

9-17-2014

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Mohammad R Rasouli

Rothman Institute of Orthopaedics, Thomas Jefferson University

Camilo Restrepo

Rothman Institute of Orthopaedics, Thomas Jefferson University, camilo.restrepo@rothmaninstitute.com

Mitchell Maltenfort, PhD

Rothman Institute of Orthopaedics, Thomas Jefferson University, mitchell.maltenfort@jeffersonhospital.org

James J Purtill

Rothman Institute of Orthopaedics, Thomas Jefferson University

Javad Parvizi

Rothman Institute of Orthopaedics, Thomas Jefferson University, parvj@aol.com

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Recommended Citation

Rasouli, Mohammad R; Restrepo, Camilo; Maltenfort, PhD, Mitchell; Purtill, James J; and Parvizi, Javad, "Risk factors for surgical site infection following total joint arthroplasty." (2014). *Rothman Institute*. Paper 55.

http://jdc.jefferson.edu/rothman_institute/55

Risk Factors for Surgical Site Infection Following Total Joint Arthroplasty

Mohammad R. Rasouli, MD, Camilo Restrepo, MD, Mitchell G. Maltenfort, PhD, James J. Purtill, MD,
and Javad Parvizi, MD, FRCS

Investigation performed at the Rothman Institute of Orthopaedics, Thomas Jefferson University, Philadelphia, Pennsylvania

Background: Currently, most hospitals in the United States are obliged to report infections that occur following total joint arthroplasty to the Centers for Disease Control and Prevention through the National Healthcare Safety Network surveillance. The objective of this study was to identify the risk factors of surgical site infections that were reported to the Centers for Disease Control and Prevention from a single institution.

Methods: For this study, 6111 primary and revision total joint arthroplasties performed from April 2010 to June 2012 were identified. Surgical site infection cases captured by infection surveillance staff on the basis of the Centers for Disease Control and Prevention definition were identified. Surgical site infection cases with index surgery performed at another institution were excluded. All cases were followed up for one year for development of surgical site infection. The model for predictors of surgical site infection was created by logistic regression and was validated by bootstrap resampling.

Results: Of all performed total joint arthroplasties, surgical site infection developed in eighty cases (1.31% [95% confidence interval, 1.02% to 1.59%]). The highest rate of surgical site infection was observed in revision total knee arthroplasty (4.57% [95% confidence interval, 2.31% to 6.83%]) followed by revision total hip arthroplasty (1.94% [95% confidence interval, 0.75% to 3.13%]). Among the variables examined, the predictive factors of surgical site infection were higher Charlson Comorbidity Index (odds ratio for a Charlson Comorbidity Index of ≥ 2 , 2.29 [95% confidence interval, 1.32 to 3.94] and odds ratio for a Charlson Comorbidity Index of 1, 2.09 [95% confidence interval, 1.06 to 4.10]), male sex (odds ratio, 1.79 [95% confidence interval, 1.11 to 2.89]), and revision total knee arthroplasty (odds ratio, 3.13 [95% confidence interval, 1.17 to 8.34]), and a higher level of preoperative hemoglobin (odds ratio, 0.85 per point [95% confidence interval, 0.73 to 0.98 per point]) was protective against surgical site infection. The C-statistic of the model was 0.709 without correction and 0.678 after bootstrap correction, indicating that the model has fair predictive power.

Conclusions: Low preoperative hemoglobin level is one of the risk factors for surgical site infection and preoperative correction of hemoglobin may reduce the likelihood of postoperative surgical site infection.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Peer Review: This article was reviewed by the Editor-in-Chief and one Deputy Editor, and it underwent blinded review by two or more outside experts. It was also reviewed by an expert in methodology and statistics. The Deputy Editor reviewed each revision of the article, and it underwent a final review by the Editor-in-Chief prior to publication. Final corrections and clarifications occurred during one or more exchanges between the author(s) and copyeditors.

