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Postoperative bleeding complications in patients with hemophilia undergoing major orthopedic surgery: A prospective multicenter observational study

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SUMMARY

BACKGROUND: Persons with hemophilia (PWH) are at risk for chronic hemophilic arthropathy (HA). Joint replacement surgery may be used to relieve intractable pain and/or restore joint function.

OBJECTIVES: This multicenter, prospective, observational cohort study evaluated the rate of bleeding during the postoperative period after total hip (THA) or knee arthroplasty (TKA).

PATIENTS/METHODS: We included PWH of any severity ≥18 years of age who were undergoing THA or TKA. Clinical decisions were made at the discretion of the treating physician according to local standards of care. Clinical data were prospectively recorded. Major bleeding was defined as bleeding in a critical site, bleeding that resulted in either a 2 g/dL or greater decrease in hemoglobin during any 24-hour period, or transfusion of two or more units of packed red blood cells.

RESULTS: One hundred thirty-one procedures (98 TKA and 33 THA) were performed, 39 (29.8%) of which were complicated by major bleeding, including 46% of THA and 25% of TKA. The risk of major bleeding was increased in THA compared to TKA (OR 2.50, p=0.05), and by the presence of an inhibitor (OR 4.29, p=0.04), increased BMI (OR 4.49 and 6.09 for overweight and obese, respectively, compared to normal BMI, each p<0.01), and non-use of an antifibrinolytic medication (OR 3.00, p=0.03). Neither continuous clotting factor infusion (versus bolus infusion) nor pharmacologic thromboprophylaxis were associated with bleeding risk.

CONCLUSIONS: The bleeding risk remains substantial after THA and TKA in PWH, despite factor replacement. Use of antifibrinolytic medications is associated with decreased risk.

Keywords

antifibrinolytics; arthroplasty; hemophilia; hemorrhage; risk factors

INTRODUCTION

Persons with hemophilia (PWH) are at risk for chronic hemophilic arthropathy (HA), a progressive disease caused by repeated intraarticular bleeding with subsequent inflammation and damage to bone, cartilage, and other joint structures. HA typically affects large joints, including knees, hips, ankles, and elbows. HA causes significant pain, disability, and impaired health-related quality of life.[1–4] The widespread adoption of prophylactic factor replacement has not conferred total protection against the development of HA; even in PWH receiving primary or secondary clotting factor prophylaxis, many still develop HA.[5–7] PWH who progress to end-stage HA are candidates for joint replacement surgery, which is considered an effective intervention for providing relief from intractable pain and restoring joint function.[8–10]

Major orthopedic surgeries, such as total knee arthroplasty (TKA) and total hip arthroplasty (THA), carry a significant risk of perioperative blood loss and need for transfusion, even in the general population.[11–13] These risks are potentially heightened in PWH due to their underlying bleeding diathesis and despite clotting factor replacement. Wang et al reported that postoperative transfusion, hospital stays, and hospital charges were greater

in patients with hemophilia after TKA and THA compared to those without hemophilia.[14] Furthermore, in a recent retrospective analysis of in-hospital and readmission data, Chiasakul et al reported greater 30-day readmission rates and prolonged length of stay, in addition to more bleeding events in PWH undergoing TKA and THA than controls without hemophilia.[15]

The American College of Chest Physicians and the American Academy of Orthopaedic Surgeons recommend that patients undergoing THA or TKA receive either pharmacologic or mechanical thromboprophylaxis postoperatively to prevent venous thromboembolism (VTE).[16, 17] However, the use of pharmacologic thromboprophylaxis potentially further exacerbates the risk of bleeding in PWH. Prospective data on short-term or long-term outcomes in PWH undergoing major lower extremity orthopedic surgery are scarce. Most existing data on perioperative complications such as major bleeding and transfusion rates come from single-center, retrospective studies.[18–21] Therefore, in this study, we prospectively collected and analyzed ‘real world’ data on bleeding events and transfusion needs during post-operative hospitalization in PWH undergoing TKA or THA.

