

# In-Hospital Complications and Readmission in Patients with Hemophilia Undergoing Hip or Knee Arthroplasty

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**Background:** Individuals with hemophilia undergoing hip or knee arthroplasty are at risk for complications such as bleeding and infection. However, data on hospital length of stay (LOS) and readmission rates compared with non-hemophilic controls are lacking. This study compared the complication rates, LOS, and unplanned 30-day readmission rates between patients with hemophilia and nonhemophilic controls.

**Methods:** This retrospective cohort study used the Pennsylvania Health Care Cost Containment Council (PHC4) database from 2007 to 2015 to compare outcomes in patients with hemophilia and nonhemophilic controls undergoing partial and total hip arthroplasty, knee arthroplasty, and revision knee arthroplasty.

**Results:** A total of 118 patients with hemophilia and 3,811 controls were identified. Compared with controls, patients with hemophilia had a higher risk of bleeding complications after hip procedures (38.7% versus 16.1%, p = 0.003), a higher risk of surgical site infection after knee procedures (8.1% versus 1.1%, p < 0.001), longer median LOS after hip (6 versus 3 days, p < 0.001) and knee (5 versus 3 days, p < 0.001) procedures, and higher rates of unplanned 30-day readmission after hip (22.6% versus 4.1%, p < 0.001) and knee (10.3% versus 4.5%, p = 0.018) procedures. The most common reason for unplanned 30-day readmission in patients with hemophilia was bleeding or the patient's underlying coagulopathy (25.1%).

**Conclusions:** Patients with hemophilia undergoing hip or knee arthroplasty had a higher incidence of postoperative bleeding (hip procedures) and surgical site infections (knee procedures), longer LOS, and higher rates of unplanned 30-day readmission compared with nonhemophilic controls. Key limitations of our study include the potential for inaccurate coding, the relatively small number of patients in the hemophilia cohort, and the uneven distribution of procedure type in the hemophilia and control cohorts.

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

emophilia A and B are congenital bleeding disorders caused by deficiency of coagulation factors VIII and IX, respectively. Severe hemophilia is characterized by

recurrent spontaneous intra-articular hemorrhage, leading to a complication known as hemophilic arthropathy<sup>1</sup>. Individuals with hemophilic arthropathy suffer from chronic pain and

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Disclaimer: The Pennsylvania Health Care Cost Containment Council (PHC4) is an independent state agency responsible for addressing the problem of escalating health costs, ensuring the quality of health care, and increasing access to health care for all citizens regardless of ability to pay. PHC4 has provided data to the authors in an effort to further PHC4's mission of educating the public and containing health-care costs in Pennsylvania. PHC4, its agents, and staff, have made no representation, guarantee, or warranty, express or implied, that the data—financial, patient, payor, and physician-specific information—provided to the authors, are error-free, or that the use of the data will avoid differences of opinion or interpretation. This analysis was not prepared by PHC4. This analysis was done by the authors. PHC4, its agents, and staff, bear no responsibility or liability for the results of the analysis, which are solely the opinion of the authors.

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restricted joint mobility that may interfere with activities of daily living and quality of life. Orthopaedic procedures of the hip or knee, such as hip or knee arthroplasties, are indicated in advanced cases to alleviate pain and restore joint function<sup>2</sup>.

Patients with hemophilia are at risk for complications following orthopaedic surgery for a number of reasons. The risk of bleeding may be increased because of inadequate coagulation factor replacement, the presence of coagulation factor inhibitors, and/or structural articular damage. A higher prevalence of comorbidities such as human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection may predispose patients with hemophilia to postoperative infection and delayed woundhealing. Indeed, previous studies reported that patients with hemophilia who underwent orthopaedic surgery had high rates of postoperative bleeding (39%), infection (7%), and delayed wound-healing (2.2%)<sup>3</sup>. Overall complication rates were reported to be as high as 31.5%4.

Published throplasty in patients with hemophilia is limited by small numbers of patients, lack of comparisons with nonhemophilic controls, and lack of information on outcomes beyond the index hospitalization, such as readmission rates<sup>3,5,6</sup>. Using a statewide database, we conducted a cohort study of hospital discharges after hip or knee arthroplasty to compare the complication rates, hospital length of stay (LOS), and unplanned 30-day readmission rates between patients with hemophilia and nonhemophilic controls.

### **Materials and Methods**

We conducted a retrospective cohort study to compare outcomes in patients with hemophilia (hemophilia cohort) and nonhemophilic patients (control cohort) undergoing hip or knee arthroplasty. The study was exempt from institutional review board approval.

