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Risk Factors for Infection Following Total Knee Arthroplasty: A Series of 3836 Cases from One Institution

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ABSTRACT

Higher PJI rates may be related to identifiable risk factors, which may or may not be modifiable. Identifying risk factors preoperatively provides opportunities for modification and potentially decreasing the incidence of PJI. The purposes of this study were to: (1) retrospectively identify and quantify risk factors for PJI following primary TKA, and (2) to classify those significant risk factors as either non-modifiable or modifiable for intervention prior to surgery. Optimization of modifiable risk factors such as *Staphylococcus aureus* colonization, and tobacco use prior to primary TKA may decrease the incidence of periprosthetic joint infection after primary TKA, thereby reducing morbidity and the costs associated with treating those infections.

Periprosthetic joint infections (PJI) following total joint arthroplasty (TJA) are rare complications but result in inferior outcomes and increased cost. The demand for TJA in the United States is expected to increase significantly in coming years. The volume of total knee arthroplasty (TKA) procedures performed is expected to reach nearly 3.5 million annually by 2030 [1]. The reported incidence of PJI following TKA ranges from 0.5% to 1.8% [2–4], and the incidence can increase significantly in high-risk groups [5]. The high volume and increased demand for TKA will result in a significant predicted future cost burden due to infection. Therefore, reducing the incidence of PJI is of significant importance to both improve outcomes and help control rising health care expenditures. The cumulative yearly expenditure from infection after TJA is expected to exceed $1.62 billion by 2020 [6], with an estimated cost related to a single PJI as high as $130,000 [7].

Numerous strategies have been employed for perioperative optimization of the surgical environment to minimize the incidence of infection including antibiotic prophylaxis, surgical site preparation, contained surgeon exhaust suits, operating room laminar airflow, and bacterial decolonization of *Staphylococcus aureus* (*S. aureus*) [8,9]. While these strategies to improve the perioperative surgical environment can help reduce PJI incidence, certain patient-related factors increase the risk of developing PJI following orthopedic surgery [10]. For example, diabetes, obesity, *S. aureus* colonization, and tobacco use have been associated with increased risk of PJI following TJA [2,8,11,12]. Optimization of potentially modifiable patient-related risk factors prior to surgery may help reduce the risk of infection following TKA. The purposes of our study were to: (1) retrospectively identify and quantify risk factors for PJI following primary TKA, and (2) to classify those significant risk factors as either non-modifiable or potentially modifiable for intervention prior to surgery.

Materials and Methods

We analyzed data from 3419 primary TKA procedures performed at our primary institution between January 1, 2009 and December 31, 2011. The cohort had overall mean age of 64.2 years (±10.25) and consisted of 2348 female patients and 1071 male patients. Among this cohort, 45 of these procedures occurred one or more days after admission ("non-same day procedure"). All patients were monitored for deep infection for a period of one year postoperatively through an aggressive hospital surveillance program involving review by our infection control department of all readmissions, returns to the operating room, and positive cultures. Diagnosis of PJI was based on the definitions set forth by the Centers for Disease Control and Prevention's National Healthcare Safety Network (CDC/NHSN) (i.e. an infection involving deep soft tissue at incision with purulent drainage, dehiscence, fever, and localized pain or tenderness) [13]. We also used the New York State Hospital Infection Control database to supplement our surveillance efforts and ensure identification of all PJI including those presenting to outside institutions. This surveillance database reports all

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Level of Evidence: Level III - Retrospective case review.

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infections presenting within New York State back to the parent institution where the primary surgery was performed. Institutional review board (IRB) approval was granted for review of patient records.

Prior to surgery, all patients were screened for nasal colonization of *S. aureus*, prescribed a 5-day course of mupirocin ointment for nasal decolonization, and provided chlorhexidine wipes for application to the skin the evening before and morning of surgery. Infection prophylaxis during the study timeframe involved administration of intravenous antibiotics within 1 hour prior to incision and continued 24 hours postoperatively. For patients who screened positive for methicillin resistant *S. aureus* (MRSA), vancomycin was administered as prophylaxis while a second-generation cephalosporin was administered for patients with a negative screen for MRSA. Surgical approach, anesthesia type, and implant type varied based on patient characteristics and surgeon preference. Postoperative wound management involved sterile dressing for a period of 1–3 days postoperatively with serial dressing changes as needed until the wound was dry. Deep vein thromboembolism (DVT) prophylaxis involved various regimens each of which adhered to the recommendations of the American College of Chest Physicians (ACCP) and the American Academy of Orthopaedic Surgeons (AAOS).

Patient demographic and comorbidity data abstracted through the medical chart review are listed in Table 1. Diabetes status that involved a positive history of diabetes mellitus and any related organ damage such as retinopathy, neuropathy and nephropathy, was noted. Patients who underwent TKA one or more days post admission were noted as "non-same day procedure." Cutoff values for operative time and surgeon case-load were selected based on the median values of 114 minutes and 72 cases per year respectively among our cohort. A total of 49 surgeons performed the operations in this cohort. Tobacco use was defined as use within one month prior to surgery. Modifiable risk factors were defined as those factors that could potentially be treated or optimized prior to elective surgery.

