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Does Sickle Cell Disease Increase Risk of Adverse Outcomes Following Total Hip and Knee Arthroplasty? A Nationwide Database Study

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ABSTRACT

Sickle cell disease (SCD) is associated with impaired vascular function and progressive vaso-occlusive injury to bones. We used the Nationwide Inpatient Sample to identify all THA and TKA admissions between 1998 and 2010. After controlling for patient age, gender, insurance, race, and comorbidities, the risk of complication among admissions with SCD was 152% higher ($P < 0.001$) for THA and 137% higher ($P = 0.001$) for TKA. Patients with SCD had a length of stay that was 42% longer ($P < 0.001$) for THA and 20% longer for TKA ($P < 0.001$), and hospital charges that were 19% higher ($P < 0.001$) for THA and 16% higher ($P = 0.001$) for TKA. Orthopedic surgeons should counsel potential THA and TKA candidates with SCD of these risks prior to admission.

Sickle cell disease (SCD), the most common congenital hemoglobinopathy in the United States, affects more than 90,000 Americans and 1 in every 500 African-Americans [1]. Sickle cell disease is an inheritable condition that is characterized by a single missense mutation on the beta globin gene and can present as homozygous hemoglobin S (HbSS) or compound heterozygous hemoglobin S (HbSC or HbS-thalassemia) [2]. Irrespective of genotype, the expression of one HbS allele in compound heterozygotes makes individuals with SCD more prone to intracellular red blood cell polymerization in physiological states of low oxygen, which can ultimately result in vaso-occlusion, tissue ischemia and osteonecrosis [2,3]. Bone microcirculation is a common site for red blood cell sickling, and clinical presentation is characterized by severe localized pain with associated edema and erythema [4]. Infarction of the cancellous trabeculae of the femoral head is a frequent complication of SCD in adults, with as many as 50% of patients with SCD suffering from femoral head osteonecrosis by the age of 35 [5]. Sickle cell disease is also a risk factor for osteonecrosis of the knee, specifically at the femoral condyles and tibial plateau, with an incidence of 10% among patients with SCD [6]. Despite the use of joint-preserving surgical interventions including core decompression, osteotomy and bone grafting, many patients with SCD progress to advanced osteonecrosis requiring total joint arthroplasty [4,6].

Modern surgical techniques and hardware, drug therapy including hydroxyurea, and stem cell transplantation have brought dramatic improvements to the quality of life and life expectancy among patients with SCD, with many living comfortably into the seventh decade [6,7]. Despite these advances, however, patients with SCD remain high-risk surgical candidates. The stress from surgical procedures can stimulate cytokine release and lead to hypoxia, hypoperfusion and acidosis, an environment that promotes red blood cell sickling and subsequent occlusion of microcirculation [8,9]. Preoperative red blood cell transfusion has been investigated as prophylaxis against sickling crises, but postoperative complication rates among this population are estimated to be as high as 30% even after preoperative transfusion [10].

Current data on short-term outcomes following total hip arthroplasty (THA) and total knee arthroplasty (TKA) are limited to small cohort studies. Our study sought to examine differences in risk of perioperative complication, length of stay and hospital charges between patients with and without SCD who were admitted for THA or TKA between 1998 and 2010 in the United States. In secondary analyses, we studied the effects of concomitant osteonecrosis and transfusion during admission on these outcomes.

Methods

Study Population

The Nationwide Inpatient Sample (NIS) is the largest all-payer inpatient care database in the United States. Each year, the NIS compiles

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records of roughly 8 million hospital stays across nearly 1000 hospitals, creating a 20% representative sample of annual U.S. hospital admissions [11]. Each patient discharge record contains demographic and clinical data, including ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) diagnosis and procedure codes. The NIS also provides discharge weights, based on the size and location of the hospital where each admission occurred, to allow researchers to calculate nationwide estimates of patient discharges. This database has been found to represent 96% of the U.S. population [12].

Cases

Admissions who received a primary total hip arthroplasty (THA) or total knee arthroplasty (TKA) between the years of 1998 and 2010 were identified using ICD-9-CM procedure codes for THA (81.51, 00.74, 00.75, 00.76, 00.77) and TKA (81.54). Patients with diagnosis codes indicating pathological fracture, malunion of fracture, traumatic femoral neck fracture, and long-term mechanical loosening associated with revisions were excluded, as these admissions are predominantly non-elective [13].

Outcomes

Perioperative complications were assessed using ICD-9-CM diagnosis codes as defined by a recent study of orthopedic-related complications [13]. We defined a "major complication" as having acute renal failure, death, myocardial infarction, pneumonia, pulmonary embolism, stroke, or tachycardia during admission. We defined a "minor complication" as having deep vein thrombosis, implant infection, implant dislocation, irrigation and debridement, sepsis, urinary tract infection, wound hemorrhage, wound disruption, or wound infection during admission [14].

For each admission, we also extracted data on length of stay and total hospital charges. Due to the right skew of these variables, we used a log transformation to increase the normality of their distributions.