Hospital discharges were identified using the Pennsylvania Health Care Cost Containment Council (PHC4)

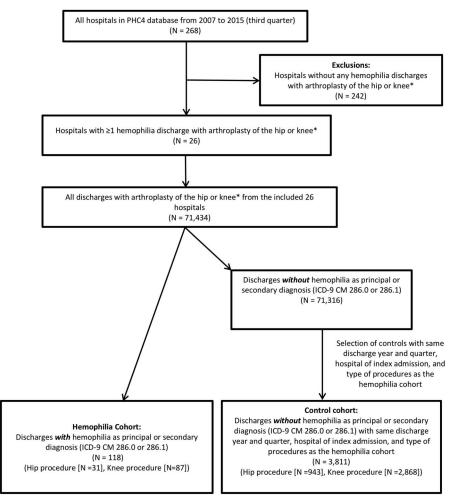


Fig. 1 Flow diagram for identification of discharges of patients with hemophilia (hemophilia cohort) and without hemophilia (control cohort). \*Discharges after hip or knee arthroplasty were required to have 1 of the following ICD-9-CM codes as the principal or secondary procedure code: 81.52 (partial hip replacement), 81.51 (total hip replacement), 00.80-82 or 00.84 (revision of knee replacement), or 81.54 (knee replacement).

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database. The PHC4 database contains information on all hospital discharges in Pennsylvania, including patient characteristics, diagnosis codes, and procedure codes.

# Inclusion and Exclusion Criteria

Hospital discharges from 2007 through the third quarter of 2015 were included. Eligible discharges were required to include 1 of the following International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes as the principal or secondary procedure code: 81.52 (partial hip

replacement), 81.51 (total hip replacement), 00.70-00.73 or 81.53 (revision of hip replacement), 81.54 (knee replacement [which includes unicompartmental, bicompartmental, and tricompartmental replacement]), or 00.80-00.82 or 00.84 (revision of knee replacement).

The hemophilia cohort included all male patients ≥15 years of age who had an ICD-9-CM code for hemophilia A or B (286.0 or 286.1, respectively) as the principal or secondary diagnosis.

The control cohort included all male patients ≥15 years of age without a hemophilia diagnosis code who underwent the

|  | Hip Procedures                   |                                |          |                                  |                                  |                      |
|--|----------------------------------|--------------------------------|----------|----------------------------------|----------------------------------|----------------------|
|  | Hemophilia<br>Cohort<br>(N = 31) | Control<br>Cohort<br>(N = 943) | P Value* | Hemophilia<br>Cohort<br>(N = 87) | Control<br>Cohort<br>(N = 2,868) | P Value <sup>*</sup> |
| Median age (IQR) (yr)                          | 57 (29)                          | 60 (17)                        | 0.146†   | 44 (23)                          | 63 (15)                          | <0.001               |
| Race/ethnicity (%)                             |                                  |                                | 0.479    |                                  |                                  | 0.024                |
| White  | 90.3                             | 83.8                           |          | 83.9                             | 81.8                             |                      |
| Black  | 6.5                              | 9.3                            |          | 8.1                              | 11.7                             |                      |
| Other  | 3.2                              | 1.9                            |          | 5.7                              | 1.5                              |                      |
| Unknown  | 0                                | 5.0                            |          | 2.3                              | 5.1                              |                      |
| Hemophilia type (%)                            |                                  |                                |          |                                  |                                  |                      |
| A  | 87.1                             | _                              |          | 92.0                             | _                                |                      |
| В  | 12.9                             | _                              |          | 8.1                              | _                                |                      |
| Admission type (%)                             |                                  |                                | 0.001    |                                  |                                  | 0.002                |
| Emergency                                      | 19.4                             | 4.6                            |          | 4.6                              | 0.4                              |                      |
| Urgent   | 9.7                              | 2.3                            |          | 1.2                              | 0.5                              |                      |
| Elective                                       | 71.0                             | 93.0                           |          | 94.3                             | 99.1                             |                      |
| Trauma   | 0                                | 0.1                            |          | 0                                | 0.1                              |                      |
| Procedure (%)                                  |                                  |                                | 0.005    |                                  |                                  | < 0.001              |
| Partial hip arthroplasty                       | 12.9                             | 2.0                            |          | _                                | _                                |                      |
| Total hip arthroplasty                         | 87.1                             | 98.0                           |          | _                                | _                                |                      |
| Knee revision                                  | _                                | _                              |          | 25.3                             | 4.1                              |                      |
| Knee arthroplasty                              | _                                | _                              |          | 74.7                             | 95.9                             |                      |
| Comorbidities (%)                              |                                  |                                |          |                                  |                                  |                      |
| Stable ischemic heart disease                  | 9.7                              | 15.3                           | 0.608    | 3.5                              | 18.2                             | < 0.001              |
| Hypertension                                   | 38.7                             | 58.6                           | 0.040    | 36.8                             | 66.1                             | < 0.001              |
| Diabetes mellitus                              | 16.1                             | 14.5                           | 0.795    | 11.5                             | 20.7                             | 0.042                |
| AIDS   | 6.5                              | 0.1                            | 0.003    | 3.5                              | 0.0                              | < 0.001              |
| Liver disease                                  | 19.4                             | 1.9                            | < 0.001  | 19.5                             | 2.0                              | < 0.001              |
| Obesity  | 9.7                              | 18.2                           | 0.339    | 8.1                              | 20.3                             | 0.004                |
| Chronic pulmonary disease                      | 3.2                              | 11.1                           | 0.241    | 5.8                              | 11.5                             | 0.120                |
| Renal failure                                  | 9.7                              | 4.2                            | 0.153    | 2.3                              | 5.5                              | 0.236                |
| Congestive heart failure                       | 6.5                              | 3.3                            | 0.283    | 2.3                              | 2.9                              | 1.000                |
| Rheumatoid arthritis/collagen vascular disease | 9.7                              | 2.3                            | 0.042    | 2.3                              | 1.4                              | 0.363                |
| Metastatic cancer                              | 0                                | 0.7                            | 1.000    | 0                                | 0.1                              | 1.000                |

