Post-Discharge Venous Thromboembolism and Bleeding in a Large Cohort of Patients Undergoing Total Hip or Total Knee Arthroplasty

Michael H. Huo, MD, Donna L. Spencer, PhD, Bijan J. Borah, MA, MSc, PhD, Roger M. Mills, MD, Ying Fan, MS, Aaron Yarlas, PhD, and Winslow Klaskala, MS, PhD

ABSTRACT

- *Objective:* To examine the incidence of and risk factors for venous thromboembolism (VTE) and bleeding in a US population of total hip or total knee arthroplasty (THA/TKA) patients.
- *Design:* Retrospective database study.
- *Setting:* Health care claims records (2004–2009) from a large insurance plan linked to an inpatient database.
- *Participants:* THA/TKA patients with no evidence of prior orthopaedic surgeries or prior VTE and no post-discharge orthopaedic surgeries.
- *Measurements:* ICD-9-CM and CPT/HCPC codes were used to identify symptomatic VTE and bleeding events up to 90 days post-surgery.
- *Results:* Of 9167 linked patients (3109 THA; 6058 TKA; median age 60 years; mean Charlson-Quan comorbidity score 0.5), 98% received thromboprophylaxis in hospital and 26% received it post-discharge. Mean overall duration of antithrombotic drug exposure was 10.7 days. 226 (2.5%) patients experienced VTE, and 324 (3.5%) had bleeding. Consistent covariates of post-discharge VTE and bleeding were inpatient VTE or bleeding events, respectively, and all-cause rehospitalization. Post-discharge thromboprophylaxis did not achieve statistical significance as a bleeding risk factor.
- *Conclusion:* Patients who experience VTE or bleeding events during index hospitalization and those rehospitalized within 90 days have higher odds of post-discharge thromboembolic and bleeding outcomes, respectively. Post-discharge thromboprophylaxis for THA/TKA does not significantly increase the risk of post-discharge bleeding.

More than 1 million total hip arthroplasties (THAs) and total knee arthroplasties (TKAs) are performed annually in the United States. Patients undergoing THA or TKA are at risk for venous thromboembolism (VTE), which encompasses both deep vein thrombosis (DVT) and pulmonary embolism (PE). Evidence-based data and guidelines [1–2] recommend VTE prophylaxis in all patients undergoing THA and TKA, and nearly all patients undergoing TKA or THA do receive some form of prophylaxis for VTE. However, there is variation in practice, and some patients do not receive guideline-recommended treatment [3–5]. In addition, anticoagulation carries the risk of bleeding complications [6,7].

The purpose of this study was to examine the thromboprophylactic approaches used in patients undergoing THA and TKA as well as occurrences and predictors of VTE and bleeding, in both the inpatient and outpatient settings. We used 2 large integrated national claims and inpatient hospital detail record databases to conduct our study using retrospective review.

METHODS

Patient Sample

Patients had to be age 18 years or older, have documented evidence of elective THA (ICD-9-CM procedure

From the Department of Orthopedic Surgery, University of Texas Southwestern Medical Center, Dallas, TX (Dr. Huo); OptumInsight, Eden Prairie, MN (Dr. Spencer and Mr. Fan); Division of Health Care Policy and Research, Mayo Clinic, Rochester, MN (Dr. Borah); Janssen Pharmaceuticals, Raritan, NJ (Drs. Mills and Klaskala); and QualityMetric, Lincoln, RI (Dr. Yarlas).

code 81.51) or elective TKA (ICD-9-CM procedure code 81.54), and be continuously enrolled in the health plan from 90 days before the index hospital admission to 90 days post-discharge. Exclusion criteria were presence of a claim for VTE or orthopaedic surgery during the 90 days before the index admission, presence of claims for both THA and TKA on the same index procedure date, and any post-discharge orthopaedic surgeries or death during the 90-day post-discharge period.

Data Source

Health care claims from a large US health plan affiliated with OptumInsight (formerly Innovus) were linked to Premier's *Perspective* database (Premier, Charlotte, NC), an inpatient hospital database that represents over 500 US hospitals. Study-eligible patient records identified in both data sources were linked using a methodology described by Hammill et al [8] employing the following variables: admission date for index hospitalization for THA/TKA, discharge date after THA/TKA, patient date of birth, hospital and/or provider name and address, hospital Medicare number (site identifier), patient's primary diagnosis (recorded using ICD-9-CM codes), patient gender, and identifier of health care provider. Only patient records that were unique for the combination of these variables were selected and included in the integrated database. The integrated dataset included data on patients' pre-index characteristics, primary and secondary diagnoses, inpatient procedures, laboratory tests administered, medications dispensed, discharge information (eg, length of stay, discharge status), and post-discharge health care utilization information from claims submitted to the health plan by hospitals, physicians, and pharmacies.