PATIENTS AND METHODS

We conducted a prospective, observational cohort study in 14 institutions to investigate outcomes associated with total hip or knee arthroplasty in PWH. Rates of postoperative VTE in the initial 46 subjects in this study were previously reported.[22] PWH scheduled for joint replacement surgery were identified prospectively by each participating center and asked to participate. We included subjects with hemophilia A or B of any severity who were at least 18 years of age, could provide informed consent and were willing to return for follow-up 4–6 weeks after surgery. The unit of analysis for this study was defined as any qualifying operative intervention (unilateral or bilateral). Individuals who participated in the study were eligible to enroll in the study again if they underwent a second qualifying procedure on a different date.

Study visits occurred immediately prior to and 4–6 weeks after surgery. For this analysis, we evaluated bleeding events that occurred during surgery or in the period of hospitalization following the procedure, as well as bleeding that led to re-hospitalization any time during the first 6 weeks after discharge. Sites also reported other clinically significant or adverse events relevant to the study. Data were recorded in real-time using a secure web-based data capture system (REDCap, Vanderbilt University). All clinical treatment decisions, including perioperative clotting factor management, postoperative rehabilitation, and VTE prophylaxis and/or treatment were made at the discretion of each treating physician according to individual local standards of care. The study was approved by each center’s institutional review board, and all subjects provided informed consent prior to enrollment.

Clinical and Outcome Variables

Clinical and outcomes data were abstracted from medical charts and obtained through patient and clinician interview. We collected information describing each subject’s type and severity of hemophilia, history or presence of inhibitors, peri-operative clotting factor product and dose, postoperative hemoglobin levels, and any VTE prophylaxis received.

We considered a participant to have an active inhibitor if he received a bypass agent (recombinant activated factor VII or activated prothrombin complex concentrate) as the primary hemostatic treatment during the peri-operative period. We classified patients as having received antifibrinolytic (aminocaproic acid or tranexamic acid) or pharmacologic thromboprophylaxis (low molecular weight heparin, direct oral anticoagulants, or warfarin) if they were administered any doses of these medications during the hospitalization. Likewise, subjects were considered to have been treated with continuous infusion of clotting factor if they received factor by this method at any time during their hospitalization.

The primary outcome for this study was major bleeding during surgical procedures or the post-operative hospitalization period. Bleeding that occurred after hospital discharge was examined separately. We used a modified version of the International Society on Thrombosis and Haemostasis definition of major postoperative bleeding, defined as follows: any bleeding that occurred in a critical site (intracranial, intraspinal, intraocular, pericardial, intraarticular other than the operative site, intramuscular with compartment syndrome, or retroperitoneal) or bleeding at any site that resulted in any of the following outcomes: 1) decrease in hemoglobin of 2 g/dL or more during any 24-hour period, 2) transfusion of two or more units of packed red blood cells (pRBC) during hospitalization, or 3) death.[23] Minor bleeding was defined as any clinically overt bleeding at a site other than the operative site that did not meet the criteria for major bleeding.

Secondary outcomes included bleeding into the surgical joint space, return to the operating room, and hospital readmission within 6 weeks of discharge. In addition to information describing hemostatic and thromboprophylactic treatments, we also recorded venous or arterial thrombotic events. Additional significant clinical events, including the development of factor VIII (FVIII) or factor IX (FIX) inhibitors prior to the postsurgical follow-up visit or documented infections in the surgical joint were reported by each site.

Statistical Analyses

We analyzed the primary study outcome using both univariate and multivariable logistical regression analyses. We examined the relationships of both patient- and treatment-related variables to the primary outcome, including age, body mass index (BMI) category (<25 kg/m^2, normal; 25–30 kg/m^2, overweight; >30 kg/m^2, obese), hemophilia type (A or B), inhibitor status, type of surgery, factor infusion strategy, use of antifibrinolytics, and use of anticoagulants. Following completion of univariate analyses, we used forward stepwise conditional multivariable logistic regression and included variables that had a p-value of 0.20 or lower in the univariate analyses. Missing data are described in Tables 1–3. We did not impute missing data for statistical analyses (complete case analysis). All statistical operations were carried out using the R and SPSS (v27) statistical packages.

