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Does Hemophilia Increase the Risk of Postoperative Blood Transfusion After Lower Extremity Total Joint Arthroplasty?

Bhaveen H. Kapadia, MD [a], Matthew R. Boylan, ScB [a, b], Randa K. Elmallah, MD [c], Viktor E. Krebs, MD [d], Carl B. Paulino, MD [a], Michael A. Mont, MD [c, *]

[a] Department of Orthopaedic Surgery, SUNY Downstate Medical Center, Brooklyn, New York
[b] Department of Epidemiology and Biostatistics, SUNY Downstate Medical Center, Brooklyn, New York
[c] Center for Joint Preservation and Reconstruction, Rubin Institute for Advanced Orthopedics, Sinai Hospital of Baltimore, Baltimore, Maryland
[d] Department of Orthopaedic Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio

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ABSTRACT

Background: Hemophilia can lead to the development of arthropathies secondary to recurrent hemarthroses. However, given these patients' bleeding tendencies, postoperative complications associated with blood loss are a considerable concern.
Methods: We identified men in the Nationwide Inpatient Sample who underwent total hip or knee arthroplasty between January 1998 and December 2010. We used propensity scores to match 332 hemophiliacs (267 hemophilia A, 65 hemophilia B) to a comparison cohort of 996 patients in a 1:3 ratio, according to the site of arthroplasty, year of admission, age, race, and Charlson and Deyo score.
Results: The incidence of any postoperative transfusion was 15.06% for hemophiliacs, compared with 9.84% for the matched comparison cohort ($P = .012$). For hemophiliacs, the odds ratio was 1.60 (95% confidence interval [CI] = 1.11-2.31; $P = .013$) for any transfusion, 1.90 (95% CI = 1.24-2.92; $P = .003$) for allogenic transfusion, and 1.05 (95% CI = 0.56-1.95; $P = .888$) for autogenic transfusion.
Conclusion: Hemophilia is associated with an increased risk of blood transfusion after lower extremity total joint arthroplasty. Patients and providers should discuss these risks before surgery, and insurers should consider incorporating this comorbidity into bundled payments for total hip and knee arthroplasty.

Hemophilia is an inherited bleeding disorder caused by insufficient production of clotting factors of the intrinsic coagulation pathway. In the United States, the prevalence of this X-linked recessive condition is 13.4 cases per 100,000 males, with 10.5 cases of hemophilia A and 2.9 cases of hemophilia B [1]. Patients with this bleeding diathesis are predisposed to musculoskeletal problems, including muscular hematoma, joint contracture, and hemarthrosis. Recurrent bleeding into joint spaces can lead to chronic synovitis and progressive cartilage destruction, ultimately resulting in hemophilic arthropathy [2-4]. The resulting swelling, pain, flexion contracture, and recurrent bleeding associated with arthropathy may be refractory to nonoperative management and are often indications for lower extremity total joint arthroplasty (TJA), such as total hip arthroplasty (THA) or total knee arthroplasty (TKA).

Lower extremity TJA has been successful in improving function and relieving pain in patients afflicted with hemophilic arthropathy, and current literature has shown favorable short- and long-term surgical outcomes within this patient population [2,5-11]. However, as with any surgery, intraoperative blood loss during lower extremity TJA may be severe enough to indicate postoperative allogenic or autogenic red blood cell transfusion. Yet, there are limited data on bleeding complications of lower extremity TJA among hemophiliacs.

With a decreased intrinsic clotting ability, we hypothesized that hemophiliacs would be more likely to require blood transfusions after lower extremity TJA than a matched comparison cohort of

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* Reprint requests: Michael A. Mont, MD, Center for Joint Preservation and Reconstruction, Rubin Institute for Advanced Orthopedics, Sinai Hospital of Baltimore, 2401 West Belvedere Avenue, Baltimore, MD, 21215.

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lower extremity TJA patients without hemophilia. To test this hypothesis, we used a large, multihospital, U.S. inpatient database and assessed: (1) the incidence of postoperative blood transfusion; (2) the risk of postoperative transfusion in hemophilic patients compared with a matched control cohort (1:3); and (3) the risk of postoperative transfusion when specifically evaluating patients who had hemophilia A or B.

Materials and Methods

Study Population

The Nationwide Inpatient Sample (NIS) is the largest all-payer inpatient database in the United States. Each year, the NIS collects medical records of nearly 8 million hospital stays across >1000 U.S. hospitals, creating a 20% representative sample of annual nationwide hospital admissions [12]. Each patient discharge record contains demographic and clinical data, including International Classification of Diseases, Ninth Revision (ICD-9) diagnosis and procedure codes. Because the NIS contains entirely deidentified medical record data, this study was given exempt status by the institutional review board at our institution.

