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Original Article

Periprosthetic Infection Recurrence After 2-Stage Exchange Arthroplasty: Failure or Fate?

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ABSTRACT

Background: Two-stage exchange arthroplasty remains the preferred method for treating a chronic periprosthetic joint infection (PJI) in North America. However, infection recurrence may occur. Previously, recurrent infections have been classified as persistent (same isolated pathogen) or new (different pathogen identified). We sought to determine (1) recurrence rates among patients with chronic hip and knee PJI, treated with 2-stage exchange arthroplasty; (2) risk factors for infection recurrence; and (3) risk factors for developing persistent vs new infection.

Methods: We retrospectively reviewed clinical characteristics of patients with chronic hip and knee PJI, treated with 2-stage revision between January 1998 and March 2014. Minimum follow-up was 24 months. Two multivariate logistic regression models were constructed to determine independent predictors for infection recurrence and persistence.

Results: In total, 548 patients were identified (283 men, 265 women). Forty-eight had a recurrent infection (8.76%). Men had 54.8% lower odds of PJI recurrence than women (odds ratio [OR] = 0.452; 95% confidence interval [CI], 0.235-0.869). Patients with heart disease had 109% higher odds of infection recurrence than patients without heart disease (OR = 2.09; 95% CI, 1.097-3.081). The risk of infection recurrence was 119% higher in patients with psychiatric disorders than in patients without psychiatric disorders (OR = 2.19; 95% CI, 1.011-4.761). Patients with recurrent knee PJI had 84.6% lower odds of persistent infection (OR = 0.154; 95% CI, 0.034-0.696) compared to hip PJI. Patients with heart disease had 5-fold increased odds for persistent PJI (OR = 5.068; 95% CI, 1.38-22.56).

Conclusion: Female gender, heart disease, and psychiatric disorders increase the risk of hip and knee PJI recurrence. Patients with PJI of the hip and with heart disease are at higher risk of infection persistence.

Infection rates after primary total joint arthroplasty are reported to range between 1% and 3% [1-4]. Revision surgery is associated with up to a 4-fold increase in the risk of periprosthetic joint infection (PJI) [5,6]. In addition to the significant increase in the number of total joint arthroplasties that is expected in the future and is fueled by the growing demands of an aging population [7], an analogous increase in the absolute number of cases complicated with infection can be expected.

The standard of treatment of late chronic PJIs (infections with insidious onset of symptoms presenting more than 4 weeks after surgery) is 2-stage exchange arthroplasty [8,9]. The first stage of the procedure consists of removal of the infected implants, debridement of infected or grossly necrotic tissues and irrigation in order to diminish the bacterial load, followed by insertion of an antibiotic-impregnated cement spacer. This is accompanied by a 6-week regimen of antibiotics which is based on the sensitivity profile of the isolated microorganism or is empirical when no pathogen is identified. After completion of the antibiotic course reimplantation follows, which is dictated by a gradual decrease in

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inflammatory markers and negative cultures after joint aspiration [10].

In larger series, the success rate of 2-stage exchange arthroplasty is reported to range from 72% to 100% [8,11-24]. Risk factors for failure (infection recurrence) have been previously identified [8,25-27]. Infection recurrence can be the result of either failure to eradicate the previous infection or an infection with a different pathogen. In this context, recurrent infections have been characterized as "persistent" (when cultures yield the same pathogen) or "new" (when a different microorganism is identified as the cause) [28]. Given their different nature, these subgroups may be associated with distinct predisposing factors, representing a topic that has not been adequately studied [9,28-30].

The purposes of our present study were to determine (1) the recurrence rates among patients with chronic PJI of the hip and knee, treated with 2-stage exchange arthroplasty; (2) the risk factors for infection recurrence; and (3) the risk factors for developing a persistent vs a new infection.

Materials and Methods

We retrospectively reviewed clinical characteristics of 548 patients with late chronic PJI of the hip and the knee, treated with 2-stage exchange arthroplasty in a tertiary teaching institution, between January 1998 and March 2014. Late chronic infections were infections with an insidious onset within more than 4 weeks after index surgery, based on the Tsukayama classification of PJIs of the hip and the knee [31,32]. Infections presenting within 4 weeks after index procedure, acute hematogenous infections with a late presentation, and cases of positive intraoperative cultures taken during a revision surgery for a reason other than infection were excluded from the study. The diagnosis was based on the Musculoskeletal Infection Society criteria [33] and was determined by either the presence of a draining sinus communicating with the joint or the isolation of a microorganism from at least 2 samples of joint fluid or tissue. If these criteria were not met, diagnosis was based on the presence of at least 3 of the following: elevated inflammatory markers (erythrocyte sedimentation rate [ESR] $\geq$ 30 mm/h and C-reactive protein [CRP] $\geq$ 1 mg/dL); elevated synovial leukocyte count (or a result of ++ in leukocyte esterase strip); elevated synovial neutrophil percentage; isolation of a pathogen in 1 periprosthetic tissue or fluid culture; and greater than 5 neutrophils per high-power field in 5 high-power fields on histologic examination. A synovial leukocyte count >1700 cells/μL and a synovial neutrophil percentage >60% were considered highly suggestive of infection. There were 283 men (51.6%) and 265 women (48.4%) in our sample. Their mean age at the time of diagnosis was 65.4 ± 12.8 years. The mean body mass index was 29.6 ± 6.9 kg/m^2. Two hundred eighty-two patients had a chronic PJI of the hip, whereas a PJI of the knee was the diagnosis in 266 patients. The present study was approved by the institutional review board.

