Influence of Preoperative Cardiovascular Risk Factor Clusters on Complications of Total Joint Arthroplasty

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Abstract

Identification of preexisting cardiovascular risk factors is important in projecting postoperative outcomes.

Using claims data for 16,317 patients who underwent total hip arthroplasty and/or total knee arthroplasty, we performed logistic regression and survival analysis to determine the effects of hypertension, diabetes, dyslipidemia, and obesity (both independently and in clusters) on incidence of myocardial infarction (MI), venous thromboembolism (VTE), and revision arthroplasty.

Our results indicated that diabetes (odds ratio [OR], 1.55; $P<.05$) and hypertension (OR, 1.56; $P<.05$) were independent risk factors for postoperative MI. Risk for MI increased significantly with the addition of each risk factor; there was a 128% increase in risk when all 4 cardiovascular risk factors were present (OR, 2.28; $P<.0001$). Risk for VTE did not change significantly with 1, 2, or 3 risk factors but reached statistical significance when all 4 risk factors were present (hazard ratio, 3.20; $P = .05$). There was no association between cardiovascular risk factors and incidence of revision arthroplasty.

Our analysis confirmed that diabetes and hypertension are risk factors for postoperative MI, but the respective significant and near significant increased risks for MI and VTE seen with cardiovascular risk factor clustering merit further evaluation of the role of metabolic syndrome in patients who undergo arthroplasty.

More than 400,000 total hip arthroplasties (THAs) and total knee arthroplasties (TKAs) are performed annually in the United States.[1] Although advances in implant materials and surgical techniques have resulted in more than 95% survivorship of THAs and TKAs,[2] investigators recently have identified optimization of preoperative health as leading to further improvement in patient outcomes. Medical comorbidities lead to a variety of poor outcomes, including mortality,[3-5] deep and superficial infections,[6,7] aseptic loosening of hardware,[8,9] postoperative complications,[10-12] non-homebound discharge,[11] and lower patient satisfaction.[13] Although many of these studies were limited by their small sample sizes, lack of control for confounding variables, and varying outcome measures, Jain and colleagues[11] rigorously designed their evaluation of the US Nationwide Inpatient Sample to overcome these limitations. They reviewed almost 1 million patients who underwent THA, TKA, or total shoulder arthroplasty and found that hypertension, diabetes, and obesity conferred an increased risk for postoperative complications and non-homebound discharge. They also found that any 2 of these risk factors further increased the risk for suboptimal outcomes. However, they evaluated only immediate postoperative in-hospital outcomes, such as postoperative infection, nonhealing wounds, pulmonary embolus, thrombophlebitis, and vascular complications.

In insulin-resistant patients, a cluster of risk factors for cardiovascular disease was first described in the late 1980s.[14] This cluster was later characterized as "metabolic syndrome" by the World Health Organization and by the US National Heart, Lung, and Blood Institute in its "Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)."[15] The ATP III definition includes abdominal obesity, atherogenic dyslipidemia, hypertension, insulin resistance with or without glucose intolerance, proinflammatory state, and prothrombotic state.[16] Although this definition and the classification of this risk factor cluster as a syndrome are not universally accepted by the medical community, diagnosing metabolic syndrome is thought by most to be an important factor in determining a person's risk for cardiovascular disease. Ten percent to 25% of the US population carries a diagnosis of metabolic syndrome, which confers increased risk for incident cardiovascular disease and all-cause mortality.[17-19] Although the high incidence of metabolic syndrome suggests that this syndrome may be an important factor in outcomes of surgical procedures, the relationship has

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Table I. Demographic Characteristics and Number of Preexisting Cardiovascular Risk Factors for Total Joint Arthroplasty Patients by Type of Surgery

Parameter	All Patients (N = 16,317)	TKA (n = 10,961)	THA (n = 5291)	TKA + THA (n = 65)
Mean (SD) age, y	64.8 (11.5)	65.2 (10.7)	64.1 (13.0)	65.1 (10.5)
Female, %	60.1	63.0	54.2	63.1
No. of preoperative risk factors, %				
0	37.6	34.7	43.8	35.4
1	35.7	36.1	34.8	41.5
2	20.0	21.4	17.0	16.9
3	6.0	7.0	4.0	4.6
4	0.7	0.8	0.4	1.5

Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty.