Lower Extremity TJA Cases

Between January 1998 and December 2010, we identified 614,861 patients with an ICD-9 procedure code for THA (81.51, 00.74, 00.75, 00.76, 00.77) and 1,165,349 patients with an ICD-9 procedure code for TKA (81.54). As hemophilia is predominant in men and female carriers of the hemophilia gene have clotting factor levels that are generally sufficient for normal hemostasis [13], we excluded the 1,097,384 female patients from this cohort. In addition, we excluded the 24,253 patients with ICD-9 diagnosis codes indicating pathologic fracture, malunion of fracture, and traumatic fracture, because these admissions are predominantly nonelective [14], *bilateral cases*, and the 183 patients who underwent THA and TKA in the same admission. This left a cohort of 658,390 male patients who underwent a primary lower extremity TJA.

Demographic Covariates

Demographic variables for each admission, including age (in years), gender (male, female), race (white, nonwhite, missing), and year of admission (1998-2010), were extracted. Comorbidities were assessed using the Charlson and Deyo scoring method for ICD-9 coding [15]. The 17 comorbidities (with point value in parentheses) included: congestive heart failure (1), peripheral vascular disease (1), dementia (1), cerebrovascular disease (1), chronic pulmonary disease (1), rheumatologic disease (1), peptic ulcer disease (1), mild liver disease (1), past myocardial infarct (1), uncomplicated diabetes (1), hemiplegia or paraplegia (2), renal disease (2), malignancy including leukemia and lymphoma (2), diabetes with end-organ damage (2), moderate or severe liver disease (3), metastatic solid tumor (6), and human immunodeficiency virus infection (6). Patients with none of these comorbidities received a score of 0 points.

Study Cohort

We identified 332 patients with a diagnosis of hemophilia at the time of their admission for primary lower extremity TJA. There were 267 patients with hemophilia A (ICD-9 diagnosis 286.0) and 65 patients with hemophilia B (ICD-9 diagnosis 286.1). The 658,058 patients without a documented diagnosis of hemophilia were placed in the comparison cohort.

A matched comparison cohort was then created to minimize the confounding bias of demographic variables on the outcome data. Using propensity scores [16], we then matched patients in the comparison cohort to hemophiliacs in a 3:1 ratio. Matching variables included site of arthroplasty (hip or knee), age, race, Charlson and Deyo score, and year of admission. Fisher exact tests (site of arthroplasty), chi-squared tests (race, year of admission), and independent sample *t* tests (age, Charlson and Deyo score) were used to calculate the significance of demographic differences between hemophiliacs and the comparison cohort. There were significant differences between hemophiliacs and the unmatched comparison cohort according to site of arthroplasty ($P = .002$), year of admission ($P = .013$), age ($P < .001$), race ($P < .001$), and Deyo comorbidity score ($P = .042$). After matching 996 patients in the comparison cohort to the 332 hemophiliacs, there were no significant differences according to site of arthroplasty ($P = .388$), year of admission ($P = .911$), mean age ($P = .590$), or race ($P = .082$). The difference in mean Charlson and Deyo score remained significant after matching ($P = .013$) and was therefore included as a covariate in all regression models (Table 1).

Outcomes

We used ICD-9 procedure codes to identify the 41,536 patients who received an allogenic blood transfusion (99.03, 99.04) and the 38,355 patients who received an autogenic blood transfusion (99.00, 99.02) during admission. The 75,917 patients with "any blood transfusion" received an allogenic and/or autogenic blood transfusion during admission. We compared the day of transfusion to the day of surgery to identify postoperative transfusions that occurred within 72 hours of surgery.

Statistical Analysis

The incidence of transfusion was calculated and compared using frequency tables and Fisher exact tests. The risk of transfusion was then modeled with logistic regression used to calculate the odds ratio (OR) and 95% confidence interval for hemophiliacs compared with the matched comparison cohort. Regression models were not adjusted for the site of arthroplasty, age, race, or year of admission, as matching for these variables already had minimized their associated confounding effects. The model was adjusted for each

Table 1
Patient Demographics of Study Cohort.

Demographics	Hemophiliacs	All Controls	*P*	Matched Controls	*P*
Admissions, N	332	658,058		996	
Surgery site, %					
Hip	28.31	36.31	.002	30.82	.388
Knee	71.69	63.69		69.18	
Year of admission, %					
1998-2000	23.19	20.21	.013	21.79	.911
2001-2003	26.20	20.65		25.70	
2004-2006	21.69	26.64		23.29	
2007-2010	28.92	32.50		29.22	
Age, mean	47.65	65.21	<.001	47.11	.590
Gender, %					
Male	100.00	100.00	.999	100.00	.999
Female	0.00	0.00		0.00	
Race, %					
White	56.93	66.32	<.001	59.84	.082
Nonwhite	17.77	9.30		12.85	
Missing	25.30	24.38		27.31	
Deyo score, mean	0.69	0.51	.042	0.46	.013

% denotes the percentage of patients.
N, number of patients.