<sup>\*</sup>Fisher exact test, except where otherwise noted. †Wilcoxon rank-sum test.

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same qualifying procedures in the same hospitals and same discharge years and quarters as the hemophilia cohort.

### Variables

For each eligible hospital discharge, the following data elements were collected: age, sex, race, year of discharge, admission type (emergency, urgent, elective, or trauma), hospital, type of procedure, comorbidities, complications during hospitalization (thromboembolic events, infection, bleeding, transfusion of red blood cells), LOS, discharge disposition, unplanned readmission within 30 days of discharge from the index admission, and reason for readmission. The ICD-9-CM codes for comorbidities, complications, and reasons for 30-day readmission are listed in Appendix Tables S1, S2, and S3, respectively. Hemophilia severity and inhibitor status were not available in the PHC4 database.

# Statistical Analysis

The Fisher exact test was used to evaluate differences in clinical characteristics, outcomes, and complications between the hemophilia and control cohorts, and the Wilcoxon rank-sum

test was used to compare median ages. Exact logistic regression was used to obtain unadjusted odds ratios (ORs), with 95% confidence intervals (CIs), between hemophilia status and other characteristics. Adjusted ORs and 95% CIs were obtained from a multivariate logistic regression model. The log-rank test was used to evaluate differences between Kaplan-Meier curves for LOS. Simple linear regression was used to evaluate changes in average LOS over time. All analyses were done using SAS/STAT software (version 9.4; SAS Institute). All graphics were created using R version 3.5.3 (R Foundation for Statistical Computing) and SAS/STAT.

### Results

# Demographic and Clinical Characteristics

A total of 118 discharges with a listing of hemophilia and 3,811 discharges without hemophilia were identified (Fig. 1). Thirty-one patients in the hemophilia cohort and 943 controls underwent hip procedures, and 87 with hemophilia and 2,868 controls underwent knee procedures. Characteristics of eligible discharges are summarized in Table I. For knee procedures,

