CLINICAL RESEARCH

Symptomatic Pulmonary Embolus After Joint Arthroplasty: Stratification of Risk Factors

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Abstract

Background Prophylaxis for pulmonary embolism (PE) after total joint arthroplasty (TJA) presents the clinical dilemma of balancing the risk of postoperative thrombotic risk and anticoagulation-related complications such as bleeding, hematoma formation, and infection. Risk stratification of patients undergoing TJA is needed to tailor prophylaxis based on thrombotic and bleeding risk.

Questions/purposes The purpose of this study was to identify the preoperative comorbidities that were associated with an increased risk of symptomatic PE after joint arthroplasty in a large group of patients who had TJAs and who were treated with either aspirin or warfarin.

Methods We conducted a retrospective study of 26,391 primary and revision TJAs performed at our institution between January 2000 and April 2011. A total of 24,567 patients received warfarin prophylaxis for 6 weeks (targeted international normalized ratio of 1.5–2.0) and 1824 patients received 325 mg aspirin twice daily. Symptomatic patients with decreased oxygen saturation were evaluated for PE using either a ventilation/perfusion scan or multidetector CT scan. Symptomatic PEs occurring in patients within 90 days postoperatively identified with CT or ventilation/perfusion scans were considered complications related to surgery, and fatal PEs were those that occurred in patients who died during the hospital admission owing to cardiopulmonary failure after PE. Using a logistic regression analysis, a nomogram was created to predict postoperative symptomatic PE risk.

Results Risk of postoperative symptomatic PE after primary and revision TJAs was 1.1%. Risk of postoperative fatal PE was 0.02%. Elevated BMI (p < 0.035), procedures on the knee (p < 0.006), higher Charlson Comorbidity Index (p < 0.015), chronic obstructive pulmonary disorder (p = 0.006), atrial fibrillation (p < 0.001), anemia (p < 0.001), presence of deep vein thrombosis (p < 0.001), and depression (p = 0.012) were independent risk factors for symptomatic PE. Based on these risk factors and derived scoring criteria, patients can be classified into low- (0.35%), medium- (1.4%), and high- (9.3%) risk categories.

Conclusions Patients who are obese, undergo knee procedures, have an elevated Charlson Comorbidity Index, chronic obstructive pulmonary disease, atrial fibrillation, anemia, depression, or postoperative deep vein thrombosis are at greater risk of having a postoperative PE develop. These risk factors should be considered when deciding on postoperative anticoagulation prophylaxis.

Level of Evidence Level IV, therapeutic study. See the Instructions for Authors for a complete description of levels of evidence.

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Introduction

During the next two decades, the number of total joint arthroplasties (TJAs) in the United States and worldwide is predicted to increase dramatically. Kurtz et al. [19] predicted that by 2030, there will be 174% and 673% increases in the number of primary THAs and primary TKAs, respectively. One of the most serious complications after TJA is pulmonary embolism (PE) [2, 6, 10, 13, 16]. The risk of symptomatic and asymptomatic PEs after TJA in patients receiving thromboprophylaxis has been reported to be 0.4% to 23% [8, 11, 18, 24, 26, 43]. In addition to patient morbidity and mortality, a PE leads to an extended hospital stay and increased treatment costs, creating an economic burden that can be expected to increase in the future [5, 30]. Consequently, patients undergoing TJA often are prescribed a postoperative anticoagulation regimen in an attempt to minimize the occurrence of postoperative venous thromboembolism (VTE), particularly PE. However, VTE prophylaxis presents the clinical dilemma of balancing postoperative thrombotic risk along with anticoagulation-related complications such as bleeding, hematoma formation, and infection [10]. Therefore, it would be helpful if risks for symptomatic PE in patients undergoing TJA could be clarified to stratify patients by their thrombotic risk to allow tailored prophylaxis.