Table II. Adjusted Odds Ratio (OR) and 95% Confidence Interval (CI) for Myocardial Infarction by Individual Cluster of Cardiovascular Risk Factors[a]

Risk Factor(s)	Adjusted OR	95% CI
All 4 risk factors	2.3	1.6-4.5
Diabetes	1.5	1.1-2.1
Hypertension	1.6	1.4-1.8
Obesity	1.4	0.9-2.1
Diabetes, hypertension	2.1	1.7-2.5
Hypertension, obesity	1.3	0.9-1.8
Hypertension, dyslipidemia	1.4	1.2-1.7
Diabetes, hypertension, dyslipidemia	2.1	1.7-2.7
Diabetes, hypertension, obesity	1.7	1.1-2.5

[a]Logistic regression models adjusted for age, sex, and type of procedure.

not been reported extensively.[20] Kasai and colleagues[21] found increased risk for postprocedure cardiac events in patients who had metabolic syndrome and underwent percutaneous coronary intervention, but few other studies of a possible association between postprocedure outcomes and metabolic syndrome have been reported.

A better understanding of the impact of preexisting cardiovascular risk factors on surgical outcomes may be of importance in efforts to optimize both the preoperative health and postoperative course of surgical patients. In the study reported here, we examined the potential association between specific clusters of cardiovascular risk factors and outcomes of THAs and TKAs. We hypothesized that there would be an additive effect of hypertension, diabetes, dyslipidemia, and obesity on the postoperative occurrence of myocardial infarction (MI), venous thromboembolism (VTE), and revision arthroplasty in patients who underwent total joint arthroplasty (TJA).

Methods

Study Population

We retrospectively analyzed data from a database of a large health benefits company encompassing approximately 3.5 million covered members who were enrolled in health maintenance organization, preferred provider organization, Medicare, or Medicaid health plans. Two electronic databases, a member file including demographic information for each member per encounter (age, sex, type of insurance) and a medical file including up to 5 recorded *International Classification of Diseases, Ninth Revision* (*ICD–9*) codes per encounter, were merged for this analysis.

We identified all members, aged 18 years or older, having a medical claim between May 1, 2002 and April 1, 2008 with a *Current Procedural Terminology* (*CPT*) code of 27447 (TKA) or 27130 (THA). These patients' cardiovascular risk factors were identified in the 3 months before the index date using *ICD–9* codes for diabetes, hypertension, abnormal lipid panel, and obesity. A 2005 study showed that using *ICD–9* codes to determine risk factors for common cardiovascular diseases and stroke had 96% specificity and 95% positive predictive value but low sensitivity (76%).[20]

The date of each member's first CPT code for TKA or THA was considered that member's index date. Patients with a diagnosis related group–defined diagnosis of MI, VTE, or revision hip or knee arthroplasty after the date of initial THA or TKA were identified. The date of the postoperative event, which was available only for VTE and revision arthroplasty, was also recorded.

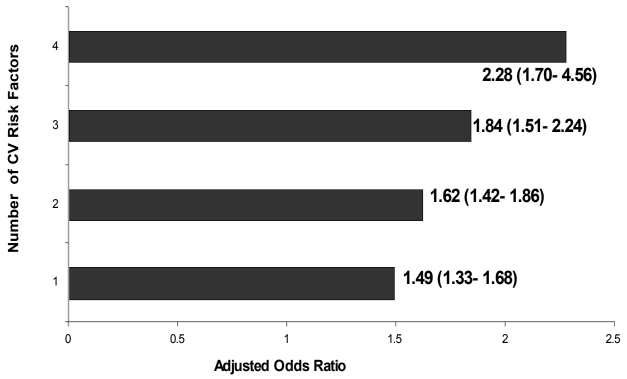

Figure 1. Results of logistic regression analyses of the number of preexisting cardiovascular (CV) risk factors and the risk of postoperative myocardial infarction in total arthroplasty patients shown as adjusted odds ratios and 95% confidence intervals. Regression models adjusted for gender, age, and type of procedure.