Data from 1 January 2004 through 30 June 2009 were used for this study. Study data were reviewed and determined to be de-identified in compliance with applicable privacy laws. Pursuant to the Health Insurance Portability and Accountability Act (HIPAA), the use of de-identified data does not require institutional review board approval or waiver of authorization. For this reason, the study was not submitted for review.

Study Variables and Coding

Study variables included patient demographic and pre-index characteristics (age, gender, geographic region, Charlson-Quan comorbidity index [9], and medications) as well as thromboprophylaxis use during hospitalization and the post-index period. Length of stay during the index hospitalization and all-cause rehospitalization were also recorded. Inpatient antithrombotic therapeutics were categorized as enoxaparin, warfarin, enoxaparin plus mechanical device, warfarin plus mechanical device, fondaparinux plus mechanical device, warfarin plus enoxaparin plus mechanical device, other pharmacologic agents (mainly antiplatelets), and no prophylaxis. A combination of validated ICD-9-CM diagnosis and procedure codes (per Current Procedural Terminology [CPT] and the Healthcare Common Procedure Coding System [HCPCS]) derived from literature and verified by clinical experts was used to identify study outcomes, which included symptomatic VTE (DVT and/or PE) and bleeding events (major, non-major, other bleeding, or hematoma). The ICD-9-CM diagnosis codes used in this study are presented in the Appendix. VTE and bleeding events were identified for the index hospitalization period (inclusive of the index date) and for the 90-day post-discharge period (exclusive of the discharge date).

Statistical Analysis

Descriptive statistics (frequencies, means, and standard deviations [SDs]) were used to evaluate distributions of study variables; the chi-square test and the independent samples *t* test were used to assess differences between the 2 patient surgery groups (THA vs TKA).

Multivariate logistic regression analyses were performed to identify independent predictors of VTE and bleeding. Results were stratified by surgery type. Although many clinically relevant risk factors for VTE and bleeding were captured by the Charlson-Quan comorbidity score, some variables not included in the index—such as obesity, thrombophilia, abdominal surgery, and history of multiple traumas—were retained as individual covariates. A binary variable for post-discharge all-cause rehospitalization was also included. Multivariate odds ratios (ORs) and 95% confidence intervals (CIs) were used to quantify the predictive relations in estimates, while 2-tailed *P* values were calculated to test for the statistical significance of each relation ($\alpha = 0.05$). Tests for multicollinearity were also conducted. The overall fit of each regression model was evaluated further by the G statistic (also referred to as the likelihood ratio test) and the Hosmer–Lemeshow goodness-of-fit test. All analyses were performed using SAS software version 9.1 (SAS Institute, Cary, NC).

Table 1. Pre-index Patient Characteristics

Patient Characteristics	Total (*n* = 9167)	THA (*n* = 3109)	TKA (*n* = 6058)	*P* Value*
Male, *n* (%)	3898 (42.5%)	1586 (51.0%)	2312 (38.2%)	< 0.001
Geographic region, *n* (%)				
Northeast	433 (4.7%)	190 (6.1%)	243 (4.0%)	< 0.001
Midwest	3372 (36.8%)	1076 (34.6%)	2296 (37.9%)	0.002
South	4192 (45.7%)	1398 (45.0%)	2794 (46.1%)	0.293
West	1170 (12.8%)	445 (14.3%)	725 (12.0%)	0.001
Mean age, y	60.4 [± 10.1]	58.6 [± 11.2]	61.3 [± 9.3]	< 0.001
Mean comorbidity score	0.53 [± 0.96]	0.48 [± 0.96]	0.56 [± 0.95]	< 0.001
Comorbidity score, *n* (%)				
0	6061 (66.1%)	2179 (70.1%)	3882 (64.1%)	< 0.001
1	2040 (22.3%)	614 (19.8%)	1426 (23.5%)	< 0.001
2	668 (7.3%)	198 (6.4%)	470 (7.8%)	0.015
3+	398 (4.3%)	118 (3.8%)	280 (4.6%)	0.066
Obesity, *n* (%)	534 (5.8%)	127 (4.1%)	407 (6.7%)	< 0.001
Thrombophilia, *n* (%)	35 (0.4%)	13 (0.4%)	22 (0.4%)	0.686
Abdominal surgery, *n* (%)	286 (3.1%)	96 (3.1%)	190 (3.1%)	0.899
Surgical resection of abdominal or pelvic cancer, *n* (%)	193 (2.1%)	53 (1.7%)	140 (2.3%)	0.056
Multiple trauma, *n* (%)	1212 (13.2%)	370 (11.9%)	842 (13.9%)	0.008
Antithrombotic drug use, *n* (%)	1191 (13.0%)	365 (11.7%)	826 (13.6%)	0.011
Mean no. of unique medications	5.0 [± 4.0]	4.6 [± 3.7]	5.2 [± 4.1]	< 0.001
Mean no. of medication dispensings	8.7 [± 8.1]	8.1 [± 7.7]	9.0 [± 8.2]	< 0.001