|   | Н                                | ip Procedures                  |          | Knee Procedures                  |                                  |          |  |  |
|---|----------------------------------|--------------------------------|----------|----------------------------------|----------------------------------|----------|--|--|
|   | Hemophilia<br>Cohort<br>(N = 31) | Control<br>Cohort<br>(N = 943) | P Value* | Hemophilia<br>Cohort<br>(N = 87) | Control<br>Cohort<br>(N = 2,868) | P Value* |  |  |
| Thromboembolic complications (%)                |                                  |                                |          |                                  |                                  |          |  |  |
| Venous thromboembolism                          | 0                                | 0.64                           | 1.000    | 1.15                             | 0.98                             | 0.581    |  |  |
| Acute coronary syndrome (STEMI/NSTEMI/UA†)      | 0                                | 0.95                           | 1.000    | 0                                | 0.28                             | 1.000    |  |  |
| Acute ischemic stroke/transient ischemic attack | 0                                | 0.21                           | 1.000    | 0                                | 0.24                             | 1.000    |  |  |
| Bleeding (%)                                    |                                  |                                |          |                                  |                                  |          |  |  |
| Bleeding complications                          | 38.71                            | 16.12                          | 0.003    | 19.54                            | 13.95                            | 0.158    |  |  |
| Intracerebral hemorrhage                        | 0                                | 0                              | _        | 0                                | 0.03                             | 1.000    |  |  |
| Transfusion of red blood cells                  | 19.35                            | 7.74                           | 0.034    | 12.64                            | 4.05                             | 0.001    |  |  |
| Infection (%)                                   |                                  |                                |          |                                  |                                  |          |  |  |
| Surgical site infection                         | 0                                | 0.21                           | 1.000    | 8.05                             | 1.12                             | < 0.001  |  |  |
| Other infection                                 | 6.45                             | 2.12                           | 0.153    | 2.30                             | 1.32                             | 0.331    |  |  |
| Discharge disposition (%)                       |                                  |                                | 0.442    |                                  |                                  | < 0.001  |  |  |
| Home  | 70.97                            | 76.25                          |          | 67.82                            | 64.19                            |          |  |  |
| Short-term care facility                        | 16.13                            | 8.70                           |          | 29.89                            | 15.27                            |          |  |  |
| Long-term care facility                         | 12.90                            | 14.42                          |          | 1.15                             | 19.56                            |          |  |  |
| Other   | 0                                | 0.42                           |          | 1.15                             | 0.84                             |          |  |  |
| Hospice   | 0                                | 0.11                           |          | 0                                | 0.03                             |          |  |  |
| Died in hospital                                | 0                                | 0.11                           |          | 0                                | 0.10                             |          |  |  |
| Median hospital length of stay (IQR)† (days)    | 6 (5)                            | 3 (1)                          | <0.001   | 5 (4)                            | 3 (2)                            | <0.001   |  |  |
| Unplanned 30-day readmission (%)                |                                  |                                | <0.001   |                                  |                                  | 0.018    |  |  |
| No  | 77.42                            | 95.86                          |          | 89.66                            | 95.54                            |          |  |  |
| Yes   | 22.58                            | 4.14                           |          | 10.34                            | 4.46                             |          |  |  |

<sup>\*</sup>Fisher exact test. †STEMI = ST-elevation myocardial infarction, NSTEMI = non-ST-elevation myocardial infarction, and UA = unstable angina. †After excluding 4 controls who died in the hospital.

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compared with the control cohort, patients in the hemophilia cohort were younger, with a median age of 44 years (interquartile range width [IQR]), 23 years) versus 63 years (IQR, 15 years) (p < 0.001). For hip procedures, the median age was not significantly different between the hemophilia and control cohorts.

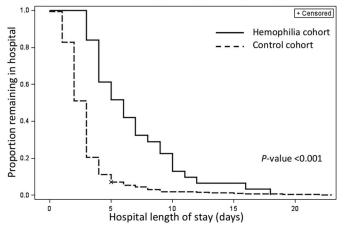
In the hemophilia cohort, hemophilia A constituted 87.1% and 92.0% of discharges after hip and knee procedures, respectively. Information on the severity of the hemophilia was not available.

For the index hospitalization, urgent or emergency admission was significantly more common in the hemophilia cohort for both hip (29.0% versus 6.9%, p < 0.001) and knee (5.8% versus 0.9%) procedures (p = 0.002). Hip procedures constituted a similar proportion of surgeries in the hemophilia

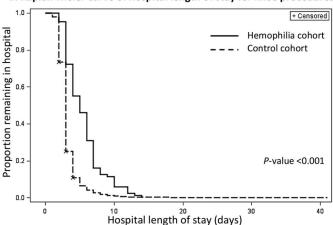
(26%) and control (25%) cohorts. Knee arthroplasty was the most common index procedure in both the hemophilia (55.1%) and control (72.2%) cohorts. However, compared with the controls, higher percentages of the hemophilia cohort underwent knee revision and partial hip arthroplasty. We did not include revision of hip arthroplasty because no patients undergoing this procedure were identified in the hemophilia cohort.

The prevalence of certain comorbidities differed between the hemophilia and control cohorts. For both hip and knee procedures, acquired immune deficiency syndrome (AIDS) and liver disease were significantly more common in the hemophilia cohort, whereas hypertension was more common in the control cohort.