RESULTS

Between February 2010 and October 2020, there were 131 procedures at the fourteen participating sites. The mean age of subjects at the time of the surgical procedure was 47.4 years (47.8 years for THA and 47.3 years for TKA), and mean weight and BMI were 89.2 kg and 27.8 kg/m^2, respectively (Table 1). Race/ethnicity were self-reported as 73.3%

white, 15.3% African American, 7.6% Hispanic, 3.1% Asian, and 0.8% other/unknown. A history of FVIII or FIX inhibitor was noted in 26.7% of subjects, and 9.2% (n=12) of procedures were performed in subjects with active inhibitors, as defined above. Study procedures included 98 TKA (74.8%) and 33 THA (25.2%) (Table 2). Four individuals underwent bilateral knee replacement, which we considered as a single procedure in this analysis.

Of the 131 procedures, 39 (29.8%) were complicated by major bleeding during the postoperative hospitalization period (Table 3). One unit of pRBC was transfused during hospitalization in 7 cases (5.3%), which were categorized as having minor bleeding. No other minor bleeding events were reported during this period. Of the 39 surgeries complicated by major bleeding events, 22 had a hemoglobin drop of more than 2 grams/dL in a 24-hour period, 10 had post-operative transfusion of 2 or more units of pRBCs, and 7 met both criteria (Figure 1). No subject had bleeding into a critical site or fatal bleeding.

Fourteen subjects experienced confirmed or suspected bleeding into the surgical joint space post-operatively. Thirteen out of fourteen (92.9%) of the suspected or confirmed operative joint bleeds occurred after TKA. One knee bleed required a return to the operating room for management. Four out of five operative joint bleeds diagnosed prior to discharge occurred in subjects who were also classified as having major or minor bleeding during hospitalization. The remaining 9 operative joint bleeds occurred after discharge from the hospital. Multiple possible causes were suspected for these outpatient bleeds, including missing doses of factor prior to physical therapy, sustaining injuries, and participating in routine physical activities such as walking. Nine subjects (6.9%) were readmitted to the hospital during the 6 weeks following initial discharge. Six were readmitted for management of symptoms concerning for bleeding into the operative joint. After evaluation in the hospital, 2 of these 6 were felt to be due to operative joint bleeding and 4 were felt to be due to other causes. The remaining patients were admitted for management of VTE (2 patients) and central line infection (1 patient).

Twelve patients with active inhibitors received recombinant activated factor VII (rFVIIa) prior to, during, and immediately following their surgical procedures. None received activated prothrombin complex concentrate (aPCC) initially, although one subject who was initially treated with FVIII experienced an anamnestic inhibitor response on post-operative day 6 and was treated with aPCC thereafter. Half the patients with active inhibitors experienced major bleeding (Table 3). Major bleeding occurred in 37/119 patients (31.1%) who did not receive pharmacologic thromboprophylaxis versus 2/7 (28.6%) who received low molecular weight heparin (no patient received aspirin or other anticoagulants). Of the nine participants noted to have cirrhosis or liver dysfunction at the time of surgery, one (11.1%) had major bleeding. The proportions of patients who had major bleeding with and without other treatment characteristics are summarized in Table 3.

In the multivariable analysis, factors independently associated with increased odds of major bleeding included THA (OR 2.50, 95% CI 1.00 – 6.28), having an active inhibitor at the time of surgery (OR 4.26, 95% CI 1.05 – 17.35), overweight or obesity (OR 4.49, 95% CI

1.35 – 14.91, and OR 6.09, 95% CI 1.81 – 20.52, respectively), and not using antifibrinolytic medication peri-operatively (OR 3.00, 95% CI 1.09 – 8.27).

Of the enrolled patients undergoing surgery, two (1.5%) had a family history of thrombosis, and 1 (0.8%) reported a personal history of VTE. By the 6-week follow-up visit, 5 of the 131 (3.8%) procedures were associated with symptomatic thrombotic events. Three of these events were deep vein thrombosis (DVT) – two isolated distal DVTs and one suspected event of unknown location (individual declined to have any imaging studies). One subject experienced a pulmonary embolus post-operatively.[22] In addition, there was one reported superficial venous thrombosis event. Four of the VTE events occurred after hospitalization, when factor levels had not been recently measured. One of the VTE events occurred prior to hospital discharge; the highest measured factor activity level post-operatively for this patient was 66%. While 2 of the 5 patients who developed VTE had received factor infusion by continuous infusion during hospitalization, at the time VTE was diagnosed all subjects were being treated with factor by bolus infusions. None of the VTE events occurred in subjects with inhibitors.