Several studies have identified risk factors involved in the development of PE after general surgery procedures [3, 7, 8, 21]. For example, Caprini et al. [3] developed scoring criteria to determine the risk of PE in the general surgery population. However, risk factors for PE after TJA have not been as well defined. Whereas a TJA may be considered a prothrombotic risk factor, it remains unclear what role other factors play in affecting postoperative PE risk. Studies currently available in the literature evaluating PE risk after TJA have several limitations including small sample size, limited followup, selective patient populations, and/or incomplete data [4, 22, 25, 37, 43]. Furthermore, some PE risk studies with large cohorts of patients [6, 13] use International Classification of Diseases, 9th Revision (ICD-9) or International Classification of Diseases, 10th Revision coding data to identify complications. Although such coding often is helpful for identifying known comorbidities, there are concerns regarding underreporting and/or inaccurate reporting of perioperative complications. Such concerns will continue to hamper studies that rely on large databases in which a significant proportion of the perioperative information is coded by hospital billing staff and not by medical personnel.

The purpose of our study is to identify risk factors for symptomatic PE after primary and revision joint arthroplasties in patients who receive either prophylactic warfarin or aspirin therapy. Our aim is to develop criteria to stratify patients according to their risk of symptomatic PE to provide targeted postoperative PE prophylaxis.

Materials and Methods

Study Design

Study data were obtained from a prospectively maintained joint arthroplasty database that includes comprehensive documentation of all admissions and discharges of patients who have undergone procedures at one institution. The database includes data from primary admissions and readmissions. After institutional review board approval, all primary and revision TJAs performed at our institution from January 2000 to April 2011 were identified. A total of 26,415 patients undergoing primary and revision TJAs were identified from the institutional database. All patient records were reviewed to identify the type of PE prophylaxis administered. A total of 24,567 patients received postoperative pharmacologic VTE prophylaxis with warfarin (targeted international normalized ratio of 1.5–2) and 1824 patients received prophylaxis with our institutional aspirin protocol (single dose of low-dose warfarin the night of surgery followed by 325 mg aspirin twice daily). All patients receiving anticoagulation other than warfarin or aspirin were excluded (enoxaparin, 21 patients; heparin, two patients; fondaparinux, one patient). From 2000 until December 2007, all surgeons at our institution used warfarin for routine postoperative VTE prophylaxis. Beginning in January 2008, one of our surgeons began using aspirin 325 mg twice a day for VTE prophylaxis, and since then, there has been a gradual trend at our institution toward using aspirin for postoperative VTE prophylaxis. Patient demographics were obtained from hospital admission information. Comorbidities were collected using ICD-9 discharge coding.

Based on clinical suspicion for PE, an imaging workup with either chest CT or ventilation/perfusion scans was obtained. Beginning in 2008, an institutional protocol was put into effect for workup of PE to reduce the overdiagnosis of PE [45]. Under the new protocol, symptomatic patients with symptoms of tachypnea greater than 20 breaths per minute, tachycardia greater than 100 beats per minute, new onset arrhythmia, hemoptysis, dyspnea, or chest pain, receive 2 L of oxygen via nasal cannula. Pulse oximetry then is rechecked after 10 minutes, and if the oxygen saturation is less than 90%, a ventilation/perfusion scan or multidetector CT scan is obtained to rule out PE. In asymptomatic patients with oxygen saturation less than 90% with otherwise normal vital signs, 2 L of oxygen is given via nasal cannula, oxygen saturation is checked 10 minutes later, and if less than 90%, a ventilation/perfusion

scan or multidetector CT scan is obtained. A positive radiologic result for PE was defined as PE seen on the CT scan, including subsegmental PEs, and high probability on ventilation/perfusion scans.

Mortality data (for purposes of 90-day mortality after hospital discharge) were obtained using the Social Security Death Index. Patients who were identified to have died within 90 days postoperatively were crossmatched to those who were identified to have had a PE develop. A detailed review of the medical record then was performed to confirm that the mortality was related to the PE.

Patients and Events

Of the 26,391 patients in the database, 1125 underwent workup for suspected PE. Overall, 1216 radiologic evaluations were performed, including 955 CT scans of the chest and 261 ventilation/perfusion scans. Diagnosis of symptomatic PE was confirmed in 281 of the 1125 patients scanned for suspected PE, yielding a symptomatic PE risk of 1.1% (281 of 26,391 patients) after TJA at our institution (Fig. 1). Two of the 24 patients who were treated with

nonwarfarin or nonaspirin anticoagulation had postoperative symptomatic PEs develop. These 24 patients were excluded from the final analysis because of inconsistency in the anticoagulation protocol.