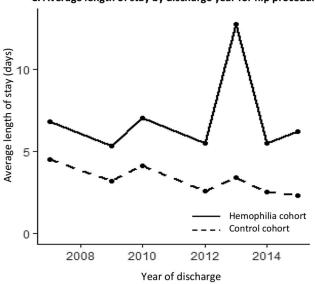
# A. Kaplan-Meier curve of hospital length of stay for hip procedures



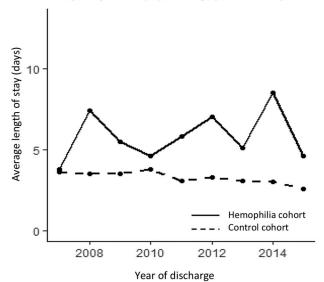
# B. Kaplan-Meier curve of hospital length of stay for knee procedures



# C. Average length of stay by discharge year for hip procedures



D. Average length of stay by discharge year for knee procedures



Figs. 2-A through 2-D Hospital length of stay. Kaplan-Meier curves for hospital length of stay in the hemophilia and control cohorts are shown for hip (Fig. 2-A) and knee (Fig. 2-B) procedures. Average length of stay over the study period (2007 to 2015) in the hemophilia and control cohorts is shown for hip (Fig. 2-C) and knee (Fig. 2-D) procedures.

### **Hospital Characteristics**

The hemophilia and control cohorts were identified among patients from 26 hospitals across Pennsylvania (Fig. 1). Of these hospitals, 13 (50%) were part of a health system with a federally funded hemophilia treatment center (HTC). Most eligible discharges (87.3% of the hemophilia cohort and 92.2% of the control cohort) were from health systems with an affiliated HTC. From 2007 to 2015, the average volume of orthopaedic procedures performed at each included hospital ranged from 2.4 to 178.8 procedures per month. Seventeen hospitals (65.4%) had an average volume of >50 procedures per month. Most of the hemophilia (89.8%) and control (98.3%) cohorts underwent surgery at one of these high-volume hospitals.

Clinical Outcomes and Complications During Hospitalization The frequencies of clinical outcomes and complications in the hemophilia and control cohorts are shown in Table II. For both hip and knee procedures, the rates of thromboembolic complications were low and similar in both cohorts. Information regarding the use of postoperative thromboprophylaxis was not available.

Compared with controls, bleeding events were significantly more common in the hemophilia cohort for hip procedures (38.7% versus 16.1%, p=0.003) but not for knee procedures (19.5% versus 14.0%, p=0.158). A higher percentage of the hemophilia cohort received transfusion of red blood cells after both hip (19.4% versus 7.7%, p=0.034) and knee (12.6% versus 4.1%, p=0.001) procedures. Information regarding administration of coagulation factor replacement therapy was not available.

Surgical site infection was significantly more common in the hemophilia cohort after knee procedures (8.1% versus 1.1%, p < 0.001) but not hip procedures (0.0% versus 0.21%, p = 1.000). Rates of non-surgical-site infection were similar

between the hemophilia and control cohorts. Independent predictive factors for any infection after a knee procedure included chronic pulmonary disease (OR, 1.9; 95% CI, 1.0 to 3.5; p=0.047) and knee revision (versus knee arthroplasty) (OR, 16.7; 95% CI, 10.2 to 27.6; p<0.001).

The majority of discharges were to home in both groups. Discharge to a short-term care facility was more frequent in the hemophilia cohort, while controls were more frequently discharged to a long-term care facility. There was no in-hospital mortality in the hemophilia cohort, whereas 4 patients in the control cohort died in the hospital (after 1 hip procedure and 3 knee procedures).

# Hospital Length of Stay

For both hip and knee procedures, the LOS was significantly longer in the hemophilia cohort than controls (p < 0.001) (Figs. 2-A and 2-B). After excluding those who died in the hospital, the median LOS in days was 6 (IQR, 5) in the hemophilia cohort versus 3 (IQR, 1) in the controls for hip procedures (p < 0.001) and 5 (IQR, 4) versus 3 (IQR, 2) for knee procedures (p < 0.001) (Table II). Over the 9-year study period (2007 to 2015), the average LOS for hip and knee procedures declined in the controls (p < 0.001 for both hip and knee procedures) (Figs. 2-C and 2-D), but this trend was not apparent in the hemophilia cohort (p = 0.817 and 0.475, respectively).