Data analysis involved univariate and multivariate regression analyses conducted using SAS version 9.3 (SAS Institute, Cary, NC) to determine significant patient-related and surgery-related predictors for risk of postoperative PJI. All statistical analyses were performed by a trained statistician (AS). Results are reported as odds ratio (OR) with 95% confidence interval (CI). Statistical significance was set at $P < 0.05$.

Results

Among the procedures reviewed, 26 of 3419 (0.76%) primary TKA procedures were complicated by PJI. Causative organisms and frequency of isolation are presented in Table 2. Multivariate analysis for primary TKA procedures revealed that significant risk factors for infection included male gender (OR 3.32, [95% CI: 1.20–9.17], $P = 0.021$), active tobacco use (OR 3.07, [95% CI: 1.02–9.37], $P = 0.047$), comorbid pulmonary disease (OR 5.27, [95% CI: 1.38–20.10], $P = 0.015$), and colonization with *S. aureus* (OR 3.97, [95% CI 1.49–10.54], $P = 0.006$).

Table 2
Isolated Organisms Among All PJI After TKA.

Organism	Frequency
Coagulase Negative Staphylococci spp.	14
S. aureus	9
Viridans *Streptococcus* spp.	3
Enterococcus faecalis	4
Morganella spp.	4
Proteus spp.	3
Other Gram Positive Rod	3
Corynebacterium spp.	1
Enterococcus faecium	1
Group B *Streptococcus*	1
Acinetobacter spp.	1
Escherichia coli	1
Enterobacter spp.	1
Pseudomonas aeruginosa	1
Serratia spp.	1
Providencia spp.	2

TKA = total knee arthroplasty; PJI = periprosthetic joint infections.

MRSA colonization was associated with increased risk of infection in the univariate analysis but was not found to be a significant independent risk factor based on the multivariate analysis (Table 3).

Risk factors that did not prove significant among this cohort for primary TKA included ASA > 2, BMI ≥ 30 kg/m^2, BMI ≥ 40 kg/m^2, operative time > 114 minutes, low surgeon case load, and the presence of various comorbid medical conditions (i.e. neurologic, autoimmune, cardiac, gastrointestinal, hepatobiliary, malignancy).

When analyzing combined risk factors for compounding effects on risk, tobacco use was an additive risk factor when combined with a BMI greater than or equal to 30 kg/m^2 (OR 8.37 [95% CI: 1.86–37.74], $P = 0.0092$). Among the significant independent risk factors identified, active tobacco use and *S. aureus* colonization are potentially modifiable risk factors for PJI.

Discussion

Periprosthetic joint infections following TKA are devastating complications leading to inferior outcomes and increased costs. This study was conducted to identify and quantify risk factors for PJI following primary TKA and to classify significant risk factors as either non-modifiable or potentially modifiable by intervention prior to surgery. Among our study population infection developed in 26 of 3419 (0.76%) primary TKA cases. Significant risk factors for infection after primary TKA included active tobacco use, comorbid pulmonary disease, and *S. aureus* colonization. Some of these risk factors such as tobacco use and *S. aureus* colonization are potentially modifiable, and efforts to minimize or eliminate these modifiable risk factors may help to improve infection rates following TKA.

Table 1
Potential Risk Factors Examined.

Male Gender	1071/3419	Comorbid Autoimmune Condition	7/3419
Diabetes Diagnosis	478/3419	Comorbid Cardiac Condition	0/3419
Catheter Associated Urinary Tract Infection	6/3419	Diabetes Related Complications	38/3419
Central Line-Associated Bloodstream Infection	0/3419	Diabetes Renal/Ophthalmologic Complications	10/3419
ASA > 2	1127/3155	End Stage Renal Disease	0/3419
BMI ≥ 40 kg/m^2	376/2940	Comorbid Gastrointestinal Condition	42/3419
BMI ≥ 30 kg/m^2	1719/2940	Comorbid Hepatobiliary Condition	24/3419
Operation Time. ≥ 114 minutes	995/2760	Comorbid Malignancy	152/3419
Tobacco Use Within One Month Prior to Surgery	251/2776	Comorbid Pulmonary Condition	102/3419
Non-Same Day Surgery	45/3419	Comorbid Skin Condition	67/3419
Case Load ≥ 72/year	1845/3419	Prior Transplant Surgery	12/3419
Age ≥ 55 years	2837/3419	Screen/Received Mupirocin	3058/3419
Age ≥ 65 years	1666/3419	*S. aureus* Colonized	586/3058
Comorbid Neurologic Condition	45/3419	MRSA Colonized	118/3058

Risk factors listed with number of patients identified possessing a specific risk factor out of total patients examined for the given risk factor.
BMI = body mass index; ASA = American Society Anesthesiologists; MRSA = methicillin resistant *S. aureus*.