The mean age of the patient population was 69.4 years (range, 11.2–99.6 years) and the average BMI was 32.0 kg/m^2 (range, 10.2–77.5 kg/m^2) (Table 1). Two hundred forty-six of the 281 (87.5%) patients who had PEs develop were diagnosed during their initial hospital stay; the remaining 35 were diagnosed on readmission. Ninety-day all-cause mortality in our study cohort was 0.33% (86 of 26,391 patients). However, only four deaths were directly attributable to PE for a risk of 0.02%, and there were no deaths documented in our hospital records that were attributable to PE prophylaxis.
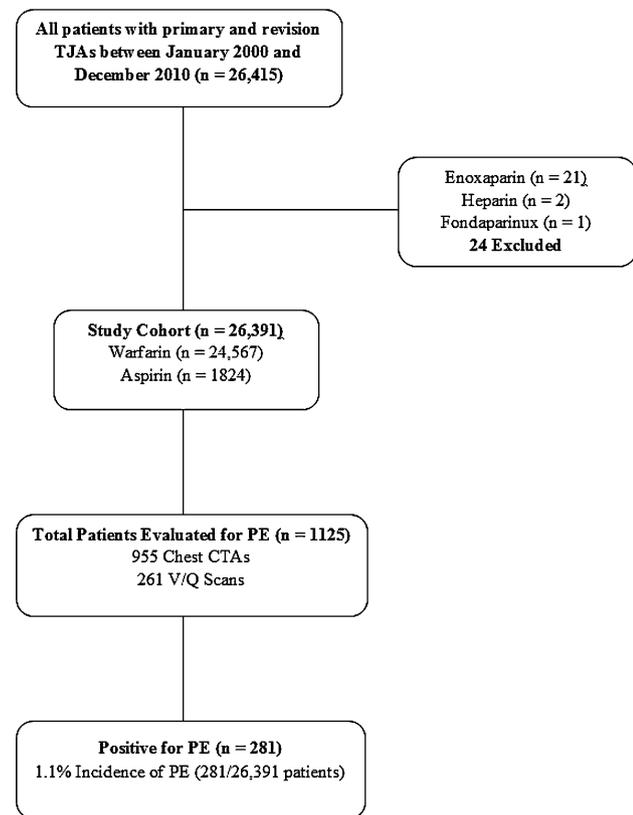

Fig. 1 The flow diagram for our study is shown. TJA = total joint arthroplasty; PE = pulmonary embolism; CTA = computed tomography angiography; V/Q = ventilation/perfusion scan.

Table 1. Multivariate analysis for pulmonary embolus risk factors

Multivariate variable	Odds ratio/95% CI	p value
BMI (kg/m^2)		
< 25	1.000 (reference value)	
≥ 25 and < 30	1.619; 0.93–2.32	0.04
≥ 30 and < 35	2.275; 1.21–3.04	< 0.001
≥ 35 and < 40	2.399; 1.15–3.23	0.001
≥ 40	2.320; 0.99–3.12	0.003
Procedure		
Primary hip	1.000 (reference value)	
Primary knee	3.690; 2.27–4.54	< 0.001
Revision hip	0.809; 0.76–2.60	0.400
Revision knee	2.152; 1.05–3.60	0.006
Charlson Comorbidity Index		
0	1.000 (reference value)	
1	1.743; 0.79–4.60	0.18
2	2.658; 1.01–5.59	0.02
3	3.791; 1.78–9.57	0.001
4	3.574; 1.60–9.22	0.002
5	4.476; 1.77–14.0	0.002
6	6.041; 1.89–32.6	0.01
Bilateral procedure		
Unilateral	1.000 (reference value)	
Staged bilateral	0.525; 0.28–0.70	0.001
Simultaneous bilateral	0.963; 0.91–1.86	0.96
Atrial fibrillation	2.455; 1.70–3.84	< 0.001
COPD	1.599; 0.98–2.10	0.006
Anemia	1.697; 1.20–2.26	< 0.001
Presence of DVT	19.338; 9.97–54.5	< 0.001
Connective tissue disease	0.371; 0.12–1.23	0.05
Depression	1.652; 1.17–2.69	0.01

COPD = chronic obstructive pulmonary disease; DVT = deep vein thrombosis.