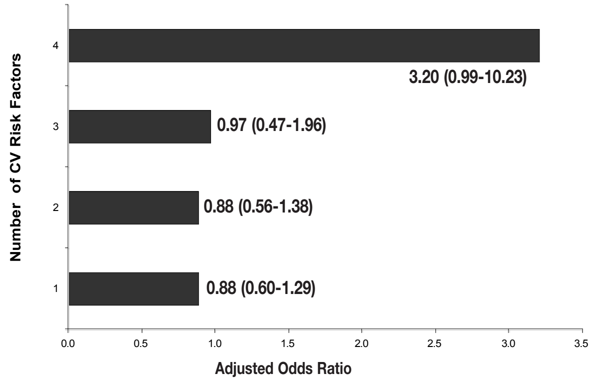

Figure 2. Results of logistic regression analysis of the number of preexisting cardiovascular (CV) risk factors and the risk of postoperative venous thromboembolism in total arthroplasty patients shown as adjusted odds ratios and 95% confidence intervals. Regression models adjusted for gender, age, and type of procedure.

Final date of follow-up was April 1, 2008. The study received a statement of exemption from review from the University of Miami institutional review board.

Definitions

Mutually exclusive groups of *ICD–9* codes were defined according to number of cardiovascular risk factors in a given patient. For example, a patient with obesity and diabetes was placed in the 2-risk-factor group, whereas a patient with diabetes, obesity, hyperlipidemia, and hypertension was placed in the 4-risk-factor group. The contribution of each risk factor alone to the outcome was also examined. In addition, the patients were classified into 1 of the 13 possible mutually exclusive cardiovascular risk factor combinations (clusters) for a separate analysis.

Statistical Analysis

Individual Cardiovascular Risk Factors. Separate bivariate logistic regression models were created for each of the postoperative outcomes (MI, VTE, revision arthroplasty) with outcome set as the dependent variable. Four logistic regression models were created for each outcome with each cardiovascular risk factor (diabetes, hypertension, dyslipidemia, obesity) included as a covariate with age and sex. All 3 covariates were entered in a blockwise manner. An odds ratio (OR) for the likelihood of an outcome occurring was calculated as the exponent of the β coefficient of the risk factor.

Number of Cardiovascular Risk Factors for MI. Because time-to-event data were unavailable for MI, a logistic regression model was created with MI as the dependent variable. Age, sex, type of procedure (THA, TKA, both), and number of cardiovascular risk factors (0, 1, 2, 3, 4) were entered as covariates in a blockwise manner. An OR with a 95% confidence interval (CI) for the likelihood of MI was calculated as the exponent of the β coefficient of the type of risk factor cluster.

Number of Cardiovascular Risk Factors for VTE and Revision. As time-to-event data were available for VTE and revision arthroplasty, we performed a survival analysis using 2 separate Cox proportional hazards regression models. In patients who experienced an event, the date of the event was used to calculate survival time; in patients who did not experience an event, data were censored at April 1, 2008 (last date of follow-up). Age, sex, type of procedure (THA, TKA, both), and number of cardiovascular risk factors (0, 1, 2, 3, 4) were entered as covariates in a blockwise manner. A hazard ratio (HR) with a 95% CI for the likelihood of an outcome occurring was calculated as the exponent of the β coefficient of the type of risk factor cluster.

Cardiovascular Risk Factor Clusters. As mentioned, each patient was placed into 1 of 13 mutually exclusive cardiovascular risk factor clusters representing all possible combinations, except for the 14th combination of all risk factors, which was already examined. Separate logistic regression (for MI) and Cox proportional hazards regression (for VTE and revision arthroplasty) were created with age, sex, type of procedure, and all 14 clusters entered into the model in a blockwise manner. Clusters with $P>.10$ were eliminated from the model in a backwards stepwise manner. ORs (for logistic regression) and HRs (for Cox regression) for the likelihood of an outcome occurring were calculated as the exponent of the β coefficient of the type of risk factor cluster. For all analyses, statistical significance was set at $P<.05$. All statistical analyses were performed using the SPSS 15.0 statistical software package (SPSS, Chicago, Illinois).