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

*Based on 2-tailed chi-squared tests of association (proportions) and independent samples *t* tests (means) for differences between THA and TKA groups.

RESULTS

Patient Characteristics

Of 72,418 patients with THA or TKA during the study period, 56,984 met the inclusion/exclusion criteria. Of those, 9167 patients (3109 THA and 6058 TKA) were successfully linked to the US hospital inpatient dataset. **Table 1** summarizes the demographic and pre-index characteristics of patients overall and by surgery type.

Mean age among the entire cohort was 60.4 years (SD 10.1), and 42.5% of the patients were male. In general, Charlson–Quan comorbidity index scores were low (mean 0.53). Relatively few patients had evidence of underlying VTE risk factors, such as obesity (5.8%), thrombophilia (< 1.0%), previous abdominal surgery (3.1%), or previous surgical resection of abdominal or pelvic cancer (2.1%). Nearly 15.0% of patients had experienced multiple traumas. On average, patients used a mean of 5.0 unique medications, including antithrombotic agents (13%) and a mean of 8.7 pre-index medication dispensings during the pre-index period.

Compared with the TKA patients, the THA patient group included more males (51.0% vs 38.2%, $P < 0.001$), was slightly younger (mean age 58.6 vs 61.3 years, $P < 0.001$), and had a lower *P* mean Charlson–Quan comorbidity score (0.48 vs 0.56, $P < 0.001$). In addition, fewer THA patients than TKA patients were obese (4.1% vs 6.7%, $P < 0.001$), had trauma events (11.9% vs 13.9%, $P = 0.008$), and had used antithrombotic medications prior to index admission (11.7% vs 13.6%, $P = 0.011$).

VTE Prophylaxis

The mean length of hospital stay was 4.4 days (SD 1.4), with no significant difference observed between types of surgery. The overwhelming majority (98.1%) of patients received thromboprophylaxis during their index

Table 2. Inpatient Thromboprophylaxis

	Total (*n* = 9167)	THA (*n* = 3109)	TKA (*n* = 6058)	*P* Value*
Mean length hospital stay, d	4.4 [± 1.4]	4.4 [± 1.4]	4.5 [± 1.4]	0.563
Inpatient thromboprophylaxis use, *n* (%)	8994 (98.1%)	3053 (98.2%)	5941 (98.1%)	0.665
Enoxaparin	1257 (13.7%)	460 (14.8%)	797 (13.2%)	0.031
Enoxaparin + MPD	2050 (22.4%)	701 (22.6%)	1349 (22.3%)	0.031
Fondaparinux + MPD	526 (5.7%)	184 (5.9%)	342 (5.7%)	0.595
Warfarin	1179 (12.9%)	414 (13.3%)	765 (12.6%)	0.351
Warfarin + MPD	2142 (23.4%)	707 (22.7%)	1435 (23.7%)	0.310
Warfarin + enoxaparin + MPD	529 (5.8%)	174 (5.6%)	355 (5.9%)	0.609
Other	1311 (14.3%)	413 (13.3%)	898 (14.8%)	0.043
None	173 (1.9%)	56 (1.8%)	117 (1.9%)	0.665

MPD = mechanical prophylaxis device; THA = total hip arthroplasty; TKA = total knee arthroplasty.

