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Factors Associated With 20-Year Cumulative Risk of Infection After Aseptic Index Revision Total Knee Arthroplasty

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ABSTRACT

Background: The purpose of this study was to calculate the cumulative risk of periprosthetic joint infection (PJI) after aseptic index knee revisions and to identify the surgical, perioperative, and medical comorbidity risk factors associated with deep infection.
Methods: We retrospectively reviewed 1802 aseptic index revision total knee arthroplasties performed at our institution from 1970 to 2000. From this cohort, there were 60 reoperations performed for deep infection.
Results: The cumulative risk of infection at 1, 5, 10, and 20 years after index revision was 1%, 2.4%, 3.3%, and 5.6%, respectively.
Conclusions: Male gender, use of constrained implants, increased operative times, increased Charlson Comorbidity Index, and a history of liver disease were all significantly associated with PJI. The development of cardiovascular disease, endocrine disorders, and renal disease were also associated with PJI.

Periprosthetic joint infection (PJI) is a devastating and quite costly complication after primary and revision total knee arthroplasty (TKA) [1]. It is estimated that the number of primary TKAs is expected to increase by >670% over the next 25 years with revision TKAs expected to also see a significant increase over the next several years [2]. Given these anticipated surgical volumes, there needs to be a more thorough understanding of the cumulative risks and risk factors associated with PJI after TKA.

Revision TKAs are known to have a higher risk of PJI than primary TKAs. [1,3,4]. PJI is often found to be the most common mode of failure after revision TKA [3,5-8]. The rates of infection after revision TKA vary within the literature, with rates being reported up to 46%. Unfortunately, many previous studies of PJI after revision TKA have included both septic and aseptic revisions and first-time revisions and multiple revised knees, which may explain the wide range in the reported risk of PJI in these studies [4,9,10]. The purpose of this study was to (1) identify the cumulative risk of PJI after aseptic index knee revisions; (2) identify surgical and medical risk factors at the time of index revision surgery associated with PJI; and (3) identify medical comorbidities that develop after index revision that may place a patient at increased risk of PJI.

Materials and Methods

From 1970 to 2000, there were 3487 revision TKAs performed in 2379 patients at our institution. This cohort included both patients who had their primary TKA performed at our institution and patients who were referred from different institutions. There were 1685 knees excluded from the final analysis because of previous knee revision, previous infection, use of a custom-type prosthesis, the use of noncondylar knee designs, or because the lack of documented institutional consent to participate in a research study. This left 1802 index knee revisions performed for aseptic reasons in the final cohort (1615 patients).

For each patient, the medical records were reviewed for surgical and demographic information at the time of the index revision TKA. This review included gender, age, body mass index (BMI), smoking status, classification score of the American Society of Anesthesiologists (ASA), reason for revision, operative time, anesthesia time, allogenic blood transfusion, antibiotic infusion timing with respect

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to the time of incision, and tourniquet time. In addition, data from our institution's total joint registry were used, which contains information on the types of prostheses used, complications of surgery, and patient clinical follow-up. These specific data are obtained from all clinical follow-up examinations in addition to total joint specific questionnaires that are given to patients as part of the standard total joint registry data collection protocol.

Medical comorbidities at the time of revision surgery were ascertained by reviewing all medical diagnostic codes in each patient's medical record. We identified unique medical codes and then grouped these into categories. These included diabetes, gastrointestinal disorders, autoimmune disorders, dementia, deep vein thrombosis, pulmonary embolus, cerebrovascular disease, cardiovascular disease, endocrine disorders, infection, leukemia, solid malignancy, metabolic bone disease, neurologic disorders, renal disease, liver disease, and pulmonary disorders. The Charlson Comorbidity Index was calculated from these medical diagnoses.

These same medical diagnoses were reviewed in a separate analysis looking at new medical diagnoses that each patient developed after index aseptic knee revision. Searching for new medical diagnostic codes that appear in the patients' record between the time of index revision surgery and most recent follow-up identified the new diagnoses that each patient developed. We then grouped these unique codes into groups as stated previously.

Using the total joint registry data and information from the medical records, we identified all reoperations or revisions after aseptic index knee revision. A reoperation was defined as any procedure in which the patient required general or regional anesthesia, and an incision was made. We then identified the reasons for each patient underwent a reoperation. There was a group of patients who underwent closed manipulation under general anesthesia that were not included in this reoperation group because of the lack of incision and were thus analyzed separately. Specifically, we identified those who had undergone a reoperation for PJI. A reoperation due to PJI was defined as a reoperation performed for positive bacterial culture from an aspiration and/or intraoperative cultures or for clinical suspicion of PJI. We also included those patients who had a reoperation performed for PJI at outside institutions that was reported by the patient in their follow-up or the surgeon who performed the reoperation provided documentation.