Surgical site infection after total joint arthroplasty is a rare but devastating complication¹⁻³, with these infections still a major cause of morbidity in surgical patients⁴. Treatment of hospital-acquired infections poses a huge economic burden on health care^{5,6}. As part of the mission to reduce the burden of hospital-acquired infections, the

Centers for Disease Control and Prevention (CDC) has issued guidelines for the prevention of surgical site infection that are currently being updated⁷. In addition, the CDC requires all hospitals to report the hospital-acquired infections through the National Healthcare Safety Network (NHSN) surveillance program.

Disclosure: None of the authors received payments or services, either directly or indirectly (i.e., via his or her institution), from a third party in support of any aspect of this work. One or more of the authors, or his or her institution, has had a financial relationship, in the thirty-six months prior to submission of this work, with an entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work. No author has had any other relationships, or has engaged in any other activities, that could be perceived to influence or have the potential to influence what is written in this work. The complete **Disclosures of Potential Conflicts of Interest** submitted by authors are always provided with the online version of the article.

Risk factors for surgical site infection can be categorized into those relating to the patient's health status, those that relate to the surgical environment, and those that arise from clinical interventions increasing the patient's inherent risk. It is believed that identification of patient-related risk factors and their reversal in some cases can lead to a reduction in surgical site infection⁸. Although several studies have been performed to determine risk factors of surgical site infection following total joint arthroplasty^{1,9-13}, risk factors for surgical site infection as defined by the CDC and required to be reported have not been fully evaluated.

The objective of this case-control study was to determine the patient-related risk factors for surgical site infection following primary and revision total joint arthroplasty using an institutional database on joint arthroplasty and the data generated by the NHSN surveillance.

Materials and Methods

After obtaining approval of the institutional review board, this retrospective study was carried out at our institution and covered the time period from April 2010 to June 2012. During this time, 2718 total hip arthroplasties, 2549 total knee arthroplasties, 516 revision total hip arthroplasties, and 328 revision total knee arthroplasties were performed at our institution. Patients who were identified by the NHSN surveillance system as developing surgical site infection during the first year after the total joint arthroplasty were noted. Patients who did not have their index arthroplasty at our institution were excluded. The institutional database (TheraDoc Infection Control Assistant; TheraDoc, Salt Lake City, Utah), which includes detailed data related to surgery, microbiology and laboratory results, radiology reports, admission information, data from the pharmacy, and numerous other data points, was used to extract the pertinent information needed for this study. Information, including demographic characteristics, Charlson Comorbidity Index¹⁴, and laboratory and intraoperative data were obtained using our digital database. At our institution, we use the Charlson Comorbidity Index to assess underlying comorbidities. The Charlson Comorbidity Index consists of seventeen items as follows: myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular accident, pulmonary disease, connective tissue disorder, peptic ulcer, mild to moderate liver disease, and diabetes (each item has a score of 1 point); hemiplegia, diabetes with complications, renal disease, and cancer (each item has a score of 2 points); severe liver disease and metastatic cancer (each item has a score of 3 points); and acquired immunodeficiency syndrome (AIDS), which scores 6 points¹⁵. We queried our institutional database using codes from the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) to identify comorbidity items, which have previously been described¹⁵. Because we included age as an independent variable in the multivariate analysis, we did not adjust the Charlson Comorbidity Index for age.

In this database, all surgical site infection events are defined on the basis of the CDC/NHSN guideline⁷. At our institution, infection surveillance staff capture all surgical site infection cases in one of the following four ways: (1) an alert is sent to the surveillance center from the microbiology laboratory whenever an organism grows on culture when a culture specimen is taken from a patient; (2) an alert is issued when, within one year of the index arthroplasty, a patient is readmitted because of infection to Thomas Jefferson University Hospital; (3) an automatic check is in place to scan the operating room schedules and to detect the names of patients who had undergone arthroplasty within the preceding year; or (4) our institution is informed of patients readmitted to other facilities, as institutions are required to share this information with each other by The Joint Commission and Act 52 (the Medical Care Availability and Reduction of Error [MCARE] Act, which requires certain health-care facilities in Pennsylvania to report health care-associated infections to the Pennsylvania Department of Health, the Pennsylvania Health Care Cost Containment Council, and the Pennsylvania Patient Safety Authority through the CDC's NHSN). Once the surveillance center has been informed of patients with possible surgical site

infection, the clinical records of these patients are evaluated to confirm the diagnosis. Each orthopaedic surgeon receives a quarterly list of the patients with surgical site infection that is communicated to the CDC.