*Based on 2-tailed chi-square tests of association (proportions) and independent samples *t* tests (means) for differences between THA and TKA groups.

Table 3. Post-Discharge (≤ 90 Days) Thromboprophylaxis

	Total (*n* = 9167)	THA (*n* = 3109)	TKA (*n* = 6058)	*P* Value*
Any post-discharge use, *n* (%)	2420 (26.4%)	800 (25.7%)	1620 (26.7%)	0.299
Warfarin	1611 (17.6%)	557 (17.9%)	1054 (17.4%)	0.538
Enoxaparin	508 (5.5%)	166 (5.3%)	342 (5.7%)	0.544
Fondaparinux	93 (1.0%)	25 (0.8%)	68 (1.1%)	0.150
Other	316 (3.5%)	109 (3.5%)	207 (3.4%)	0.825
MPD	77 (0.8%)	7 (0.2%)	70 (1.2%)	< 0.0001
None	6747 (73.6%)	2309 (74.3%)	4438 (73.3%)	0.299

MPD = mechanical prophylaxis device; THA = total hip arthroplasty; TKA = total knee arthroplasty.

*Based on 2-tailed chi-square tests of association (proportions) and independent samples *t* tests (means) for differences between THA and TKA groups.

hospitalization; 57.2% received both pharmacoprophylaxis plus mechanical prophylaxis (**Table 2**). While the 2 surgery groups did not differ significantly in terms of prophylaxis use, slightly more THA than TKA patients received enoxaparin only (14.8% vs 13.2%; $P = 0.031$) and slightly fewer THA than TKA patients received "other" prophylaxis (13.3 vs 14.8%, $P = 0.043$).

During the post-discharge period, only 26.4% of patients received some form of thromboprophylaxis: 17.6% received warfarin, 5.5% enoxaparin, 1.0% fondaparinux, and 3.5% other therapeutics (**Table 3**). There were no significant differences in post-discharge prophylaxis distribution by surgery type except for the use of mechanical device prophylaxis. However, use of these devices in the post-index period was low for both THA and TKA patient groups (0.2% and 1.2%, respectively). Patients who received either warfarin or enoxaparin in hospital were more likely to receive the same medications post-discharge (data not shown). The mean overall (inpatient and outpatient) antithrombotic drug exposure for the entire cohort was 10.7 days, including a mean 3.3 days during hospitalization and mean 7.4 days post-discharge. The total antithrombotic drug exposure (hospitalization period and/or up to 90 days post-discharge) ranged from 0 days to 100 days with a median of 4 days.

VTE and Bleeding Outcomes

As shown in **Table 4**, 226 (2.5%) patients experienced VTE and 324 (3.5%) patients experienced bleeding during the index inpatient stay and/or the post-discharge

Table 4. VTE and Bleeding Outcomes

	Total (*n* = 9167)	THA (*n* = 3109)	TKA (*n* = 6058)	*P* Value*
Patients with VTE events, n (%)	226 (2.5%)	61 (2.0%)	165 (2.7%)	0.026
During index inpatient stay	33 (0.4%)	10 (0.3%)	23 (0.4%)	0.661
During post-discharge period	159 (1.7%)	45 (1.5%)	114 (1.9%)	0.131
During inpatient stay and post-discharge	34 (0.4%)	6 (0.2%)	28 (0.5%)	0.045
Patients with bleeding events, n (%)	324 (3.5%)	114 (3.7%)	210 (3.5%)	0.623
During index inpatient stay	53 (0.6%)	23 (0.7%)	30 (0.5%)	0.144
During post-discharge period	255 (2.8%)	83 (2.7%)	172 (2.8%)	0.640
During inpatient stay and post-discharge	16 (0.2%)	8 (0.3%)	8 (0.1%)	0.174

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

*Based on 2-tailed chi-square tests of association (proportions) for differences between THA and TKA groups.

period. Compared with THA patients, a slightly higher proportion of TKA patients had VTE (2.7% vs 2.0%, $P = 0.026$), but there was no statistical difference in bleeding rates between the patient groups. The majority of patients with a VTE or any bleeding experienced these adverse events after hospitalization (70.4% and 78.7%, respectively; data not shown).