In the 1802 index knee revisions, the male-to-female ratio was 47%-53%, respectively. There was an even distribution of right- and left-sided knee revisions. The median BMI was 29.4 (range, 16.4-52.5). Fifty-six percent of the patients had primary TKAs performed at our institution with 44% having their primary TKA performed elsewhere. The median age of the patient at the time of index revision was 70 years (range, 22-92 years). The median time from primary TKA to index knee revision was 6.0 years (range, 0 days-28.8 years). The median time from index knee revision until reoperation or until the most recent follow-up was 9.9 years (range, 1 day-30.2 years). At the time of this most recent review, 980 of the knees were followed until the patient's death without any reoperation, and 376 knees were followed until undergoing additional reoperation as defined previously.

Statistical Analysis

The analysis was centered on the outcome of infection after aseptic index knee revision. The cumulative probability of PJI was calculated using Kaplan-Meier survival curves. The risk of PJI associated with patient demographics, surgical factors, and medical comorbidities was evaluated using Cox proportional hazards regression models. Because some patients contributed 2 observations each to the analysis cohort (ie, both right and left knees underwent aseptic revision), the robust sandwich estimate of the variance was used to properly account for the within-patient correlation. Medical comorbidities identified before the index knee revision surgery were analyzed in 2 ways: univariately as individual covariates and by calculating the Charlson Index. Comorbidities that were identified after the index revision surgery were incorporated into the proportional hazards regression models as time-dependent covariates. When necessary due to low event counts for some risk factors, Firth's penalized likelihood was used in the Cox models to minimize bias in the parameter estimates. All statistical tests were 2-sided, and the threshold of statistical significance was set at $\alpha = 0.05$. The analysis was conducted using SAS, version 9.2 (SAS Institute Inc, Cary, NC).

Results

Of the 1802 aseptic index revision knees, 375 (20.8%) underwent a reoperation during the study period. The 3 most common reasons for reoperation were extensor mechanism problems, loosening, and infection, respectively [7]. Seventy-five reoperations (20%) were performed for extensor mechanism problems, 70 (18.7%) for loosening, and 60 (16.0%) because of PJI.

The 60 reoperations for PJI occurred from 13 days to 18.6 years after revision. Of these 60 reoperations, 18 (30%) were within the first year after revision surgery, with 40 (67%) within 5 years and 50 (83%) within 10 years. Forty-two of these reoperations for PJI were performed at our institution, whereas the other 18 were performed elsewhere. The most common organisms isolated from these infected reoperations were *Staphylococcus aureus* (32%) and *Streptococcus* species (7%). There were 36 culture-positive infections, and 7 were culture-negative infections, with 17 reoperations performed elsewhere and it is unknown whether they were culture positive or negative.

The cumulative risk for undergoing a reoperation because of PJI at 1, 5, 10, and 20 years after index revision was 1% (95% confidence interval [CI]: 0.6-1.5), 2.4% (95% CI: 1.7-3.2), 3.3% (95% CI: 2.4-4.2), and 5.6% (95% CI: 3.7-7.4), respectively (see Fig. 1).

The analysis of surgical risk factors showed that an operative time of >180 minutes (hazard ratio [HR] = 1.7, 95% CI: 1.0-2.9, $P = .04$) and an anesthesia time of >240 minutes (HR = 1.9, 95% CI: 1.1-3.3, $P = .02$) were both associated with increased risk of undergoing reoperation for PJI. Implants with increased varus-valgus constrained or hinged implants were associated with an increased risk of reoperation for PJI (HR = 2.0, 95% CI: 1.2-3.4, $P = .01$; see Table 1). Not included in this group of reoperations, there were 60 knees that underwent closed manipulation under anesthesia after their index revision surgery, which was not associated with increased risk of infection (HR = 0.8, 95% CI: 0.2-3.1, $P = .7$).

Risk factors associated with specific patient characteristics and their medical comorbidities at the time of index knee revision surgery showed that increased age had a statistically significant protective effect with regard to reoperation for PJI (HR for 10-year increase in age: 0.70, 95% CI: 0.57-0.86, $P < .001$). The median time from index revision to reoperation for infection was 3.4 years for patients younger than 65 years at the time of index revision, whereas, it was 3.2 years for patients of 65 years and older which was not statistically significant ($P = .46$). Male gender had an increased risk of reoperation for PJI (HR 2.3, 95% CI [1.3, 3.9], $P = .002$). There was an increased risk of reoperation for PJI in those patients who had a history of liver disease at the time of index knee revision (HR = 3.1, 95% CI: 1.3-7.8, $P = .01$). Patients who had a Charlson Comorbidity Index score of ≥ 3 also showed an increased risk of reoperation for PJI (HR = 2.9, 95% CI: 1.1-7.4, $P = .03$) (see Table 2).

Medical comorbidities that the patients developed after undergoing revision surgery were analyzed separately from those