DISCUSSION

This is the largest prospective observational study of postoperative bleeding complications in PWH undergoing total knee or total hip arthroplasty. The rate of major bleeding in our population was 29.8%. Previous studies reported bleeding rates between 20 – 50% in patients with hemophilia undergoing TKA or THA, a wide range that includes our study's observed rate of bleeding.[18–20] Overall, 18% of patients required post-operative red cell transfusion, with 13% receiving at least 2 units pRBCs and 5.3% receiving 1 unit of pRBC during hospitalization. These findings are in line with a large retrospective cohort of patients with hemophilia undergoing TKA or THA reported by Kapadia et al to have a 15% transfusion rate compared to 9.8% in matched patients without hemophilia.[24] Given that blood product administration is not without potentially serious risks, the increased need for transfusions in the hemophilia population warrants future mitigation efforts. It is also true, however, that thresholds for transfusion vary by institution and by provider, and postoperative transfusion could potentially be reduced by implementation of more conservative transfusion guidelines. Other approaches to reducing the need for transfusion have been described and tested in patients both with and without hemophilia, such as the multimodal blood loss prevention method, an approach that incorporates the use of intra-articular tranexamic acid, a tourniquet during the procedure, and sealing the femoral canal with bone graft. [25]

One challenge in interpreting the existing literature on bleeding after orthopedic surgery is the use of different criteria to define bleeding.[26] The 29.8% major bleed rate in PWH observed in our cohort is strikingly higher than the 0.6% incidence of major bleeding after THA and TKA reported in one study of patients without hemophilia who were receiving postoperative pharmacologic thromboprophylaxis (aspirin, enoxaparin, or rivaroxaban).[27] However, comparing the definitions of bleeding utilized in the two studies provides an illustrative example of the importance of clear, objective, and consistent measures of bleeding. Lindquist defined major bleeding using the same criteria used in our study, with a

notable exception: transfusion of two or more units of blood and hemoglobin decreases of at least 2 g/dL were only considered to meet the criteria for major bleeding if these were judged to have been the result of “clinically overt” bleeding. In contrast, we did not require a subjective assessment of clinically overt bleeding; rather, the need for transfusion and rapid decline of hemoglobin were categorized in our study as being clinically relevant, regardless of whether there was clinical evidence of overt bleeding. We chose to use the term “major bleed” to signify this clinical relevance.

Furthermore, the Lindquist study’s primary outcome was “any bleeding,” which included both major bleeding as described above and clinically relevant nonmajor bleeding. The incidence of any bleeding in their study sample was 4.1%. This number does not include the large number of patients who required blood transfusions postoperatively, who represented another 23.2% of subjects.[27] Other studies of THA and TKA in the general population report transfusions in sizable proportions of patients. A single center experience found that 16.4% of patients were transfused after these procedures when a blood-conservation algorithm was not utilized; the average decline in hemoglobin observed in these patients was 4.0 g/dL after THA and 3.8 g/dL after TKA.[28] Prior to institution of more stringent blood transfusion guidelines, the rate of transfusion was even higher than that seen in our study, with up to 46% of patients receiving blood transfusions (30% autologous and 16% allogenic) after more than 9400 THA and TKA procedures performed in 1996 – 1997. On average, patients who were transfused in this study received 1.8 units of pRBC (2.1 units for those receiving allogenic transfusions).[29]

Given the differing definitions of bleeding among studies, comparing patients in the general population to those with hemophilia should be performed with caution. It should also be noted that most patients with hemophilia undergo major orthopedic surgery for a different indication (usually hemophilic arthropathy), in which the specific arthropathic changes may contribute to increased peri-operative bleeding risk. Furthermore, patients with hemophilia have an underlying predisposition to bleeding that may be mitigated but perhaps not eliminated by peri-operative treatment with clotting factor. The perceived increased bleeding risk in PWH may impact providers’ clinical management decisions, particularly regarding reducing the threshold for pRBC transfusion. Regardless of differences in bleeding rates between the two patient groups, there is room for improvement in PWH undergoing major joint replacement surgery. Whether reduction of early postoperative bleeding impacts long-term functional outcomes is unknown. The present study will continue to collect annual follow up data to address this question.

Nine of the 131 participants (6.9%) required hospital re-admission within 6 weeks after discharge. Two individuals were readmitted after being clinically diagnosed with bleeding in the surgical joint. Four readmissions occurred for evaluation of lower extremity symptoms suggestive of, but ultimately felt not to be due to bleeding within the surgical joint. Most were managed conservatively with factor replacement and analgesic medications.