For patients who experienced an adverse outcome during the post-index period, the type of VTE and bleeding as well as the number of weeks to the first event were examined (data not shown). Some patients experienced more than one type of VTE event. Of 193 patients with post-discharge VTE, 149 (77.2%) had DVT, 59 (30.6%) had PE, and 11 (5.7%) had DVT and PE. Almost two-thirds of patients (64.8%) had their VTE event(s) during the 30 days after hospital discharge.

Of 271 (3.0%) patients who had evidence of any bleeding after hospitalization, 45 (16.6%) had major bleeding, 104 (38.4%) had hematoma, and 126 (46.5%) had non-major bleeding, with some patients having more than one type of bleeding outcome. Eighty percent of major bleeding occurred within 30 days following hospital discharge; however, 75% of patients who had hematoma experienced that event(s) up to 2 months after discharge. The rate and timing of bleeding events following index hospitalization did not differ significantly between THA and TKA patients (data not shown).

Among the 173 patients who did not receive thromboprophylaxis during hospitalization, none experienced VTE and 5 (2.9%) experienced bleeding during the index inpatient stay and/or during the post-discharge period.

Predictors of VTE and Bleeding Events

The consistent predictors of post-discharge VTE (**Table 5**) included an in-patient VTE event during the index hospitalization (OR 54.3 and OR 63.6 for THA and TKA patient groups, respectively; $P < 0.001$) and all-cause rehospitalization during the 90-day follow-up period (OR 9.6 and OR 8.3 for THA and TKA patient groups, respectively; $P < 0.001$). In the THA group, 2 additional risk factors—pre-admission thrombophilia and longer index hospitalization length of stay—were statistically significant predictors of post-discharge VTE (OR 13.5; $P = 0.002$ and OR 1.2; $P = 0.006$, respectively).

The consistent predictors of post-discharge bleeding (**Table 6**) included an inpatient bleeding event during index hospitalization (OR 12.3 and OR 6.6; $P < 0.001$) and all-cause rehospitalization (OR 6.7 and OR 3.7; $P < 0.001$) during the 90-day follow-up period for the THA and TKA patient groups, respectively. In the TKA group, male gender and a higher baseline count of unique medications demonstrated a statistically significant association with post-discharge bleeding (OR 2.1 and OR 1.1; $P < 0.001$, respectively). Both the VTE and bleeding regression models offered a good fit for the data per the goodness-of-fit statistics.

DISCUSSION

Despite important advances in thromboprophylaxis following THA and TKA, patients continue to develop clinically relevant VTE events. These events occur predominantly within the first 90 days following surgery [10]. The incidence estimates of VTE and bleeding

Table 5. Multivariate Analysis of Predictors of Post-Discharge VTE

	THA (n = 3109)			TKA (n = 6058)		
Risk Factor	**OR**	**95% CI**	***P* Value**	**OR**	**95% CI**	***P* Value**
Male gender	1.67	0.90–3.09	0.102	1.37	0.95–1.98	0.094
Age > 60 years	0.92	0.50–1.70	0.798	0.97	0.67–1.40	0.867
Comorbidity score*	0.81	0.58–1.12	0.200	0.91	0.75–1.11	0.341
Pre-index unique medications	1.02	0.94–1.10	0.610	1.04	1.00–1.09	0.059
Pre-index comorbidities						
Obesity	1.50	0.45–5.07	0.512	1.58	0.87–2.87	0.135
Thrombophilia	13.52	2.56–71.44	0.002	3.87	0.66–22.78	0.135
Surgical resection of abdominal or pelvic cancer	1.25	0.34–4.54	0.734	0.70	0.27–1.80	0.456
Multiple trauma	0.61	0.22–1.72	0.351	0.81	0.47–1.39	0.451
Length of inpatient stay	1.21	1.06–1.38	0.006	1.04	0.95–1.15	0.377
VTE event during inpatient stay	54.28	16.83–175.03	< 0.001	63.55	32.85–122.97	< 0.001
Post-discharge all-cause rehospitalization	9.63	4.90–18.93	< 0.001	8.28	5.40–12.69	< 0.001
Goodness-of-fit test						
Likelihood ratio	χ^2 = 81.62, DF = 11, P < 0.001			χ^2 = 232.85, DF = 11, P < 0.001		

OR = odds ratio; THA = total hip arthroplasty; TKA = total knee arthroplasty.