# Unplanned 30-Day Readmission

A significantly higher percentage of the hemophilia cohort had an unplanned 30-day readmission compared with the controls for both hip (22.6% versus 4.1%, p < 0.001) and knee (10.3% versus 4.5%) procedures (p = 0.018) (Table II). For patients undergoing hip procedures, hemophilia was an independent predictive factor for unplanned 30-day readmission, with an OR of 6.7 (95% CI, 2.3 to 17.4; p = 0.001). For patients

|                           | Hip Procedures |          |         |                      |          |         | Knee Procedures |         |         |                      |         |         |
|---------------------------|----------------|----------|---------|----------------------|----------|---------|-----------------|---------|---------|----------------------|---------|---------|
|                           | Univariate     |          |         | Reduced Multivariate |          |         | Univariate      |         |         | Reduced Multivariate |         |         |
|                           | OR             | 95% CI   | P Value | OR                   | 95% CI   | P Value | OR              | 95% CI  | P Value | OR                   | 95% CI  | P Value |
| Hemophilia                | 6.7            | 2.3-17.4 | 0.001   | 6.7                  | 2.3-17.4 | 0.001   | 2.5             | 1.1-5.1 | 0.036   | 2.2                  | 1.0-4.6 | 0.041   |
| Age <50 yr                | 0.8            | 0.3- 1.9 | 0.777   | _                    | _        | _       | 1.4             | 0.8-2.3 | 0.247   | _                    | _       | _       |
| Diabetes                  | 1.1            | 0.4-2.4  | 1.000   | _                    | _        | _       | 1.5             | 1.0-2.2 | 0.071   | 1.5                  | 1.0-2.2 | 0.039   |
| Liver disease             | 3.0            | 0.6-10.7 | 0.199   | _                    | _        | _       | 1.5             | 0.5-3.7 | 0.533   | _                    | _       | _       |
| Obesity                   | 0.7            | 0.2-1.6  | 0.501   | _                    | _        | _       | 0.7             | 0.4-1.2 | 0.198   | _                    | _       | _       |
| Chronic pulmonary disease | 1.0            | 0.3-2.6  | 1.000   | _                    | _        | _       | 1.4             | 0.8-2.2 | 0.281   | _                    | _       | _       |
| Procedure type            |                |          |         |                      |          |         |                 |         |         |                      |         |         |
| Partial hip arthroplasty  | 4.5            | 1.1-14.5 | 0.040   | _                    | _        | _       | _               | _       | _       | _                    | _       | _       |
| Total hip arthroplasty    | Ref.           |          |         | _                    | _        | _       | _               | _       | _       | _                    | _       | _       |
| Knee revision             | _              | _        | _       | _                    | _        |         | 2.2             | 1.1-4.1 | 0.022   | 2.0                  | 1.1-3.7 | 0.031   |
| Knee arthroplasty         | _              | _        |         | _                    |          | _       | Ref.            |         |         | Ref.                 |         |         |

| Diagnosis for Unplanned<br>30-Day Readmission | Hin Prop                     | edures (%)                 | Knoo Pro                     | cedures (%)                 | Hip and Knee Procedures (%)      |                               |  |
|---|------------------------------|----------------------------|------------------------------|-----------------------------|----------------------------------|-------------------------------|--|
|   | Hemophilia<br>Cohort (N = 7) | Control<br>Cohort (N = 39) | Hemophilia<br>Cohort (N = 9) | Control<br>Cohort (N = 128) | Hemophilia<br>Cohort<br>(N = 16) | Control<br>Cohort<br>(N = 167 |  |
| Hemophilia/coagulation<br>defect              | 14.3                         | 0                          | 22.2                         | 0.8                         | 18.8                             | 0.6                           |  |
| Bleeding or anemia                            | 0                            | 7.7                        | 11.1                         | 7.8                         | 6.3                              | 7.8                           |  |
| Venous thromboembolism                        | 0                            | 5.1                        | 0                            | 7.0                         | 0                                | 6.6                           |  |
| Surgical complications                        | 14.3                         | 35.9                       | 22.2                         | 20.3                        | 18.8                             | 24.0                          |  |
| Infection                                     | 0                            | 2.6                        | 0                            | 10.2                        | 0                                | 8.4                           |  |
| Respiratory diagnosis                         | 42.9                         | 5.1                        | 0                            | 7.0                         | 18.8                             | 6.6                           |  |
| Cardiovascular diagnosis                      | 0                            | 15.4                       | 0                            | 7.0                         | 0                                | 9.0                           |  |
| Gastrointestinal diagnosis                    | 0                            | 2.6                        | 11.1                         | 3.1                         | 6.3                              | 3.0                           |  |
| Kidney/electrolytes                           | 0                            | 5.1                        | 0                            | 0                           | 0                                | 1.2                           |  |
| Neurological diagnosis                        | 0                            | 0                          | 0                            | 7.0                         | 0                                | 5.4                           |  |
| Orthopaedic diagnosis                         | 0                            | 2.6                        | 0                            | 3.1                         | 0                                | 3.0                           |  |
| Trauma/injuries                               | 0                            | 2.6                        | 0                            | 0                           | 0                                | 0.6                           |  |
| Unspecified pain                              | 0                            | 7.7                        | 22.2                         | 12.5                        | 12.5                             | 11.4                          |  |
| Others/nonspecific symptoms                   | 28.6                         | 7.7                        | 11.1                         | 14.1                        | 18.8                             | 12.6                          |  |

