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Risk Factors for Recurrence of Periprosthetic Knee Infection

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ABSTRACT

We retrospectively reviewed 110 patients who underwent two-stage revision surgery in order to identify potential risk factors for recurrence of periprosthetic infection. We found that patients with inflammatory arthritis ($P = 0.0125$), perioperative hematoma formation ($P = 0.0422$), wound dehiscence ($P = 0.042$), and those who are chronic *Staphylococcus* carriers ($P = 0.0177$) were associated with an increased incidence of re-infection. The duration of intravenous antibiotic therapy less than 6 weeks was associated with a reduced risk of reinfection to greater than 6 weeks ($P = 0.03$). Multivariate analysis indicated that wound dehiscence (odds ratio [OR], 5.119; 95% confidence interval [CI], 1.367–19.17), and *Staphylococcus* carriers (OR, 11.419; 95% CI, 1.376–94.727) are significant predictors of recurrence ($P = 0.0153$ and 0.0241, respectively).

Periprosthetic infection (PI) after total knee arthroplasty (TKA) occurs in approximately 2% of patients and is associated with significant morbidity and high socioeconomic cost. [1] Eradication of PI and the prevention of recurrence – while maintaining knee function – are the primary goals in the management of these complex cases. Risk factors for infection after TKA have been extensively described in the literature [2–7].

For chronic periprosthetic infection, two-stage exchange arthroplasty is considered the gold standard for treatment, and includes prosthesis removal, extensive debridement of all infected tissue, and insertion of an antibiotic spacer [4]. Following a six-week course of parenteral antibiotics, and a negative joint aspiration, the second stage includes reimplantation of a new prosthesis.

Recurrence of PI after surgical treatment ranges from 9% to 33% and carries significant additional patient morbidity and cost [2,4,8,9]. Factors for failure after two-stage treatment include medical status, pathogen virulence and antibiotic resistance in addition to the condition of bone and soft tissue envelope [3,4]. However, the risk factors of recurrence of periprosthetic joint infection after a two-stage procedure have not yet been extensively studied.

Therefore, the purpose of this study was 1) to determine the efficacy of two-stage revision arthroplasty followed by delayed re-implantation for infected TKA in a large number of patients treated in a single institution during a 10-year period, 2) to identify the incidence of recurrence, and 3) to identify potential risk factors for recurrence of periprosthetic infection, focusing specifically on the impact of various perioperative medical and surgical factors.

Patients and Methods

We retrospectively reviewed a cohort of 110 TKAs in 118 patients diagnosed with a periprosthetic knee infection between January 2000 and June 2011 based on a prospectively collected database. Our study was approved by our Institutional Review Board. There were 51 (46.7%) male and 59 (53.6%) female patients with a mean age of 64.3 years (range 36 to 90). Their average body mass index (BMI) was 33.9 kg/m^2 (range 18 to 61). TKA was performed in 88 (80%) cases with a background of idiopathic osteoarthritis, 14 cases (12.7%) with posttraumatic OA and 8 cases (7.3%) with an inflammatory etiology. All TKAs included into the present study cohort were primary unilateral; revision cases, simultaneous bilateral and staged bilateral cases were excluded from the study.

Treatment consisted of a two-stage revision surgery performed by an orthopaedic surgeon specialized in adult reconstruction and joint arthroplasty in our institution. The first stage included prosthetic joint resection, extensive debridement, and placement of temporary antibiotic loaded cement spacer. Patients subsequently received 3–8 weeks of intravenous antibiotics, determined by the antibiotic sensitivity of the pathogen(s) isolated from the joint fluid and culture samples obtained intra-operatively. Clinical signs of infection, inflammatory markers (ESR and CRP) and negative joint aspiration were used to determine the time of re-implantation, which on average was 3.2 weeks post completion of IV antibiotic treatment (range, 2 to 8 weeks).

Failure of the second stage (implantation of a new prosthesis) was defined as clinical and/or laboratory evidence of re-infection: elevated inflammatory markers (i.e. ESR > 30 mm and CRP > 1 mg/dL), a positive

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Table 1
Characteristics of Patients with Recurrent Infection.

	Age	Gender	Etiology	Time Interval	Pathogen First Infection	Pathogen Re-Infection	Outcome
1	78	F	OA	210	*Staph. lugdunensis*	*Staph. lugdunensis*	2 stage revision
2	65	F	OA	160	MRSA	*Strep. viridanse*	Fusion after 4 debridements
3	67	M	OA	103	*Strep. viridanse*	*Strep. viridanse*	2 stage revision
4	67	M	OA	14	*Staph epidermidis*	*Staph epidermidis*	2 stage revision
5	66	F	Inflammatory	22	*Staph aureus*	*Staph aureus*/VRE/*Pseudomonas*	Quad rupture/2 debridements/Fusion
6	65	M	OA	25	*Staph aureus*	*Staph aureus*	2 stage revision
7	50	M	OA	22	*Staph aureus*	MRSA	2 stage revision
8	44	F	Inflammatory	18	MRSA	MRSA	2 stage revision
9	68	F	Postraumatic	40	MRSA	MRSA	2 stage revision
10	80	M	OA	145	*Staph epidermidis*	*Staph epidermidis* and *P. acnes*	2 stage revision
11	70	M	OA	70	*Staph aureus*	*Enter. faecalis* and *Staph aureus*	2 stage revision
12	59	F	Inflammatory	13	*Staph epidermidis*	*Staph. epidermidis*/MRSA/*Cand. albicans*	1 stage repeated twice/Ex Fix/Fusion
13	44	M	Postraumatic	13	*Pseudomonas*	*Pseudomonas*	3 debridements/Ex Fix/Fusion/Amputation
14	66	M	OA	22	*Enterococcus/Proteus/E. Coli*	*Enterococcus/Proteus/E. Coli*	3 debridements/Fusion
15	59	F	Inflammatory	25	MRSA	*Staph. epidermidis*/MRSA/*Cand. albicans*	2 debridements/Ex Fix/Fusion

joint fluid and/or intraoperative soft tissue and/or bone culture, and/or the presence of purulence or sinus tract communicating with the joint. Successful two-stage outcome was defined as the one that did not develop re-infection and therefore did not require further medical or surgical intervention.