*Presented as a continuous variable.

risk found in this analysis were consistent with rates reported in other studies [11–18]. With analysis by surgery type, the post-discharge incidence of VTE was slightly lower among THA than TKA patients. The post-discharge incidence of bleeding was slightly higher among TKA patients when compared with reports of bleeding events in the literature. The data demonstrated that post-discharge thromboprophylaxis did not significantly increase the risk of post-discharge bleeding complications.

In this study, compared with patients without in-hospital events, those who experienced VTE or bleeding during the index hospitalization were significantly more likely to experience the same type of adverse event following their discharge from the hospital. The other significant covariate for both post-discharge VTE and bleeding was all-cause rehospitalization within 90 days post-discharge. As reported by other studies, some of these rehospitalizations could have been due to post-surgical wound complications, including prosthetic joint infections and hematoma formation [19,20]. Our study did not examine the timing of rehospitalization relative to the VTE or bleeding outcome and did not examine the reason for rehospitalization.

Unlike a previous study by Anderson and White [21], our analysis did not identify male gender as a risk factor for VTE. Other reports have found contradictory evidence of the effect of gender on risk for VTE [14,16]. Similar inconsistencies were found with respect to patient baseline comorbidities, including obesity. Whereas our results indicating that pre-index thrombophilia is associated with higher odds of VTE in the THA group and is consistent with previous reports [22], the evidence that obesity is not a significant predictor of VTE is in contrast to previous findings [11,12,16,23]. This could be due to under-reporting, because obesity cannot be captured by the ICD-9 codes and is not recorded in the patients' medical charts.

There are inconsistent findings in the literature with respect to patient-related risk factors for post-discharge VTE and bleeding complications [24–26]. Post-discharge bleeding can occur in THA and TKA patients even in the absence of thromboprophylaxis [22].

Patterns of antithrombotic strategies in this study were consistent with those reported by the Hip and Knee Registry of over 23,000 THA and TKA patients [27]. In our study, most patients received mechanical device prophylaxis along with a pharmaceutical anticoagulant

Table 6. Multivariate Analysis of Predictors of Post-Discharge Bleeding Events

Risk Factor	THA (*n* = 3109)			TKA (*n* = 6058)		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Male gender	1.28	0.82–1.99	0.279	2.05	1.51–2.78	< 0.001
Age > 65 years	1.04	0.63–1.71	0.889	1.00	0.72–1.40	0.993
Comorbidity score*	1.12	0.94–1.35	0.214	1.06	0.92–1.22	0.439
Pre-index unique medications	1.05	0.99–1.11	0.079	1.06	1.03–1.10	< 0.001
Length of inpatient stay	1.07	0.95–1.20	0.266	1.05	0.97–1.14	0.198
Bleeding event during inpatient stay	12.33	5.05–30.11	< 0.001	6.55	2.78–15.42	< 0.001
Post-discharge thromboprophylaxis use†	0.91	0.56–1.48	0.689	0.98	0.70–1.37	0.909
Post-discharge all-cause rehospitalization	6.66	3.85–11.53	< 0.001	3.74	2.45–5.69	< 0.001
Goodness-of-fit test						
Likelihood ratio	χ^2 = 72.25, DF = 8, *P* < 0.001			χ^2 = 88.68, DF = 8, *P* < 0.001		

OR = odds ratio; THA = total hip arthroplasty; TKA = total knee arthroplasty.

*Presented as a continuous variable.

†Includes only pre-outcome thromboprophylaxis medication/device use. For patients with bleeding during the post-discharge period, this variable indicates any medication/device use before the bleeding outcome occurred. For patients without bleeding during the post-discharge period, this variable indicates any medication/device use during the entire follow-up period.

(mainly warfarin or enoxaparin) during their hospital stay. Nearly all patients received thromboprophylaxis during hospitalization, but only a relatively small proportion (26%) received anticoagulation (in most cases either warfarin or enoxaparin) post-discharge. These findings are consistent with previous reports [21,28,29].

This analysis has some limitations: (1) claims data may result in variability in the quality of the data collected; (2) the claims data may have under-reported comorbid conditions in the multivariate analysis; (3) although we adjusted for pre-index (baseline) characteristics in the regression models, unmeasured confounders may still limit statistical inferences from the data; and (4) the results of this study reflected the health utilization patterns of adult patients enrolled in a large healthcare plan and may not be generalizable to other insured or uninsured populations in the United States. Further, it is important to note that the study may be limited by the sample attrition observed for the eligible subjects for whom linkage with the hospital detail data was not achieved. Although a complete comparison between those included and excluded was not possible, an examination of the overall VTE and bleeding rates for the entire THA/TKA claims-only dataset of eligible patients found the rates (2.4% and 3.1%, respectively) similar to those observed for the linked study cohort (2.5% and 3.5%, respectively).