Statistics

All analyses were implemented in the package "rms" for the statistical language R (R Foundation for Statistical Computing, www.r-project.org). Comorbidities were identified by ICD-9 codes and were studied as risk factors for postoperative PE (Table 2). Additional risk factors studied, but not reported in Table 2, included age, BMI, race, sex, procedure, Charlson Comorbidity Index, simultaneous bilateral procedure, and type of anticoagulation (warfarin or aspirin).

Table 2. International Classification of Diseases, 9th Revision (ICD-9) coding definitions for comorbidities

Comorbidity	ICD-9 codes
Diabetes mellitus	249-249.79; 250-250.79
Hypothyroidism	244-244.99
Ischemic heart disease	412-414.99
Congestive heart failure	428-428.99
Hypertension	401-405.99
Peripheral vascular disease	443-443.99
Atrial fibrillation	427.3-427.31
Valvulopathy	V42.2; 424-424.3
Chronic obstructive pulmonary disease	490-496.99
Smoking history	V15.82; 305.1
Sleep apnea	327.23; 780.51; 780.57
Anemia	280-285.99
Presence of deep vein thrombosis	453.4-453.49
History of venous thromboembolism	V12.51; V12.55
History of malignancy	V10-V10.99
Active malignancy	140-208.99
Leukemia	V10.6-V10.69; 204-208.99
Lymphoma	200-202.99
HIV	V08-V08.99; V42-V42.99; 42-42.99; 79.53; 795.71
Connective tissue disease	710-710.99; 714-714.99
Crystalline arthropathy	274-274.99; 712.1-712.3
Renal disease	V56-V56.99
Dialysis	V45.1-V45.12
Benign prostatic hypertrophy	600-600.01
Liver disease	570-573.99
Cerebrovascular disease	V12.54; V17.1; 435-435.99; 437-438.99
Depression	V79.0;296.2-296.39; 311-311.99
Anxiety	300-300.02
Peptic ulcer disease	531-533.99
Gastrointestinal reflux disease	530.11; 530.81
Diverticulosis or gastrointestinal bleeding	562-562.99; 578-578.99
Inflammatory bowel disease	555-556.99

Chi-square and independent t-tests were used to identify the individual association of each proposed risk factor with the occurrence of PE. Backward stepwise elimination was used in a logistic regression model to analyze the association of risk factors with postoperative PE occurrence accounting for potential confounders. A p value less than 0.05 was considered statistically significant.

A nomogram was created using a logistic regression model to predict the risk of PE. Initially, logistic regression models were built using the full set of possible predictive variables. This full model then was pruned using a backward elimination algorithm that removed variables with little impact on the prediction. Finally, penalized maximum likelihood estimation was used to constrain the regression coefficients to improve reliability of the model [41]. These steps are intended to prevent overfitting in the model and improve predictive reliability. Internal validation tools based on bootstrapping were used to confirm that the final logistic regression model was not unduly optimistic. A nomogram was generated using the coefficients of the final model to estimate a linear predictor and map the linear predictor to estimated probabilities of the event. The regression coefficients used to create the nomogram indicated independent effect that each risk factor contributed to the risk of symptomatic PE, relative to one another. We used the relative size of the regression coefficients for each independent risk factor to create a whole number system that was clinically feasible to use.

Results

Pulmonary Embolism Risk by Procedure

The risk of symptomatic PE after primary THA was 0.4% (49 of 12,017 procedures), 1.8% after primary TKA (197 of 10,844 procedures), 0.7% after revision hip arthroplasty (16 of 2188 procedures), and 1.4% after revision knee arthroplasty (19 of 1340 procedures). Furthermore, the risk of symptomatic PE after unilateral procedures was 1.1% (202 of 18,612 procedures), 0.7% after staged bilateral TJAs (31 of 4563 procedures), and 1.5% after simultaneous bilateral TJAs (48 of 3216 procedures).