Results

Baseline Characteristics

We analyzed 16,317 TJA cases (Table I): 10,961 TKA (67.2%), 5291 THA (32.4%), and 65 TKA-plus-THA

(0.4%). Mean (SD) age of patients was 64.8 (11.5) years (range, 18-102 years). Most (60.1%) of the patients were female. Fewer than half (37.6%) of the patients had no cardiovascular risk factors, 35.7% had 1 risk factor, 20% had 2 risk factors, 6% had 3 risk factors, and 0.7% had 4 risk factors. Mean follow-up (index date to April 1, 2008) was 48 months (range, 24-71 months).

Crude Event Rates

Myocardial infarction was the most common postoperative outcome, occurring in 1966 of the 16,317 patients (12%). VTE occurred in 148 patients (0.9%), and revision arthroplasty was performed in 300 patients (1.8%). Mean (SD) time to VTE was 297.6 (88.8) days, and mean (SD) time to revision arthroplasty was 352.8 (343.2) days.

Event Risks for Individual Cardiovascular Risk Factors

Logistic regression modeling for individual risk factors, adjusted for age and sex, showed that MI was significantly associated with preoperative hypertension (OR, 1.56; 95% CI, 1.41-1.73) and diabetes (OR, 1.55; 95% CI, 1.37-1.75). Dyslipidemia and obesity were not associated with increased risk for postoperative MI. None of the 4 cardiovascular risk factors in this study were individually associated with increased risk for postoperative VTE or revision arthroplasty.

Event Risks by Number of Preexisting Cardiovascular Risk Factors

Logistic regression analysis showed increased risk for MI, adjusted for age, sex, and procedure, associated with 1 to 4 preexisting cardiovascular risk factors (Figure 1). Adjusted OR for MI was 1.49 (95% CI, 1.33-1.68) with 1 cardiovascular risk factor, 1.62 (95% CI, 1.42-1.86) with 2 cardiovascular risk factors, 1.84 (95% CI, 1.51-2.24) with 3 cardiovascular risk factors, and 2.28 (95% CI, 1.70-4.56) with all 4 cardiovascular risk factors.

Cox proportional hazards regression modeling, adjusted for age, sex, procedure, and number of risk factors, showed no increase in risk for VTE with 1 to 3 preexisting cardiovascular risk factors (Figure 2). Presence of all 4 cardiovascular risk factors approached a statistically significant increase in likelihood of postoperative VTE (HR, 3.20; 95% CI, 0.99-10.23; $P = .05$).

Cox proportional hazards regression modeling for risk of requiring revision arthroplasty, adjusted for age, sex, procedure, and number of cardiovascular risk factors as covariates, showed no association with presence of any number of cardiovascular risk factors.

Event Risks by Cluster of Cardiovascular Risk Factors

Logistic regression modeling for MI, adjusted for age, sex, type of procedure, and risk factor clusters, showed a significantly increased risk in the presence of 9 of the 13 clusters not already examined (Table II). The highest risk was associated with the cluster of diabetes and hypertension (OR, 2.1; 95% CI, 1.7-2.5) and the cluster of diabetes, hypertension, and dyslipidemia (OR, 2.1; 95% CI, 1.7-2.7). Separate Cox proportional hazards regression models, adjusted for age, sex, type of procedure, and risk factor cluster, showed no increase in risk for VTE and revision arthroplasty in any of the 13 risk factor clusters.

Discussion

In this study, we evaluated the association of preoperative cardiovascular risk factors, individually and in clusters, with MI, VTE, and revision arthroplasty after THA and TKA. Although the relationship between preoperative comorbidities and postoperative outcomes already has been evaluated,[3-13] most of the studies had important methodologic limitations that reduced the generalizability of their findings. We believe that the present study is the first to identify an association between specific clusters of cardiovascular risk factors and long-term postsurgical outcomes in a very large population of patients who underwent THA and/or TKA.