Despite these limitations, we believe that this study contributes to a better understanding of the risk factors for VTE and bleeding following hospital discharge in the THA and TKA patient populations. The strength of this analysis was the use of an integrated dataset of medical claims linked to hospitalization data across the inpatient and outpatient continuum of care. While results of most studies are presented in an aggregate format (ie, with THAs and TKAs combined), we examined clinical outcomes separately by the type of surgery. When evaluating thromboprophylaxis patterns, we included mechanical device prophylaxis, which were often omitted in previous analyses.

Conclusion

Post-discharge use of VTE prophylaxis has been shown to be effective for the prevention of symptomatic DVT and PE. In this large sample of patients, post-discharge thromboprophylaxis did not significantly increase the risk of post-discharge bleeding complications.

Acknowledgments: The authors would like to thank Dr. Mark Maruish from QualityMetric, who provided valuable assistance with the literature review and composition of the initial draft version of this manuscript. The authors would also like to acknowledge Ruth Sussman, PhD, who provided editorial support.

Appendix. ICD-9-CM Diagnosis Codes for Identifying VTE and Bleeding Outcomes

Diagnosis	ICD-9-CM Diagnosis Codes
DVT	451.1, 451.11, 451.19, 451.2, 451.81, 453.2, 453.4, 453.40, 453.41, 453.42, 453.8, 453.9
Pulmonary embolism	415.1x
Major bleeding	360.43, 362.81, 363.61-363.62, 372.72, 376.32, 379.23, 430, 431, 432.x, 531.0x, 531.2x, 531.4x, 531.6x, 534.0x, 534.2x, 534.4x, 534.6x, 537.83, 568.81, 569.83, 578, 596.7, 719.1x, 786.3, 852
Non-major bleeding	530.82, 532.0x, 532.2x, 532.4x, 532.6x, 562.02, 562.03, 562.12, 562.13, 569.3, 599.7x, 599.89, 626.6, 782.7, 784.7, 784.8
Other bleeding	287.9, 374.81, 448.9, 459.0, 533.0x, 533.2x, 533.4x, 533.6x, 958.2

Corresponding author: Donna Spencer, PhD, Optum-Insight, 12125 Technology Dr., Eden Prairie, MN 55344, donna.spencer@optum.com.

Funding/support: This study was sponsored by Janssen Pharmaceuticals.

Financial disclosures: Dr. Huo is a consultant for Stryker and DePuy and serves on the speakers bureaus for Cadence and Janssen.