At our institution, routine infection prevention protocols are in place for patients undergoing elective arthroplasty that include skin cleansing with 4% chlorhexidine wipes twenty-four hours prior to surgery and administration of perioperative antibiotics within one hour of surgery and for twenty-four hours following the surgery.

Statistical Analysis

Because the number of surgical site infection events was relatively small, we only collected the variables, which were more likely to affect the development of surgical site infection. Only these variables were included in the logistic regression analysis to avoid the negative effect of including a large number of variables in the model when the number of events is small. The models were then systematically pruned using the Akaike information criterion (AIC)¹⁶, which combines model error with model complexity, until the AIC could not be further optimized. The model included an interaction term between the type of joint (knee or hip) and the type of surgery (primary or revision) to allow for revision hip arthroplasties and revision knee arthroplasties having different outcomes. Multiple imputation was used to compensate for 398 missing preoperative hemoglobin values out of the 6111 samples. When the model was rerun with only the complete cases, similar parameter values and significance resulted.

Bootstrap resampling, in which new data sets are randomly generated using the existing data, was used to validate the model by estimating the potential bias due to overfitting. The predictive power of the model was estimated by the C-statistic, also known as the area under the curve (AUC) in receiver operating characteristic (ROC) plots; an AUC of 1.0 is perfect prediction, and an AUC of 0.5 is equivalent to a coin flip. The C-statistic was adjusted downward on the basis of the bootstrap results to produce a bias-corrected estimate of the model's reliability.

Source of Funding

There was no external source of funding for this study.

Results

During the study interval, 6111 total joint arthroplasties were performed in 3414 women and 2697 men with a mean patient age (and standard deviation) of 63.0 ± 11.4 years. Surgical site infection developed in eighty cases (1.31% [95% confidence interval (CI), 1.02% to 1.59%]) during the period of study. The highest rate of surgical site infection was observed following revision total knee arthroplasty at 4.57% (95% CI, 2.31% to 6.83%). The incidence of infection was 1.94% (95% CI, 0.75% to 3.13%) after revision total hip arthroplasty, 1.18% (95% CI, 0.77% to 1.58%) after primary total hip arthroplasty, and 0.90% (95% CI, 0.54% to 1.27%) following primary total knee arthroplasty.

Surgical site infection developed in forty-three patients (1.10% [95% CI, 0.74% to 1.36%]) with a Charlson Comorbidity Index of 0, fifteen patients (1.17% [95% CI, 0.58% to 1.76%]) with a Charlson Comorbidity Index of 1, twelve patients (2.69% [95% CI, 1.1% to 4.19%]) with a Charlson Comorbidity Index of 2, and ten patients (3.44% [95% CI, 1.34% to 5.53%]) with a Charlson Comorbidity Index of ≥ 3 . Surgical site infection was observed in thirty-six women (1.05% [95% CI, 0.71% to 1.40%]) and forty-four men (1.63% [95% CI, 1.15% to 2.11%]). The highest rate of surgical site infection at 4.23% (95% CI, 0.92% to 7.53%) was in patients with a preoperative hemoglobin level of ≤ 10 g/dL. Patients with a preoperative hemoglobin level of 12 to 13 g/dL had the lowest rate of surgical site infection at 0.84% (95% CI, 0.35% to 1.34%).