Risk Factors for Pulmonary Embolism

Elevated BMI, procedures on the knee (especially bilateral procedures), higher Charlson Comorbidity Index, chronic obstructive pulmonary disease, atrial fibrillation, anemia, depression, and presence of postoperative deep vein thrombosis were identified as independent risk factors for

Table 3. Preoperative risk factors for pulmonary embolism

Variable	No pulmonary embolism (N = 26,110)	Pulmonary embolism (N = 281)	p value
Age (years)	64.0 ± 12.2	68.8 ± 10.3	< 0.001
BMI (kg/m^2)	30.1 ± 6.7	31.6 ± 6.3	0.001
Sex			
Male	11,261 (43.1%)	97 (34.5%)	0.004
Female	14,849 (56.9%)	184 (65.5%)	
Race			
White	19,355 (74.1%)	216 (76.9%)	0.17
Black	2781 (10.7%)	36 (12.8%)	
Hispanic	153 (0.6%)	1 (0.4%)	
Asian	109 (0.4%)	0 (0.0%)	
Other	3712 (14.2%)	28 (10.0%)	
Procedure			
Primary hip	11,968 (45.8%)	49 (17.4%)	
Primary knee	10,647 (40.8%)	197 (70.1%)	
Revision hip	2172 (8.3%)	16 (5.7%)	< 0.001
Revision knee	1321 (5.1%)	19 (6.8%)	
ASA class			
1	565 (3.4%)	1 (0.4%)	
2	7521 (44.7%)	78 (33.6%)	< 0.001
3	8610 (51.1%)	151 (65.1%)	
	138 (0.8%)	2 (0.9%)	
Charlson Comorbidity Index			
0	2844 (10.9%)	7 (2.5%)	
1	5727 (21.9%)	35 (12.5%)	
2	7085 (27.1%)	73 (26.0%)	
3	6352 (24.3%)	98 (34.9%)	< 0.001
4	3270 (12.5%)	52 (18.5%)	
5	628 (2.4%)	13 (4.6%)	
6	138 (0.5%)	3 (1.1%)	
≥ 7	66 (0.4%)	0 (0.0%)	
Bilateral procedure			
Unilateral	18,410 (70.5%)	202 (71.9%)	0.002
Staged bilateral (within 1 year)	4532 (17.4%)	31 (11.0%)	
Simultaneous bilateral	3168 (12.1%)	48 (17.1%)	
Anticoagulation			
Warfarin	24,290 (93.0%)	277 (98.6%)	< 0.01
Aspirin	1820 (7.0%)	4 (1.4%)	
Diabetes mellitus			
Yes	2997 (11.5%)	48 (17.1%)	0.003
No	23,113 (88.5%)	233 (82.9%)	
Hypothyroidism			
Yes	2857 (10.9%)	35 (12.5%)	0.42
No	23,253 (89.1%)	246 (87.5%)	
Ischemic heart disease			
Yes	3110 (11.9%)	45 (16.0%)	0.035
No	23,000 (88.1%)	236 (84.0%)	
Congestive heart failure			
Yes	402 (1.5%)	10 (3.6%)	0.007
No	25,708 (98.5%)	271 (96.4%)	