Covariates

We used ICD-9-CM diagnosis codes to identify THA and TKA admissions that had sickle cell disease (282.41, 282.42, 282.60, 282.61, 282.62, 282.63, 282.64, 282.68, 282.69), and classified all other admissions as not having sickle cell disease [15]. Diagnosis codes were also used to identify patients with osteonecrosis (733.4, 733.40, 733.42, 733.43, 733.49) and procedure codes were used to identify admissions requiring transfusion of red blood cells (99.00, 99.01, 99.01, 99.03, 99.04). We extracted demographic data on each admission including age (in years), gender, race (white, black, Hispanic, other), insurance (Medicare, Medicaid, private, other), and year of admission (1998–2010). We assessed comorbidities using the Charlson and Deyo method for ICD-9-CM coding [16], which uses a weighted scoring system to predict the ten-year mortality for patients based on their comorbidities. One point is assigned to congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, past myocardial infarct, or uncomplicated diabetes. Two points are assigned to hemiplegia or paraplegia, renal disease, malignancy including leukemia and lymphoma, or diabetes with end organ damage. Three points are assigned to moderate or severe liver disease, while six points are assigned to metastatic solid tumor, or HIV/AIDS. Patients with no comorbidities are given a score of zero points [16].

Statistical Analysis

We used logistic regression (proc surveylogistic) to calculate the odds ratio (OR) of having a perioperative complication during the course of admission. We used linear regression (proc surveyreg) to calculate parameter estimates for mean length of stay and mean total charges of admission. We interpreted the results of our linear regressions as percent differences, using the formula $100^*(e^b - 1)$, where b is the regression coefficient of a log-transformed outcome variable [17]. Our regression models were adjusted for the confounding effects of age, gender, race, insurance type, and Deyo comorbidity score. Admissions with missing age (THA = 3,287; TKA = 4,194), gender (THA = 8,786; TKA = 13,467), race (THA = 678,604; TKA = 1,402,920), and insurance (THA = 4,568; TKA = 10,784) could not be included in multivariable regression models. However, to rule out the possibility that the exclusion of this subset of admissions with missing demographic data biased our results, we also performed sensitivity analyses on our data, where we removed each covariate from our regression model, thereby including all patients with missing demographic data. We also used regression models with SCD (no, yes) as the outcome variable, and age, sex, race, insurance, comorbidities, osteonecrosis and transfusion as independent predictor variables, to assess the effect size of each demographic variable. We used weighting variables in all our analyses to simulate national U.S. rates of THA and TKA admission.

All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina). All P-values were two-tailed, and $P < 0.05$ was interpreted as statistically significant. All figures were generated using Microsoft Excel 2010 (Microsoft Corporation, Redmond, Washington).

Results

After exclusions, our study population consisted of 3,532 patients with SCD and 2,653,653 patients without SCD admitted for THA, as well as 724 patients with SCD and 5,660,896 patients without SCD admitted for TKA. Relative to the number of total admissions for THA and TKA, the proportion that had SCD remained steady during the study period. Between 1998 and 2010, there were 1.33 THA admissions with SCD per 1,000 total THA admissions ($m = -0.10$, $r = 0.64$, $P = 0.025$), while there were 0.13 TKA admissions with SCD per 1,000 total TKA admissions ($m = 0.01$, $r = 0.75$, $P = 0.003$) (Fig. 1).

For both THA and TKA, patients with SCD were more likely to be younger (THA: $P < 0.001$; TKA: $P < 0.001$), were more likely to be female (THA: $P = 0.003$; TKA: $P = 0.002$), were more likely to be black (THA: $P < 0.001$; TKA: $P < 0.001$), and were more likely to pay with Medicaid (THA: $P < 0.001$; TKA: $P < 0.001$). For THA but not TKA, fewer patients with SCD had a Charlson and Deyo score of 1 ($P < 0.001$) and ≥ 2 ($P < 0.001$). Osteonecrosis was observed in 87% of THA and 25% of TKA patients with SCD, compared to 11% of THA patients and 1% of TKA patients without SCD (THA: $P < 0.001$; TKA: $P < 0.001$). Blood transfusion was performed in 52% of THA and 47% of TKA admissions with SCD,

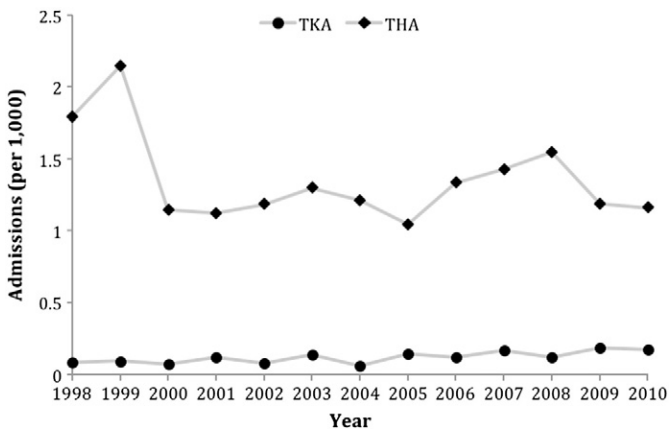

Fig. 1. Number of patients with sickle cell disease per 1000 admissions for THA and TKA (1998–2010).