TABLE I Results of Multivariate Analysis for Identifying Independent Variables of Surgical Site Infection

Variable	Odds Ratio*	P Value
Sex		0.01
Female	1 (Reference)	
Male	1.79 (1.11 to 2.89)	
Charlson Comorbidity Index		0.01
0	1 (Reference)	
≥2	2.29 (1.32 to 3.94)	
Preoperative hemoglobin level		0.03
≤10 g/dL	1 (Reference)	
12 to 13 g/dL	0.85 (0.73 to 0.98)	
Type of surgery		0.48
Primary total joint arthroplasty	1 (Reference)	
Revision total joint arthroplasty	1.30 (0.62 to 2.75)	
Type of primary total joint arthroplasty		0.29
Total hip arthroplasty	1 (Reference)	
Total knee arthroplasty	0.75 (0.44 to 1.29)	
Interaction between joint and surgery		0.02
Primary surgery and hip joint	1 (Reference)	
Revision surgery and knee joint	3.13 (1.17 to 8.34)	

*The values are given as the odds ratios, with the 95% CI in parentheses.

Multivariate logistic regression was used to examine potential predictors of surgical site infection, including age, sex, body mass index, unadjusted Charlson Comorbidity Index, month of surgery, type of surgery, and preoperative measurements of serum albumin, serum glucose, and hemoglobin. Among these, the predictive factors were higher Charlson Comorbidity Index (the odds ratios for the Charlson Comorbidity Index of ≥2 were 2.29 [95% CI, 1.32 to 3.94] compared with the Charlson Comorbidity Index of 0 and 2.09 [95% CI, 1.06 to 4.10] compared with the Charlson Comorbidity Index of 1), male sex (odds ratio, 1.79 [95% CI, 1.11 to 2.89]), and revision total knee arthroplasty (odds ratio, 3.13 [95% CI, 1.17 to 8.34]), and a higher preoperative hemoglobin level (odds ratio, 0.85 per point [95% CI, 0.73 to 0.98 per point]) was protective against the surgical site infection (Table I). The C-statistic or AUC of the model was 0.709 without correction and 0.678 after bootstrap correction for model optimism (200 bootstrap samples). These similar values indicate that there was very little bias because of overfitting and that the model has fair predictive power.

Discussion

Hospital-acquired infections place an immense economic burden on health-care costs^{1-3,5,6}. The CDC and other regulatory bodies have provided mandates and guidelines that are intended to reduce the burden of hospital-acquired infections. Part of the CDC mandate is the reporting of hospital-acquired infections through the NHSN surveillance system. Although several studies have been carried out to determine risk factors of surgical site infection in patients undergoing total joint

arthroplasty^{1,9-13}, the risk factors for developing surgical site infection, as defined by the CDC and NHSN criteria, have not been well established. The present study was conducted to identify all of the risk factors for surgical site infection following total joint arthroplasty in a single, high-volume arthroplasty center.

In the present study, using comprehensive arthroplasty as well as the surgical site infection database, the potential role of numerous risk factors for surgical site infection was evaluated. One of the strengths of this study was that detailed data on all patients who had undergone arthroplasty were collected in a prospective manner. Thus, as there were few missing data on the entire cohort, the intended analyses were allowed. Our infection surveillance center constantly updates the surgical site infection database and reports its findings to the CDC as mandated by the Commonwealth of Pennsylvania (Act 52). Thus, we are confident that the data set in this relatively large cohort enabled us to perform a meaningful analysis to identify the risk factors for surgical site infection. The detailed data collected from the patients with surgical site infection were compared with the entire cohort, and appropriate statistical analyses, including multivariate analyses, were performed. To avoid a negative effect of a small number of surgical site infections on the logistic regression analysis, only variables with the highest probability of effect on surgical site infection were entered into the model.