One subject required surgical intervention during hospitalization for intraarticular bleeding. Bleeding into the surgical joint may have been precipitated by use of the joint (physical therapy, ambulation), but these interventions are necessary to maximize potential gains of

function after surgery. Optimizing postoperative factor replacement during physical therapy and ambulation might be a focus for improving future hemostatic outcomes, especially when the frequency or timing of factor replacement may not coincide with the frequency or timing of physical therapy, thereby preventing achievement of optimal factor levels at physical therapy. When postoperative bleeding occurs, not only is optimal factor treatment required but also reduced joint activity and rest, which may slow the rehabilitation progress.

It is common practice in many institutions to utilize intra-operative antifibrinolytic agents in major lower extremity orthopedic surgery to reduce blood loss, with no apparent increased risk of postoperative VTE.[30] A number of clinical trials in the non-hemophilia population have supported this practice and shown antifibrinolytics to be safe and efficacious for preventing intra- and post-operative blood loss after THA and TKA.[31, 32] We observed in our cohort that only 21% of those who received any antifibrinolytic medication during hospitalization exhibited major bleeding, compared to 36% of those who did not receive these medications. Our findings support the routine use of antifibrinolytic agents in PWH undergoing major orthopedic surgery, though identification of the most effective and safe dosing regimens requires further investigation.

The risk of bleeding during the perioperative period must be balanced against the risk of thrombosis, particularly VTE. In 131 TKA or THA procedures, we identified 3 symptomatic deep venous thromboses (2.3%) and 1 pulmonary embolus (0.8%), despite only 7 of 131 (5.3%) participants receiving pharmacologic thromboprophylaxis. Notably, the majority of participants (57.3%) received some form of thromboprophylaxis (pharmacologic and/or mechanical) during hospitalization (Table 2).

Our ability to control for and study all clinical practices related to THA and TKA in PWH was limited by the observational nature of our study. For instance, the low number of subjects receiving pharmacologic thromboprophylaxis limited our ability to investigate the impact of this intervention on bleeding risk. Our findings must also be considered in light of differences in practice patterns in the surgical and medical management of PWH undergoing major lower extremity orthopedic surgery. It is also possible that some of the patients included in the study had joint disease due to osteoarthritis rather than hemophilic arthropathy. This study did not collect data describing number and locations of joint hemorrhages prior to hip or knee replacement, and findings from histopathologic examinations of joint tissues, if performed, were not assessed by the study. It is therefore unclear whether the underlying condition that led to the need for arthroplasty might have impacted bleeding outcomes. That said, the study's prospective, multicenter approach to recruitment, data collection, and analysis captured a representative, real-world sample of men with hemophilia who underwent TKA or THA across 14 centers in the United States. Moreover, the variability in practice and patient characteristics observed in this study underscores the need for more uniform guidance to reduce post-surgical bleeding in PWH, as well as standard approaches to post-operative physical rehabilitation.

Although our study was not designed to establish a comparison group that would allow matching patients with hemophilia with non-hemophilic controls, other retrospective cohort studies have demonstrated that PWH undergoing TKA and THA face unique

risks compared to those in the general population, and thus should be cared for by experienced multidisciplinary teams supported by on site laboratories capable of performing rapid turnaround clotting factor assays.[33–35] Future prospective research and quality improvement initiatives should focus on narrowing the gap in complication rates between patients in the general population and PWH undergoing major lower extremity orthopedic surgery.

In conclusion, this prospective, multicenter observational study of men with hemophilia undergoing major lower extremity orthopedic surgery highlights that perioperative bleeding is relatively common despite the use of factor replacement. Our data suggest that this risk may be mitigated by treating with an antifibrinolytic medication, though further study is needed. These considerations and the data from this study can help inform the shared decision-making process when PWH and their providers discuss the potential risks and benefits of joint replacement surgery.

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ESSENTIALS

- Risk factors for bleeding after orthopedic surgery in patients with hemophilia are unknown.
- Bleeding outcomes in adults with hemophilia were assessed in a prospective, multicenter study.
- Thirty percent of patients with hemophilia had major bleeding after hip or knee arthroplasty.
- Bleeding risk was impacted by inhibitor status, body mass index and use of antifibrinolytics.

