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Development and Evaluation of a Prognostic Calculator for the Surgical Treatment of Periprosthetic Joint Infection

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ABSTRACT

Background: Preoperative identification of patients at risk of failing surgical treatment for periprosthetic joint infection (PJI) is imperative to allow medical optimization and targeted prevention. The purpose of this study was to create a preoperative prognostic calculator for PJI treatment by assessing a patient's individual risk for treatment failure based on many preoperative variables.
Methods: A retrospective review was performed of 1438 PJIs, treated at 2 institutions from 2000 to 2014. Minimum follow-up was 1 year. A total of 63 risk factors, including patient characteristics, microbiology data, and surgical variables were evaluated using logistic regression, in which coefficients were scaled to produce weighted scores.
Results: The 10 significant risk factors for PJI treatment failure were in descending order of relative weight: irrigation and debridement (30 points), history of myocardial infarction (15 points), revision surgery (11 points), presence of sinus tract (10 points), resistant organisms (9 points), ever smoker (6 points), prior surgery (2.86 points per prior operation), synovial white blood cell count (8.3 $\times$ natural log of cell count), body mass index (0.66 per increment), and erythrocyte sedimentation rate (depends on both smoking and 2 stage, as these are higher order interaction factors). The area under the curve for this risk model was 0.6904 (95% confidence interval: 0.6476-0.7331).
Conclusion: In this large cohort study, we were able to identify risk factors and their relative weight for predicting PJI treatment failure. Some of the identified factors are indeed modifiable and should be addressed before treating a patient for PJI.

The population undergoing total joint arthroplasty is growing yearly and now covers a complex population over a large spectrum of ages. This has led to a surge in both the number and complexity of prosthetic joint infections (PJIs), a dreaded and costly complication of total joint arthroplasty. Patients with PJI often require numerous surgical interventions to control their condition and are at increased risk for mortality [1–4].

With interest in preventing the burden of PJI, several studies have attempted to identify the subset of population most at risk for developing PJI [5–12]. However, few studies have investigated risk factors for failure of surgical management of PJI, and even fewer have effectively elucidated the relative influence of such factors [13,14]. Furthermore, comparison of these studies is difficult because of heterogeneous definitions of infection, various postoperative antibiotic regimens, and a lack of agreement regarding treatment failure. There are very few studies in the literature that have developed predictive models, using nomograms, for probability of successful infection eradication based on the demographics and medical characteristics of the patient [13,14]. However, these are limited due to use of a single institution, the limited number of variables used in assessing treatment success, limited follow-up, and a limited or nonstandardized definition of treatment success. Thus, it is difficult to extrapolate these predictive models to the diverse population representative of the joint arthroplasty population. This may explain the lack of a universal preoperative

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prognosis predictor for PJI that is widely used in the orthopedic community.

An effective preoperative tool to quantify risk for treatment failure would guide surgeons in planning before surgery, including accurately explaining risk of failure during the consent process with patients and effectively intervening for medical optimization to increase the probability of treatment success. Preoperative knowledge of the probability that a treatment strategy will eradicate a patient's PJI is imperative for developing a strategy that will specifically target this patient. In the era of personalized medicine, treatment success targeted to the individual based on their specific factors and the surgical and medical factors involved would increase the utility of this strategy, ultimately reduce costs, and justify its clinical use. This is especially crucial given the morbidity and repeat surgeries associated with treating PJI.

To date, there is no calculator that exists for predicting treatment failure following surgical intervention for PJI. We aim to produce a prognostic calculator for prosthetic joint infection that is individually tailored to the patient based on their present comorbidities, type of procedure, cultured organism profile, and medical treatment, among other factors. By identifying the factors that influence the treatment of PJI, the physician would be able to individually assess and optimize the general medical condition of the patient.

Methods

After the institutional review board approval, a retrospective review was performed at 2 nonaffiliated institutions in distinct geographic regions. Logistic regression analysis was performed to create a statistical predictive model for PJI treatment success based on the previous variables and relative weighting for these factors were assigned.