REFERENCES

1. Jacobs JJ, Mont MA, Bozic KJ, et al. Preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty: evidence-based guideline and evidence report. 2011. American Academy of Orthopaedic Surgeons. Accessed 1 Oct 2011 at www.aaos.org/Research/guidelines/VTE/VTE_full_guideline.pdf.
2. Guyatt GH, Akl EA, Crowther M, et al. Executive summary: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2012;141(suppl 2): 7S–47S.
3. Michota FA. Prevention of venous thromboembolism after surgery. Cleve Clin J Med 2009;76(Suppl 4):S45–S52.
4. Warwick D, Friedman RJ, Agnelli G, et al. Insufficient duration of venous thromboembolism prophylaxis after total hip or knee replacement when compared with the time course of thromboembolic events: Findings from the global orthopaedic registry. J Bone Joint Surg Br 2007;89:799–807.
5. Yu HT, Dylan ML, Lin J, Dubois RW. Hospitals' compliance with prophylaxis guidelines for venous thromboembolism. Am J Health Syst Pharm 2007;64:69–76.
6. Quinlan JO, Bergqvist D, Eikelboom J. A critical appraisal of bleeding events reported in venous thromboembolism prevention trials of patients undergoing hip and knee arthroplasty. J Thromb Haemost 2010;8:1966–75.
7. Crowther MA, Warkentin TE. Bleeding risk and the management of bleeding complications in patients undergoing anticoagulant therapy: focus on new anticoagulant agents. Blood 2008;111:4871–9.
8. Hammill BG, Hernandez AF, Peterson ED, et al. Linking inpatient clinical registry data to Medicare claims data using indirect identifiers. Am Heart J 2009;157:995–1000.
9. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43:1130–9.
10. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):381S–453S.
11. Douketis JD, Eikelboom JW, Quinlan DJ, et al. Short-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of prospective studies investigating symptomatic outcomes. Arch Intern Med 2002;162:1465–71.
12. Kapoor A, Labonte AJ, Winter MR, et al. Risk of venous thromboembolism after total hip and knee replacement in older adults with comorbidity and co-occurring comorbidities in the Nationwide Inpatient Sample (2003-2006). BMC Geriatr 2010;10:63.
13. Wells PS, Borah BJ, Sengupta N, et al. Analysis of venous thromboprophylaxis duration and outcomes in orthopedic patients. Am J Manag Care 2010;16:857–63.
14. White RH, Romano PS, Zhou H, et al. Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. Arch Intern Med 1998;158:1525–31.
15. Colwell CW Jr, Collis DK, Paulson R, et al. Comparison of enoxaparin and warfarin for the prevention of venous thromboembolic disease after total hip arthroplasty. Evaluation during hospitalization and three months after discharge. J Bone Joint Surg Am 1999;81:932–40.
16. White RH, Henderson MC. Risk factors for venous thromboembolism after total hip and knee replacement surgery. Curr Opin Pulm Med 2002;8:365–71.
17. Callaghan JJ, Warth LC, Hoballah JJ, Liu SS, Wells CW. Evaluation of deep venous thrombosis prophylaxis in low-risk patients undergoing total knee arthroplasty. J Arthroplasty 2008;23:20–4.
18. Samama CM, Vray M, Barre J, et al. Extended venous thromboembolism prophylaxis after total hip replacement: a comparison of low-molecular-weight heparin with oral

anticoagulant. Arch Intern Med 2002;162:2191–6.
19. Husted H, Otte KS, Kristensen BB, et al. Low risk of thromboembolic complications after fast-track hip and knee arthroplasty. Acta Orthop 2010;81:599–605.
20. Bini SA, Fithian DC, Paxton LW, et al. Does discharge disposition after primary total joint arthroplasty affect readmission rates? J Arthroplasty 2010;25:114–7.
21. Anderson FA Jr, White K. Prolonged prophylaxis in orthopedic surgery: insights from the United States. Semin Thromb Haemost 2002;28 Suppl 3:43–6.
22. Wu O, Robertson L, Twaddle S, et al. Screening for thrombophilia in high-risk situations: systematic review and cost-effectiveness analysis. The Thrombosis: Risk and Economic Assessment of Thrombophilia Screening (TREATS) study. Health Technol Assess 2006;10:1–110.
23. Samama CM, Ravaud P, Parent F, et al. Epidemiology of venous thromboembolism after lower limb arthroplasty: the FOTO study. J Thromb Haemost 2007; 5:2360–7.
24. Freedman KB, Brookenthal KR, Fitzgerald RH Jr, et al. A meta-analysis of thromboembolic prophylaxis following elective total hip arthroplasty. J Bone Joint Surg Am 2000;82:929–38.
25. Mismetti P, Laporte S, Zufferey P, et al. Prevention of venous thromboembolism in orthopedic surgery with vitamin K antagonists: a meta-analysis. J Thromb Haemost 2004;2:1058–70.
26. Muntz J, Scott DA, Lloyd A, Egger M. Major bleeding rates after prophylaxis against venous thromboembolism: systematic review, meta-analysis, and cost implications. Int J Technol Assess Health Care 2004;20:405–14.
27. Anderson FA Jr, Hirsh J, White K, Fitzgerald RH Jr. Temporal trends in prevention of venous thromboembolism following primary total hip or knee arthroplasty 1996-2001: findings from the Hip and Knee Registry. Chest 2003;124:349S–356S.
28. Merli GJ, Malangone E, Lin J, et al. Real-world practices to prevent venous thromboembolism with pharmacological prophylaxis in US orthopedic surgery patients: an analysis of an integrated healthcare database. J Thromb Thrombolysis 2011;32:89–95.
29. Fisher WD. New oral anticoagulants and outpatient prophylaxis of venous thromboembolism. Am J Manag Care 2011;17:S15–S21.