0.48
Infecting organism		
Gram-positive	0.1 (0.0 to 1.2)	0.06
Staphylococcus	1.7 (0.0 to 75.3)	0.78
Methicillin-sensitive S. aureus	1.1 (0.1 to 21.4)	0.97
Methicillin-resistant S. aureus	1.5 (0.1 to 5.3)	0.79
Coagulase-negative Staphylococcus	0.7 (0.0 to 14.3)	0.84
Streptococcus	1.1 (0.1 to 10.8)	0.97
Gram-negative	0.3 (0.0 to 2.9)	0.31
Polymicrobial	6.3 (1.3 to 30.8)	0.02
Culture-negative	0.1 (0.0 to 1.4)	0.09

*The values are given as the odds ratio, with the 95% confidence interval in parentheses.

Discussion

Periprosthetic joint infection remains a major complication of total joint arthroplasty[43]. The outcome following treatment for periprosthetic joint infection ranges from a return to full function to the possible need for amputation or arthrodesis[33,41,44,45]. Of rising concern throughout the joint replacement community is infection involving MRSA, as it is often resistant to aggressive treatment, resulting in suboptimal outcome[46-49]. Additionally, patient health status has been implicated in predicting the outcome of periprosthetic joint infection treatment[50]. This study investigated the impact of periprosthetic joint infection on mortality and the predictors of mortality in patients with periprosthetic joint infection.

There was a significant increase in mortality in patients undergoing surgical intervention for periprosthetic joint infection compared with patients undergoing aseptic revision arthroplasty. Periprosthetic joint infection increased the risk of death more than fivefold when controlling for other potential confounding variables. McGarry et al. reported a fivefold increase in the ninety-day mortality risk after surgical site infection in an elderly population undergoing various surgical procedures[30]. This is similar to the fivefold increase in the unadjusted mortality risk at ninety days found for patients with periprosthetic joint infection. Interestingly, the effect of periprosthetic joint infection on mortality is greatest between thirty days and one year, with no statistical difference in mortality between one and five years. Despite this, the relative survival rate of patients with periprosthetic joint infection compared with those requiring aseptic revision was 87.3% at five years. For comparison, the five-year relative survival rates for the top five most common cancers are 99% for prostate cancer, 89% for breast cancer, 16% for lung and bronchial cancer, 64% for colorectal cancer, and 91% for melanoma[51]. The effect of periprosthetic joint infection on patient mortality within thirty days is inconclusive, possibly stemming from a type-II error or an indication that no difference exists in the initial insult required in treating periprosthetic joint infection compared with aseptic failure. Other authors have provided anecdotal evidence of increased mortality in patients receiving treatment for periprosthetic joint infection[52-54]. Most recently, Berend et al. reported 4% mortality within ninety days[52]. Previously identified risk factors for periprosthetic joint infection include male sex, advanced age, increased BMI, increased number of comorbidities, and knee arthroplasty, among others[11,15,20-23]. Many risk factors are also associated with an increased risk of mortality, implying that the association between mortality and periprosthetic joint infection is secondary to poor health status. However, after adjusting for such factors, periprosthetic joint infection remained a significant predictor of mortality, suggesting that the disease process or the treatment itself contributes to the increased risk of death.

Independent predictors of first-year mortality were advanced age, increased Charlson Comorbidity Index, cardiac disease, and history of cerebrovascular accident. In multivariate analysis, the number of procedures within one year had a protective effect on mortality. Although surgical intervention carries the risk of death, the number of procedures was likely protective because it signaled that patients had a level of health allowing for repeated surgical intervention. From a microbiological standpoint, patients with multiple organisms on culture, MRSA, and gram-negative organisms had increased first-year mortality. Marculescu and Cantey found that patient age greater than sixty-five years was an independent risk factor for polymicrobial periprosthetic joint infection compared with monomicrobial periprosthetic joint infection, which may account for the moderate increase in mortality[55]. However, polymicrobial infections were a predictor of mortality independent of age and overall

health, suggesting another mechanism by which polymicrobial infections predispose to early death. Gram-negative infections are also expected to be associated with poor overall health. This is evident in an analysis of success in treating gram-negative periprosthetic joint infection at this institution, where the current authors (B.Z. and J.P.) found that a large proportion of patients (26% [six of twenty-three]) did not complete a two-stage exchange because of death[53]. Lastly, MRSA is a particularly virulent organism that can cause persistent periprosthetic joint infection and increased cost of treatment[49,53,56]. Evidence provided by Nixon et al. demonstrated that, following femoral fracture and admission to an orthopaedic ward, infection with MRSA doubled the risk of first-year mortality[31]. Similarly, Leung et al. reported that 24% of patients receiving treatment for periprosthetic joint infection due to MRSA had died at a mean follow-up of nearly five years[54]. The current study also found a trend of MRSA predicting mortality, and MRSA has once again been proven to predict a dismal outcome.

The limitations of this study included its retrospective nature and reliance upon an electronic database to identify patients and other factors investigated. However, the Social Security Death Index has been validated as a tool for identifying deceased patients[57]. In attempts to mitigate the inaccuracy of periprosthetic joint infection classification, all periprosthetic joint infection cases were confirmed with use of a stringent and recently proposed standard definition for periprosthetic joint infection[36]. However, because not all variables were available for this analysis, it was necessary to eliminate the cases that could not be confirmed, limiting our study cohort and likely eliminating some cases of true periprosthetic joint infection that had negative cultures. Furthermore, this definition cannot be used in patients not requiring surgical intervention as it includes tissue specimen for culture, joint appearance, and histological analysis in its defining criteria. Thus, this analysis is limited to only the patients with periprosthetic joint infection who underwent surgical treatment. Additionally, operative variables such as operative time and blood loss were not reliably available for the entire cohort and were not reported. However, we do not believe that this weakens the findings, as the mortality rate of patients with periprosthetic joint infection was no different in the early postoperative period (thirty days) compared with the control group. Attempts were made to determine whether periprosthetic joint infection is an independent predictor of mortality by controlling for age, sex, ethnicity, number of surgical procedures, involved joint, BMI, and Charlson Comorbidity Index. Although it is believed that this adjustment sufficiently accounts for differences between the cohorts, it is not possible to identify all potential predictors of mortality that may vary between the groups.

In conclusion, undergoing treatment for periprosthetic joint infection significantly and independently increases the risk of mortality. It is evident that increased risk of mortality is due to a direct adverse effect of periprosthetic joint infection, as well as the fact that periprosthetic joint infection is a reflection of a decreased health status. Thus, in addition to the many efforts invested to control infection in patients diagnosed with periprosthetic joint infection, it is paramount to also ensure a tight control of the chronic diseases.

Appendix

_eA_ A table comparing the infecting organism between patients who died and those who survived the first year following treatment is available with the online version of this article as a data supplement at jbjs.org. ∎

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