undergoing knee procedures, independent predictive factors for unplanned 30-day readmission included hemophilia (OR, 2.2; 95% CI, 1.0 to 4.6; p = 0.041), diabetes mellitus (OR, 1.5; 95% CI, 1.0 to 2.2; p = 0.039), and a knee revision procedure (OR, 2.0; 95% CI, 1.1 to 3.7; p = 0.031) (Table III).

In the hemophilia cohort, 25.1% of unplanned readmissions within 30 days were attributed to bleeding or the patient's underlying coagulopathy. Other common causes for unplanned readmission in the hemophilia cohort were surgical complications (18.8%), respiratory diagnosis (18.8%), other/nonspecific symptoms (18.8%), and unspecified pain (12.5%). The most common cause of unplanned readmission in the control cohort (24%) was surgical complications (Table IV).

# **Discussion**

We compared complications and outcomes after hip or knee arthroplasty in patients with hemophilia and non-hemophilic controls using an administrative hospital discharge database. Key findings of our study include a higher risk of bleeding complications (significant after hip procedures), a higher risk of surgical site infection (significant after knee procedures), longer LOS, and higher rates of unplanned 30-day readmission in patients with hemophilia compared with controls.

The hemophilia cohort was younger than the controls, likely reflecting the development of degenerative joint disease at a younger age because of the effects of recurrent hemarthrosis. Most admissions were classified as elective in both cohorts, although there was a greater percentage of urgent and

emergency admissions in the hemophilia cohort (Table I), possibly resulting from a higher incidence of urgent indications for arthroplasty such as hemarthrosis, infection, and/or fracture in this population.

Thromboprophylaxis after hip and knee arthroplasty is considered the standard of care in the nonhemophilic population<sup>7</sup>. However, a consensus in patients with hemophilia is lacking and current practice varies among physicians and treatment centers<sup>8,9</sup>. The true incidence of symptomatic venous thromboembolism (VTE) in patients with hemophilia undergoing such surgeries is still uncertain. The estimated incidence in previous retrospective studies ranged from 0% to 1%<sup>10-12</sup>, whereas the incidence of symptomatic VTE was as high as 4.3% in 1 prospective multicenter study<sup>13</sup>. In our study, the incidence of VTE was comparable between the hemophilia and control cohorts for both hip (0% versus 0.64%) and knee (1.15% versus 0.98%) procedures.

Consistent with our clinical experience, we observed a higher rate of bleeding complications in patients with hemophilia after hip procedures, as well as an increased rate after knee procedures that did not reach significance. Because information on hemostatic therapy and laboratory test results is not available in the PHC4 database, we cannot determine whether bleeding complications in patients with hemophilia occurred because of suboptimal coagulation factor replacement therapy.

Postoperative infection has consistently been reported to be higher in patients with hemophilia compared with the general population<sup>4,14,15</sup>. Our results confirm these observations. The rate of surgical site infection in the hemophilia

cohort undergoing knee procedures was 8.05% compared with 1.12% in the controls (p < 0.001). The increased risk of infection in patients with hemophilia may be due to several factors, including HIV and/or HCV infection, a greater need for intravenous access, an increased rate of surgical site bleeding, and more frequent transfusion of blood components. We observed a higher risk of any infection in the knee revision group compared with the knee arthroplasty group. It is unclear if some of these infections were present before the surgery, prompting the knee revision, or developed following the revision.