This study identified a number of risk factors for surgical site infection. Consistent with previous studies^{1,13,17,18}, this study also identified underlying comorbidities as a risk factor for surgical site infection following total joint arthroplasty. We utilized the Charlson Comorbidity Index to overcome the

limitation of other comorbidity scales such as the subjectivity of the American Society of Anesthesiologists (ASA) score. The undisputed association between medical comorbidities and the potential risk for surgical site infection highlights the need for optimization of these patients prior to surgery that may translate to a reduction in surgical site infection. One of the most important modifiable factors strongly associated with surgical site infection is preoperative anemia. This finding was in agreement with a prior study from our institution on 15,722 patients that also found anemia to be a predisposing factor for periprosthetic joint infection¹⁹. There are many reasons that may account for the higher incidence of surgical site infection in patients with anemia. The higher incidence of blood transfusion, with all its adverse effects such as immunomodulation, may be one of the main reasons for the association between preoperative anemia and subsequent surgical site infection^{18,20}. However, it should be pointed out that a hemoglobin level of ≤ 10 g/dL is very low and may indicate an underlying disease such as renal failure, inflammatory arthropathies, and malnutrition causing anemia, and it might not be possible to simply correct the hemoglobin level without addressing the underlying disorder. In the present study, we entered ASA score and Charlson Comorbidity Index in the multivariate model to adjust our findings for the possible effect of comorbidities on the surgical site infection. However, the preoperative hemoglobin level was still associated with a higher risk of surgical site infection, and its effect seems to be independent of patients' comorbidities.

In the present study, revision surgery in general and revision total knee arthroplasty in particular were associated with a greater risk of surgical site infection. The latter is in agreement with other studies and may be explained by the complexity of these cases, longer operative time, larger blood loss, and unrecognized and occult infections that led to the failure of these cases in the first instance^{17,21}.

This study, again in agreement with a previously published report¹⁷, found male sex to be a risk factor for surgical site infection. However, female sex was not a risk factor for surgical site infection. This phenomenon may be explained by the effect of sex hormones on the immune system in that estrogen enhances the immune function²² while testosterone suppresses the immune function^{22,23}. Moreover, variations in societal roles and differences in exposure to infecting organisms between men and women may also have an effect²².

This study had many strengths, including completeness of the database, a large consecutive cohort of primary and revision arthroplasty that allowed us to conduct a multivariate analysis, and the uniformity in our care protocols that minimized the confounding effect of issues such as perioperative antibiotics. Finally, this study utilized the CDC/NHSN defini-

tion of surgical site infection, which removes the variability that may exist in defining infection.

The study also had some limitations. Despite the availability of a comprehensive database, this retrospective study has the shortcomings of a study design such as nonuniformity of data collection and bias. Despite all efforts to capture every surgical site infection that occurred following total joint arthroplasty in this cohort, it is possible that some cases of surgical site infection seen and treated on an outpatient basis may have been missed. We believe that the latter is unlikely, as ordering of culture from any specimens would have led to the notification of the infection surveillance center. We included only variables with the highest probability of affecting surgical site infection in the model to avoid the potential negative effect that entering too many variables in the presence of a small number of events could have on the model. This might be considered as one of the limitations of this study; however, we used various statistical tests to make sure that the model output is accurate.

In conclusion, this study comprising a relatively large cohort of patients undergoing total joint arthroplasty at a single institution has identified various risk factors of surgical site infection. We recognized that a low hemoglobin level may be associated with other comorbidities and various states of chronic disease. As such, correcting a low hemoglobin level, in isolation, may not mitigate its apparent effect on the incidence of surgical site infection. To make a definitive statement, a study would be required evaluating the impact of preoperative optimization of hemoglobin in which one group had optimized preoperative hemoglobin and one group had preoperative hemoglobin that was not optimized. However, such a study may not be possible under current guidelines for human experimentation. As rigorous statistical analysis suggests that a low hemoglobin level is an independent risk factor, it is our current recommendation that a preoperative hemoglobin level of < 10 mg/dL be corrected directly or any identifiable underlying chronic disease be addressed, prior to total joint arthroplasty. ■

Mohammad R. Rasouli, MD
Camilo Restrepo, MD
Mitchell G. Maltenfort, PhD
James J. Purtill, MD
Javad Parvizi, MD, FRCS
Rothman Institute of Orthopaedics,
Thomas Jefferson University,
The Sheridan Building,
125 South 9th Street, Suite 1000,
Philadelphia, PA 19107.
E-mail address for J. Parvizi: research@rothmaninstitute.com

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