A retrospective study of 1723 PJI cases performed between 2000 and 2014 at 2 institutions was conducted to create a PJI prognostic calculator and model. A total of 1438 PJI cases had a minimum of 1-year follow-up or failure. All patients who underwent surgical treatment for PJI were included in the analysis, and patients with a megaprosthesis or missing surgical or demographic data were excluded. Using an electronic database followed by a manual chart review, 63 potential variables, including patient demographics, comorbidities, microbiology data, and surgical variables were obtained (Appendix Table 1) including age, sex, race, joint, body mass index (BMI), type of surgical treatment (2-stage exchange, 1-stage exchange, irrigation and debridement [I&D]), PJI chronicity, cultured organisms, purulence, sinus tract, preoperative laboratory values (serum erythrocyte sedimentation rate, serum C-reactive protein [CRP], synovial fluid CRP, synovial fluid white blood cell count, synovial fluid polymorphonucleocyte percentage, synovial fluid leukocyte esterase, and hemoglobin), Charlson and Elixhauser comorbidities [15,16], alcohol abuse, drug abuse, tobacco use, cigarette pack years, psychoses, depression, anxiety, bipolar disorder, schizophrenia disorder, insurance (private vs government), American Society of Anesthesiologists score, number of prior open surgeries on that joint (including primary arthroplasty), last surgery (primary vs revision), total number of joint arthroplasties, bilateral PJI involvement, and treatment success based on the previously established Delphi criteria by Diaz-Ledezma et al [17] These criteria include (1) infection eradication characterized by a healed wound without pain or infection recurrence caused by the same organism strain, (2) no subsequent surgical intervention for infection after reimplantation surgery, and (3) no occurrence of PJI-related mortality. Patient demographics by institution are displayed in Table 1. Information regarding smoking and drug use were obtained from anesthesia reports. Psychiatric disorders were identified through International Classification of Diseases, Ninth Revision codes or patients actively taking antipsychotic medications, followed by a manual chart review to confirm diagnoses.

Table 1
Patient Demographics by Institution.

	Institution 1 (n = 819)	Institution 2 (n = 619)	*P* Value
Age (y)	64.3 ± 11.8	64.0 ± 12.3	.558
Sex			
Male	400 (48.8%)	328 (53.0%)	
Female	419 (51.2%)	291 (47.0%)	.123
Body mass index (kg/m^2)	31.7 ± 7.5	33.2 ± 9.0	<.001
Joint			
Hip	355 (43.3%)	118 (19.1%)	
Knee	464 (56.7%)	501 (80.9%)	<.001
Charlson index score (age adjusted)	3.5 ± 1.8	6.3 ± 2.8	<.001
Elixhauser index score	2.3 ± 1.4	3.3 ± 2.9	<.001

The diagnosis of PJI was then determined based on a cross-match with a prospectively collected institutional database created from querying International Classification of Diseases, Ninth Revision codes 996.6, 996.66, 996.67, 998.5, and 998.59. From this query, a manual review of the medical record was performed to confirm that surgery was further performed for PJI. PJI was defined by the International Consensus Meeting criteria [18]. Patients with inadequate data in our prospective PJI data registry were interviewed by telephone to collect the missing data. Additionally, information regarding the culture results from intraoperative tissue samples and the date of infection was extracted. Categories of organisms included resistant, atypical, polymicrobial, gram-positive, gram-negative, culture-negative, methicillin-sensitive *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, *Enterococcus* species, *Escherichia coli*, fungal, and acid-fast organisms. Atypical organisms comprised all organisms that are not among the 5 most commonly cultured organisms in PJI. Antibiotic-resistant organisms that were considered included vancomycin-resistant *Enterococcus*, methicillin-resistant *S aureus*, and methicillin-resistant *Staphylococcus epidermidis*.

All statistical analyses were performed with the use of R 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria) using the regression modeling strategies package for logistic regression. An initial logistic regression model was created using all potential predictors associated with an increased risk of PJI. Predictors were pruned from the logistic regression model based on the Akaike information criterion for one of the 2 reasons: either they were not statistically significant or their effect was negligibly small. After insignificant factors were removed, the model was refitted, and the regression coefficients from the final model were used to make a point system for risk of treatment failure. Points were assigned for each risk factor in the model by rescaling the regression coefficients by dividing the minimum absolute value among all coefficients and then multiplying each coefficient by a constant. The patient's risk score could then be computed as the aggregate number of points from the weighted risk factors. To assess the strength of the predictive model, an area under the receiver operating curve or area under the curve (AUC) analysis was performed. Prediction scores are typically considered acceptable if its AUC is 0.7, with an AUC of 0.5 representing a poor test (toss of a coin) and an AUC of 1.0 signifying a perfect test. In addition, calibration curves were also created to determine the model performance.

Results

Overall the treatment success rate was 62.2% (895/1438); stratified by procedure, it was 47.5% (242/509), 71.2% (79/111), and 70.2% (574/