Table 3. continued

Variable	No pulmonary embolism (N = 26,110)	Pulmonary embolism (N = 281)	p value
Hypertension			
Yes	12,555 (48.1%)	166 (59.1%)	< 0.001
No	13,555 (51.9%)	115 (40.9%)	
Peripheral vascular disease			
Yes	229 (0.9%)	1 (0.4%)	0.35
No	25,881 (99.1%)	280 (99.6%)	
Atrial fibrillation			
Yes	1164 (4.5%)	39 (13.9%)	< 0.001
No	24,946 (95.5%)	242 (86.1%)	
Valvulopathy			
Yes	1123 (4.3%)	10 (3.6%)	0.54
No	24,987 (95.7%)	271 (96.4%)	
Chronic obstructive pulmonary disease			
Yes	2514 (9.6%)	44 (15.7%)	0.001
No	23,596 (90.4%)	237 (84.3%)	
Smoking history			
Yes	693 (2.7%)	9 (3.2%)	0.57
No	25,417 (97.3%)	272 (96.8%)	
Sleep apnea			
Yes	2310 (8.8%)	35 (12.5%)	0.03
No	23,800 (91.2%)	246 (87.5%)	
Anemia			
Yes	4152 (15.9%)	68 (24.2%)	< 0.001
No	25,881 (99.1%)	280 (99.6%)	
Presence of deep vein thrombosis			
Yes	40 (0.2%)	11 (3.9%)	< 0.001
No	26,070 (99.8%)	270 (96.1%)	
History of venous thromboembolism			
Yes	649 (2.5%)	8 (2.8%)	0.70
No	25,461 (97.5%)	273 (97.2%)	
History of malignancy			
Yes	2486 (9.5%)	32 (11.4%)	0.29
No	23,624 (90.5%)	249 (88.6%)	
Active malignancy			
Yes	322 (1.2%)	2 (0.7%)	0.43
No	25,788 (98.8%)	279 (99.3%)	
Leukemia			
Yes	55 (0.2%)	0 (0.0%)	0.44
No	26,055 (99.8%)	281 (100.0%)	
Lymphoma			
Yes	54 (0.9%)	0 (0.0%)	0.45
No	26,056 (99.8%)	281 (100.0%)	
HIV			
Yes	188 (0.7%)	2 (0.7%)	0.99
No	25,922 (99.3%)	279 (99.3%)	
Connective tissue disease			
Yes	808 (3.1%)	4 (1.4%)	0.11
No	25,302 (96.9%)	277 (98.6%)	
Crystalline arthropathy			
Yes	547 (2.1%)	5 (1.8%)	0.71
No	25,563 (97.9%)	276 (98.2%)	

Table 3. continued

Variable	No pulmonary embolism (N = 26,110)	Pulmonary embolism (N = 281)	p value
Renal disease			
Yes	43 (0.2%)	0 (0.0%)	0.50
No	26,067 (99.8%)	281 (100.0%)	
Dialysis			
Yes	14 (0.1%)	0 (0.0%)	0.70
No	26,096 (99.9%)	281 (100.0%)	
Benign prostatic hypertrophy			
Yes	1186 (4.5%)	14 (5.0%)	0.73
No	24,924 (95.5%)	267 (95.0%)	
Liver disease			
Yes	103 (0.4%)	0 (0.0%)	0.29
No	26,007 (99.6%)	281 (100.0%)	
Cerebrovascular disease			
Yes	311 (1.2%)	5 (1.8%)	0.37
No	25,799 (98.8%)	276 (98.2%)	
Depression			
Yes	1688 (6.5%)	30 (10.7%)	0.004
No	24,422 (93.5%)	251 (89.3%)	
Anxiety			
Yes	1132 (4.3%)	15 (5.3%)	0.41
No	24,978 (95.7%)	266 (94.7%)	
Peptic ulcer disease			
Yes	125 (0.5%)	3 (1.1%)	0.16
No	25,985 (99.5%)	278 (98.9%)	
Gastrointestinal reflux disease			
Yes	6087 (23.3%)	79 (28.1%)	0.06
No	20,023 (76.7%)	202 (71.9%)	
Diverticulosis or gastrointestinal bleeding			
Yes	230 (0.9%)	2 (0.7%)	0.76
No	25,880 (99.1%)	279 (99.3%)	
Inflammatory bowel disease			
Yes	119 (0.5%)	1 (0.4%)	0.80
No	25,991 (99.5%)	280 (99.6%)	

ASA = American Society of Anesthesiologists.

symptomatic PE (based on the multivariate analysis; Table 3). A univariate analysis found a longer list of potential risk factors (Table 1); however, because of the likelihood of confounding, the multivariate analysis should be considered more definitive.

Patients receiving postoperative 325 mg aspirin twice a day for prophylaxis had a symptomatic PE rate of 0.2% (four of 1824 patients). This was significantly lower (p < 0.01) than the rate of 1.1% (277 of 24,567 patients) for patients receiving warfarin with a target international normalized ratio of 1.5 to 1.8. However, after accounting for confounding variables, anticoagulation was not found to be an independent predictor of the occurrence of symptomatic PE.