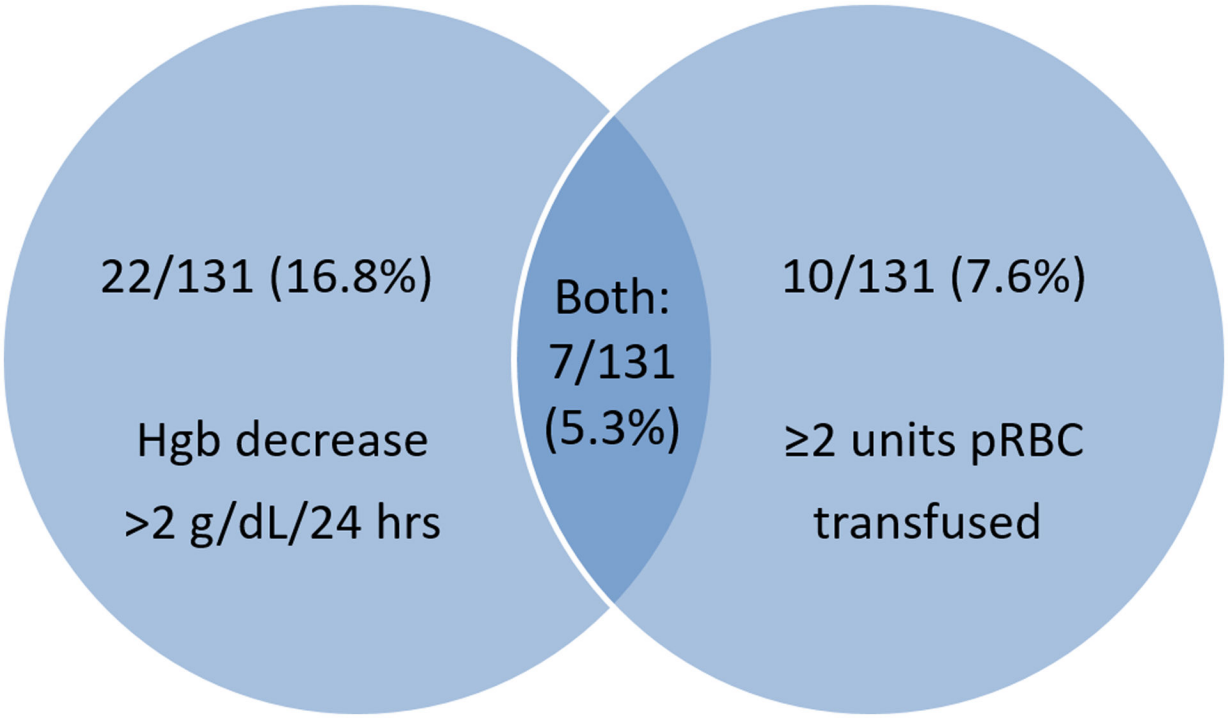

Figure 1: Major bleeding events during hospitalization following 131 total hip and knee arthroplasty procedures in men with hemophilia A or B. No patients had fatal or critical site bleeds.

Hgb=hemoglobin, pRBC=packed red blood cells

Table 1:

Demographic and Clinical Characteristics of 131 THA and TKA Procedures in PWH.

Patient Characteristic	
Age in years, mean (median, range)	47.4 (49.6, 22.2 – 72.2)
Hemophilia type, n (%)	
A	107 (81.7)
B	22 (16.8)
Missing	2 (1.5)
Hemophilia severity, n (%)	
Severe	86 (65.6)
Moderate	20 (15.2)
Mild	22 (16.8)
Missing	3 (2.3)
Active inhibitor at time of surgery, n (%)	12 (9.2)
Weight (kg), mean (median, range)	89.2 (85, 51.0 – 148.6)
Body mass index category, n (%)	
Normal / underweight (<25 kg/m^2)	38 (29.0)
Overweight (25–30 kg/m^2)	44 (33.6)
Obese (>30 kg/m^2)	43 (32.8)
Missing	6 (4.6)
Viral infection history, n (%)	
HIV	24 (18.3)
HCV	95 (72.5)

THA=total hip arthroplasty, TKA=total knee arthroplasty, PWH=persons with hemophilia, HIV=human immunodeficiency virus, HCV=hepatitis C virus

Table 2:

Procedures Performed by Hemophilia Type / Severity and Clinical Management Strategies.