We found that hospital LOS was significantly longer in the hemophilia cohort than the controls. This finding may be attributable to the need for perioperative coagulation factor infusion and higher rates of postoperative complications such as bleeding and surgical site infection in patients with hemophilia. LOS for patients with hemophilia may also be increased because of difficulty arranging for coagulation factor administration at home or at a rehabilitation facility. Patients with hemophilia also experienced more frequent unplanned 30-day readmissions, a quarter of which were related to bleeding or the patient's underlying coagulopathy. This increased risk of readmission suggests that close follow-up of patients with hemophilia is essential for the first several weeks after surgery. Clinicians should carefully consider whether patients may benefit from more aggressive interventions to prevent postoperative bleeding and the need for hospital readmission.

We did not examine differences in outcomes between centers with and without HTCs, because it was not possible to determine whether an individual patient was managed in partnership with a hematologist associated with an HTC. We were also unable to examine the impact of an individual surgeon's level of experience with patients with hemophilia, which could potentially impact surgical outcomes given the complex nature of hemophilic arthropathy. Whether hospital teams, surgeons, and hematologists who have experience and expertise in working with patients with hemophilia undergoing orthopaedic surgery achieve superior outcomes compared with those with less experience is an important question worthy of further study.

Similar to our study, a recently published Taiwanese database study found higher rates of transfusion and longer LOS in patients with hemophilia than controls<sup>16</sup>. In contrast, that study did not find any significant difference in the 30-day and 90-day postoperative complication rates. This divergence from our findings may be due to differences in the coding used to define complications between the Taiwanese study and ours. The median LOS for patients with hemophilia in the Taiwanese study was notably longer than in our study (11 versus 5 to 6 days) and the rate of red blood cell transfusion was substantially higher (92% versus 13% to 19%), reflecting differences between 2 different health-care systems.

Our study has several limitations. First, because it was a retrospective study utilizing an administrative hospital discharge database, the data used for the analysis relied heavily on

the accuracy of coding of diagnoses and complications. Thus, it is possible that some diagnoses or outcomes of interest were incorrectly coded or missed altogether. Second, the database did not allow for a more thorough exploration of clinical factors impacting postoperative outcomes in individual patients. For example, we did not have information on the severity of hemophilia, inhibitor status, use of coagulation factor replacement therapy, or use of thromboprophylaxis. Third, because of the relatively small number of arthroplasties in the hemophilia cohort, we chose to pool heterogeneous procedures in our analysis. For example, hip surgeries included both partial and total hip arthroplasty, whereas knee surgeries included both knee arthroplasty and revision. These surgeries differ with respect to indication, complexity, and complication profile. Thus, the greater percentages of partial hip arthroplasty and revision knee arthroplasty in the hemophilia cohort are potential confounders that could have influenced our results. Fourth, the complication rates that we reported were restricted to those occurring during the index hospitalization. We did not have information on outcomes occurring after discharge, although the greater 30-day readmission rate in the hemophilia cohort suggests increased post-discharge complications in this population. Fifth, we did not include any patients who underwent revision total hip arthroplasty in our study because we did not identify any patients in the hemophilia cohort who underwent this procedure. Sixth, because there is a single ICD-9-CM code for unicompartmental, bicompartmental, and tricompartmental knee arthroplasties, we were not able to determine how many patients in each cohort underwent partial versus total knee arthroplasty and whether outcomes may have differed based on the type of knee arthroplasty. Finally, although our sample size is larger than most other published studies of hip and knee arthroplasty in patients with hemophilia<sup>3-6</sup>, the number of patients in the hemophilia cohort, particularly in the hip procedure group, was small and limits the power of our study.

Our study also has several strengths. Use of the PHC4 database allowed us to explore scarcely reported outcomes in patients with hemophilia, including LOS and unplanned 30-day readmission. Moreover, data in this study were derived from all hospitals across Pennsylvania, with most patients drawn from 1 of 13 hospitals affiliated with an HTC. Thus, the results provide an overview of treatment outcomes that may be more generalizable than previously published single-center experiences. Finally, to our knowledge, this is the first study of hip and knee arthroplasty in patients with hemophilia in the United States to include a control cohort, allowing direct comparison with nonhemophilic controls in the same settings.

In summary, patients with hemophilia undergoing hip or knee arthroplasty had higher rates of postoperative bleeding (significant after hip procedures) and surgical site infection (significant after knee procedures), longer LOS, and higher rates of unplanned 30-day readmission compared with nonhemophilic controls. Among other limitations, our results may be confounded by differences in the distribution of procedure JBJS Open Access • 2020:e0085. openaccess.jbjs.org 9

types between the 2 cohorts (i.e., there were more partial hip arthroplasties and more knee revisions in the hemophilia cohort).

# **Appendix**

Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJSOA/A174).

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