Of the 4 study-defined cardiovascular risk factors, only diabetes and hypertension were found to be significant independent risk factors for postoperative MI. These same risk factors were associated with short-term postarthroplasty morbidities, as reported by Jain and colleagues.[11] Of note, our analysis showed that risk for postoperative MI rises with an increase in the number of cardiovascular risk factors. Although neither dyslipidemia alone nor obesity alone was significantly associated with increased risk for MI, each of these risk factors was associated with increased risk for MI in the presence of diabetes or hypertension. Presence of diabetes in each of the 4 most hazardous risk factor clusters for postoperative MI supports the hypothesis that the pathophysiologic pathway of insulin resistance portends a poor prognosis in these patients. This idea is consistent with the finding, by Gandhi and colleagues,[22] that diabetes was a significant predictor of MI in the first days after TJA. Although metabolic syndrome already has been shown to be a risk factor for cardiovascular events,[17-19] it is possible that the physiologic insult of surgery may accelerate or potentiate the pathophysiologic process resulting in an acute MI in patients with metabolic syndrome.

Kikura and colleagues[23] described the elevated risk for arterial and venous thromboembolic events in the perioperative period for a variety of general, orthopedic, and thoracic surgical interventions in patients with cardiac and metabolic comorbidities. Consequently, it is distinctly plausible that the perioperative acute thromboembolic syndrome described by Kikura and colleagues may be a manifestation of metabolic syndrome in the surgical population. This theory was first posited by Saad and colleagues,[24] who described a single case of fatal fat embolism after TKA in a patient with diabetes, hypertension, and obesity—3 of the factors comprising metabolic syndrome. We found that risk for postoperative VTE significantly increased in patients with all 4 cardiovascular risk factors associated with metabolic syndrome. It is possible that the proinflammatory and prothrombotic milieu favoring the formation of venous thromboemboli may not manifest clinically until abnormal glucose metabolism, hypertension, dyslipidemia, and obesity are all present.[25]

Our study had several limitations. Most notably, we had no direct measurement of cardiovascular risk factors and relied on the surrogate obesity, hypertension, dyslipidemia, and hyperglycemia information found in claims data. However, identification of cardiovascular risk factors from administrative databases has been found to have 96% specificity and 95% positive predictive value.[26] In addition, data regarding other factors that may influence arthroplasty outcomes—including patient ethnicity, medical comorbidities other than cardiovascular risk factors, reasons for revision arthroplasty, and hospital and surgeon TJA volume—were not available for this analysis. Medication data, also unavailable, may have been helpful in establishing the influence of chemoprophylaxis on the occurrence of postoperative thromboemboli. In addition, mean time to VTE was 297.6 days, which is beyond the time frame in which postoperative events are usually captured.[22] The extended time frame in which VTE events occurred in our study is not consistent with classic postoperative VTE pathophysiology, but may be related to a longer term effect of cardiovascular risk factor clustering. In addition, time-to-event data for MI were not available because of database limitations, which precluded us from completing a true survival analysis for this outcome. This limitation prevents us from classifying postoperative events within a traditional perioperative window of time and from comparing our data with data from other investigations of MI after TJA.[22,26] Finally, the dataset did not include other long-term functional outcomes of importance—strength, range of motion, ambulation, and satisfaction.

Although our findings show the importance of identifying cardiovascular risk factors in the preoperative period, we were unable to investigate the severity of each risk factor and the impact of severity on postoperative outcomes. In addition, we were unable to gauge the significance of pharmacologic and lifestyle therapy for each risk factor to possibly reduce the risk for postoperative complications. Both are areas for future investigation. Furthermore, studies should be conducted to address whether aggressive care should be given to patients with clustering of cardiovascular risk factors.

With there being more than 400,000 TJAs performed annually in the United States, identification of potentially modifiable preoperative risk factors has important implications for both improving patient outcomes and controlling the health care costs associated with these procedures and subsequent morbidities. From our results, it is clear that diabetes and hypertension are important independent risk factors for serious postarthroplasty cardiovascular complications and that increasing numbers of these risk factors are associated with increased risk for postoperative MI and VTE. Our findings emphasize the importance of preoperative evaluation of potential TJA patients for cardiovascular risk factors and metabolic syndrome. The results of these evaluations can inform appropriate preoperative interventions as well as decisions regarding the selection of the optimal procedure to optimize outcomes in patients with substantial hip or knee disease requiring surgery. Long-term follow-up of these patients is needed to better characterize the type, incidence, and causes of significant postoperative morbidities.

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This paper will be judged for the Resident Writer's Award.