Characteristic	THA, n	TKA**, n	Total, n
Hemophilia type and severity *			
A (total)	26	81	107
Severe	16	47	63
Moderate	1	15	16
Mild	5	10	15
Active inhibitor	3	9	12***
Missing severity	1	0	1
B (total)	7	15	22
Severe	3	10	13
Moderate	1	3	4
Mild	3	2	5
Clotting factor administration			
Continuous infusion	9	37	46
Bolus infusions only	23	52	75
Missing	1	9	10
Antifibrinolytic therapy			
Yes	7	31	38
No	25	62	87
Missing	1	5	6
Postoperative thromboprophylaxis			
None	14	37	51
Pharmacologic only	0	1	1
Mechanical only	17	51	68
Pharmacologic + Mechanical	1	5	6
Missing	1	4	5

* Two participants missing hemophilia type.

** Four participants underwent bilateral total knee arthroplasty procedures.

*** 10 with severe hemophilia A, 2 with mild hemophilia A

THA=total hip arthroplasty; TKA=total knee arthroplasty.

Table 3:

Clinical factors potentially related to bleeding risk in men with hemophilia A or B during hospitalization following THA or TKA.

Variable	Number with Major Bleeding, n/total (%)
Procedure type	
THA	15/33 (45.5)
TKA	24/98 (24.5)
Hemophilia type	
A	33/107 (30.8)
B	6/22 (27.3)
Hemophilia severity	
Severe	25/86 (29.1)
Moderate	7/20 (35)
Mild	7/22 (31.8)
Active inhibitor *	
Present	6/12 (50)
Not present	33/110 (30.0)
Body mass index category	
Normal/underweight (<25 kg/m^2)	5/38 (13.2)
Overweight (25–30 kg/m^2)	16/44 (36.4)
Obese (>30 kg/m^2)	18/43 (41.9)
Clotting factor administration approach	
Continuous infusion	13/46 (28.3)
Bolus only	24/75 (32)
Use of antifibrinolytic medication	
Yes	8/38 (21.1)
No	31/87 (35.6)
Use of pharmacologic thromboprophylaxis	
Yes (low molecular weight heparin)	2/7 (28.6)
No	37/119 (31.1)

* defined as use of bypass agent as primary hemostatic medication during / after procedure

THA=total hip arthroplasty, TKA=total knee arthroplasty

Table 4:

Univariable analysis of major bleeding in hemophilia patients undergoing hip or knee arthroplasty.

Variable	n	OR	95% CI	p value
Procedure type: THA	125	2.54	1.10 – 5.85	**0.03**
Age (continuous)	125	0.99	0.96 – 1.03	0.61
Hemophilia type: A	125	1.26	0.45 – 3.51	0.66
Hemophilia severity	125	0.90	0.55 – 1.47	0.68
Active inhibitor	122	2.44	0.73 – 8.13	**0.15**
Overweight vs. normal BMI	124	3.66	1.19 – 11.27	**0.02**
Obese vs. normal BMI	124	4.61	1.50 – 14.13	**0.01**
Thromboprophylaxis	125	0.88	0.16 – 4.72	0.88
No antifibrinolytic used	125	2.08	0.85 – 5.08	**0.11**
Continuous factor infusion	121	1.20	0.53 – 2.67	0.67

P values in bold (less than 0.2) indicate variables included in multivariable analysis.

OR=odds ratio, CI=confidence interval, THA=total hip arthroplasty, BMI=body mass index

* includes individuals with BMI data available (see Table 1)

Table 5:

Odds of major bleeding based on patient characteristics and surgical factors: multivariable analysis (n=121).

Variable	OR	95% CI	p value
Procedure type: THA	2.50	1.00 – 6.28	0.05
Active inhibitor	4.26	1.05 – 17.35	0.04
BMI:			
overweight vs. normal	4.49	1.35 – 14.91	0.01
obese vs. normal	6.09	1.81 – 20.52	<0.01
No antifibrinolytic used	3.00	1.09 – 8.27	0.03

OR=odds ratio, CI=confidence interval, THA=total hip arthroplasty, BMI=body mass index