Table 4. Pulmonary embolus risk stratification criteria

Risk factor	Points for each risk factor
Knee surgery	5
Charlson Comorbidity Index (CCI)	$1 \times CCI$
Atrial fibrillation	4
Postoperative deep vein thrombosis	14
Chronic obstructive pulmonary disease	2
Anemia	2
Depression	2
BMI (kg/m²)	
≤ 25	0
25–30	1
> 30	2

Nomogram of Risk for Pulmonary Embolism

A nomogram was created using a logistic regression model to predict the risk of symptomatic PE (Table 4). Low-risk patients (0.35% cumulative risk; range, 0%–0.7%) are classified as those with a score of 0 to 6 points, medium-risk patients (1.4% cumulative risk; range, 1.1%–2.8%) as those with a score between 7 and 15 points, and high-risk patients (9.3% cumulative risk; range, 4.3%–66.7%) as those with a score of 16 points or greater (Table 5).

Discussion

The risk of VTE, mainly PEs and fatal PEs, is the impetus for administration of anticoagulation agents after TJA [2, 5–8, 10, 13, 16, 18–21, 24, 26, 30, 44]. Unfortunately, the administration of chemical prophylaxis is associated with many complications such as increased hematoma formation, wound-related problems, and infection [31, 32, 36]. Sharrock et al. [39] reported that all-cause mortality is greater in patients who received aggressive anticoagulation after TJA. It therefore would be appealing to have a strategy that allows for individualization of postoperative anticoagulation for patients undergoing TJAs based on their risk for the development of PE. To develop such a strategy, we must identify the factors that place patients at the greatest risk for PE. We have provided identification of such risk factors in patients who received routine warfarin or aspirin prophylaxis.

Our study has some limitations. First, this study was limited to the evaluation of symptomatic PEs. We may have missed subclinical PEs in asymptomatic patients. However, we felt that it would have not been possible or medically appropriate to screen all patients for PE. Second,

Table 5. Risk of PE based on risk group

Risk group	Total score	Number of patients	Number of PEs	Risk of PE	Patients in each risk group (% of total patients)	PEs in each risk group (% of total PEs)	Cumulative risk in each group
Low	0	743	0	0%			
	1	1423	0	0%			
	2	2382	7	0.3%			
	3	2866	10	0.3%	13,324 (50.4)	47 (16.7)	0.35%
	4	2534	7	0.3%			
	5	1709	11	0.6%			
	6	1667	12	0.7%			
Medium	7	2094	22	1.1%			
	8	2847	34	1.2%			
	9	2934	37	1.3%			
	10	2062	34	1.6%			
	11	1048	17	1.6%			
	12	545	14	2.6%	12,474 (47.3)	179 (63.7)	1.4%
	13	373	9	2.4%			
	14	318	5	1.6%			
	15	253	7	2.8%			
High	16	187	8	4.3%			
	17	138	8	5.8%			
	18	56	1	1.8%			
	19	20	1	5.0%			
	20	22	1	4.5%			
	21	27	6	22.2%			
	22	30	7	23.3%			
	23	33	4	12.1%	593 (2.3)	55 (19.6)	9.3%
	24	37	8	21.6%			
	25	21	5	23.8%			
	26	7	2	28.6%			
	27	4	1	25.0%			
	28	3	2	66.7%			
	29	1	0	0%			
	30	5	1	20.0%			
	32	2	0	0%			

PE = pulmonary embolism.

comorbidities were identified using ICD-9 coding data from discharge records at one institution. These records are assumed to be complete and accurate because they generally report known preoperative diagnoses, but underreporting of diagnoses can occur. Third, another shortcoming is that the study design only identifies patients who had their PE diagnosed at this institution and, therefore, misses those who had a PE identified elsewhere. Nonetheless it is reasonable that nearly all of the PEs that occurred were captured, especially given that the majority of PEs occur during the immediate postoperative period [1, 12]. Fourth, 90-day mortality was determined using the Social Security Death Index. Of the 86 patients who died during the postoperative period, we were able to confirm only who four died owing to PE, and no death was directly attributable to PE prophylaxis. However, it was not possible to identify cause of death if the patient died after discharge. Although our rate of documented fatal postoperative PEs is low at 0.02%, a recent meta-analysis by Poultsides et al. showed that non-PE cardiac causes were the leading cause of death after TJA, with PE as the second leading cause at a 0.1% rate of fatal postoperative PEs with pharmacologic prophylaxis [34]. Fifth, in 2008, a new PE screening protocol was instituted at our institution to avoid