Potential risk factors for the recurrence of periprosthetic knee joint infection were tabulated into a database. Demographic data (age, gender, BMI, American Society of Anesthesiologists [ASA] classification score, prior surgeries), smoking and alcohol use, first stage surgical variables (operative time, total room time, tourniquet use, tourniquet time, use of Foley catheter, type of anesthesia [femoral nerve block, peri-articular injections], antibiotic use in the cement, length of stay [LOS], disposition after discharge, estimated intraoperative blood loss, use of drains and drain output) were recorded. Inter-stage data included time to infection, pathogen type and virulence, identification of *Staphylococcus aureus* carriers, and duration of IV antibiotics. We identified *Staphylococcus* carriers using swabs. Specifically, nasal cultures were received by rotating a sterile swab four times in the anterior nasal cavities. The swabs were immediately plated on blood agar plate medium and submerged in phenol red mannitol broth. The agar plates were evaluated on the 1st and 2nd day post incubation, whereas the broths were evaluated on the 3rd day. Broths with a color change from red to orange–yellow were considered positive and were subcultured on blood agar plates. Identification of *S. aureus* was based on gram stain and colony morphology. Latex agglutination test and catalase tests were also performed.

Complications following the second-stage were recorded and included hematoma formation, development of postoperative cellulitis, Deep Vein Thrombosis (DVT), and wound dehiscence. We determined hematoma, wound dehiscence and cellulitis as follows: those considered positive for hematoma formation were the cases with clinically evident intra-articular edema and postoperative intra-articular collection of hematoma under tension necessitating emergent evacuation either by needle aspiration or by arthroscopic debridement. Wound dehiscence was defined as the early or delayed disruption of the surgical wound exposing the subcutaneous tissue that required secondary intervention such as debridement and closure. Cellulitis was defined as the presence of an area of redness, which increased in size over a couple of days. The borders of the area of redness are generally not sharp and the skin may be swollen. Lymphatic vessels may occasionally be involved and clinical image of lymphedema may be evident. Constitutional symptomatology may include fever and/or tiredness. The diagnosis of hematoma, wound dehiscence or cellulitis was verified on a physician and infectious disease specialist basis, by confirming the above criteria. Any documentation was recorded in the patient's chart by either an orthopaedic surgeon or an infectious disease specialist.

The medical records of these patients were reviewed to confirm the presence of deep surgical site infection or cellulitis as described by the Centers for Disease Control (CDC)/NNIS guidelines [10]. According to those guidelines, the definition also encompasses a physician diagnosis of such an infection [11].

All patients were followed for a minimum of 2-years after the treatment of infection, or until recurrence.

Statistical Method

Continuous variables are presented as mean ± SD (range) and categorical variables are described as frequency (percentage). Patient characteristics, etiologic background of index surgery, history and type of prior surgeries, comorbidity, various surgical variables, type of pathogen, staphylococcus carriage, ASA, type of nerve block, and postoperative complications were compared between patients who developed recurrence and those who had a successful outcome with univariate analysis using t test or chi-square/Fisher's exact test (Tables 2–8).

Logistic regression was performed to identify risk factors for re-infection (Table 9). Model fitting for the logistic regression started with a full model including all risk factors that were significant in univariate analysis. These risk factors were then selected using backward elimination. The Hosmer–Lemeshow test of goodness-of-fit was

Table 2
Univariate Analysis of Demographic Factors (Age, Gender and Body Mass Index).

	Total	Infected	Non-Infected	*P* value
Mean Age (range min and max)	64.3 (36–90)	63.2(44–80)	64.79 (36–90)	0.605
Gender				
Males (% rate)	51 (46.7%)	8 (53.3%)	43 (45.3%)	0.5602
Females (% rate)	59 (53.6%)	7 (46.7%)	52 (54.7%)	
Mean BMI (range min max)	33.9 (18–61)	31.51 (20–59)	34.5 (18–61)	0.2676

Table 3
Analysis of Etiologic Background of Initial Operation and History of Prior Surgeries on the Same Knee, as Potential Risk Factors for Re-Infection.

	Total	Infected	Non-Infected	*P* Value
Etiology				
Idiopathic	88 (80%)	8 (53.3%)	80 (84.2%)	0.0038[a]
Post traumatic	14 (12.7%)	3 (20%)	11 (11.6%)	0.4084[b]
Inflammatory	8 (7.3%)	4 (26.7%)	4 (4.2%)	0.0125[c] 0.0042[d]
Prior surgery				
yes	72 (65.4%)	11 (73.3%)	61 (64.2%)	0.2345
no	38 (34.6%)	4 (26.7%)	34 (35.8%)	

[a] Idiopathic vs post traumatic.
[b] idiopathic vs inflammatory.
[c] post traumatic vs inflammatory.
[d] Idiopathic vs post-traumatic vs inflammatory.