Preoperatively, all patients underwent a comprehensive diagnostic evaluation, which included ESR, CRP, and joint aspiration for synovial fluid microscopic examination and culture. Comorbidities, including diabetes mellitus, malignancy, heart disease, peripheral vascular disease, connective tissue disorders, thyroid disease, pulmonary disease, smoking, psychiatric disorders, and chronic kidney disease, were recorded (Table 1). Two hundred and two patients (36.9%) were under treatment with antibiotics at home, which were discontinued for at least 5 days before joint aspiration, in order to diminish the possibility of a false-negative result. Thirty-four patients (6.2%) had been unsuccessfully treated with a prior irrigation and debridement (I&D) without removal of implants.

The patients of the present study were treated by 12 different surgeons. Different types of administered anesthesia were also recorded (Table 1). The first stage of the treatment protocol consisted of removal of infected implants and cement mantle. As per institutional protocol, at least 6 specimens were taken for cultures in all patients and/or frozen section when this was deemed necessary. Tissue samples were cultured for aerobic and anaerobic bacteria, as well as fungi, within appropriate culture media. Isolated microorganisms were categorized into staphylococcal species (including methicillin-resistant *Staphylococcus aureus* [MRSA], methicillin-sensitive *Staphylococcus aureus* [MSSA], methicillin-resistant *Staphylococcus epidermidis* [MRSE], methicillin-sensitive *Staphylococcus epidermidis* [MSSE] and other staphylococcal species), other Gram-positive pathogens, and Gram-negative microorganisms (Table 2). Notably, in 57 patients (10.4%), intraoperative cultures failed to identify a pathogen; these patients also had negative aspiration cultures preoperatively. A meticulous I&D of the joint was then conducted. This was followed by insertion of an antibiotic-laden cement spacer, with the purpose of maintaining joint space and limb length, preventing fibrosis and soft-tissue contractures, as well as locally delivering antibiotics to the infection site for a prolonged period of time. Different spacer types used are listed in Table 1. After the operation, patients received a 2-week course of parenterally administrated antibiotics, followed by oral

Table 1
Characteristics of Patients Subjected to Successful or Failed 2-Staged Exchange Arthroplasty for the Initial Periprosthetic Infection.

Variable[a]	Success	Failure (Infection Recurrence)	*P* Value	
			Univariate Analysis	Logistic Regression Analysis
Gender				
Men	265 (53.0)	18 (37.5)	.0401*	.0473*
Women	235 (47.0)	30 (62.5)		
Age (y)	65.6 ± 12.8	63.1 ± 11.6	.1269	—
BMI	29.4 ± 7.1	30.7 ± 5.8	.0921	—
Comorbidities				
Diabetes	81 (16.2)	6 (12.5)	.5028	—
Malignancy	64 (12.8)	7 (14.6)	.7253	—
Heart disease	173 (34.6)	23 (47.9)	.066	—
Thyroid disease	66 (13.2)	4 (8.3)	.3346	—
Connective tissue disease	57 (11.4)	10 (20.8)	.0567	—
Pulmonary disease	98 (19.6)	10 (20.8)	.8427	—
Smoking	46 (9.2)	3 (6.3)	.7896	—
Psychiatric disorder	56 (11.2)	12 (25.0)	.0056*	—
Peripheral vascular disease	19 (3.8)	2 (4.2)	.705	—
Chronic kidney failure	16 (3.2)	0 (0.0)	.3831	—
ASA score				
ASA 1	3 (0.6)	0 (0.0)	.4825	—
ASA 2	248 (49.6)	21 (43.8)		
ASA 3	235 (47.0)	27 (56.2)		
ASA 4	14 (2.8)	0 (0.0)		
Anesthesia				
Regional	478 (95.6)	45 (93.8)	.4732	—
General	22 (4.4)	3 (6.2)		
Joint				
Hip	261 (52.2)	24 (50.0)	.7681	—
Knee	239 (47.8)	24 (50.0)		
Prior irrigation and debridement	35 (7.0)	2 (4.2)	.7612	—
Spacer antibiotic type				
Unknown	94 (18.8)	10 (20.8)	.8678	—
Vancomycin	36 (7.2)	2 (4.2)		
Aminoglucoside	56 (11.2)	5 (10.4)		
Combination	314 (62.8)	31 (64.6)		

The asterisk (*) indicates statistical significance.
BMI, body mass index; ASA, American Society of Anesthesiologists.
[a] Continuous and categorical variables are reported using mean ± standard deviation and frequency (%), respectively.