overdiagnosis of subclinical PEs, and we gradually began to transition from warfarin to aspirin for VTE prophylaxis. It is unclear how these changes affected the risk of PE, but we did not see any increase in the risk of symptomatic PE with use of aspirin for VTE prophylaxis.

A major strength of this study was that all PEs were identified and verified by reviewing radiologic reports and not simply by relying on ICD-9 coding data. When only ICD-9 coding data (ICD-9 codes 415, 415.11, 415.19, 451, 451.0, 451.11, 451.19, 451.2, 451.81, 453, and 453.9) were reviewed, only 205 of the total 283 postoperative PE events were identified. This highlights the potential significant underreporting of adverse events when only ICD-9 coding from databases is used.

Patients with greater BMI, multiple medical comorbidities (as reflected by an elevated Charlson Comorbidity Index), chronic obstructive pulmonary disease, hypertension, and history of atrial fibrillation were more likely to have a PE develop after TJA. There are theoretical bases for the associations between some of these conditions and VTE. Patients with chronic obstructive pulmonary disease, for example, are more likely to have inflammation of the pulmonary vessels and/or experience pulmonary hypertension that leads to stagnation of blood in the inflamed or damaged vessels and subsequent thrombus formation [33]. Patients with arrhythmia such as atrial fibrillation have a high risk of thrombi developing in cardiac atria leading to elevated rates of PE and stroke [29]. Patients with postoperative deep vein thrombosis formation are, as expected, at higher risk for PEs. This is likely the result of the contribution of deep vein thrombosis to embolic phenomena such as PE. Obesity and elevated comorbidity index have been shown to be associated with an increased risk of VTE [9, 14, 17, 40]. This may be secondary to an inflammatory state in these patients that may contribute to increased thrombus formation and subsequent embolization [9, 40]. Simultaneous bilateral TJAs also have been suggested as a higher risk for the development of PE when compared with unilateral TJA [35]. This may be the result of multiple factors, including the difficulty of early mobilization and a higher embolic load from intramedullary debris from bilateral surgery. Other risk factors for PE development such as preoperative anemia and depression are not as easily explained. Subsets of anemia including sickle cell, hemolytic, and even iron deficiency anemia have been associated with PEs [27, 28, 42]. Despite this, it is unclear whether anemia has a direct mechanism to lead to increased risk of PE. Depression has been suggested to be associated with PE. Schulte et al. found depression to be an independent risk factor of PE after spinal surgery [38]. Furthermore, in the psychiatric literature, studies have suggested an association between the lack of physical activity in patients in catatonic and depressive states to

development of VTE [15, 23]. Patients with depression may experience self-neglect, which may have resulted in noncompliance with anticoagulation prophylaxis or lack of mobility, both of which may have increased the risk of PE.

Although a goal of our study was to identify risk factors associated with postoperative symptomatic PE development in patients who have undergone TJA, the ultimate purpose of this study is to use this information in making clinical choices regarding patients undergoing TJAs. Therefore, using a logistic regression model, the risk factors identified in this study have been ranked according to their relative risk (Table 4). Using these scoring criteria, three clinically significant risk groups (low, medium, and high) have been created. The application of these relative risk criteria to individual patients may help to determine the type of postoperative anticoagulation that best balances the overall risk of the development of PE with that of postsurgical bleeding.

We found that patients who have an elevated BMI, Charlson Comorbidity Index, chronic obstructive pulmonary disease, atrial fibrillation, postoperative deep vein thrombosis, or anemia, and patients who undergo knee surgery (particularly bilateral knee surgery), are at greater risk of having a postoperative PE develop. These risks should be considered when deciding on postoperative anticoagulation prophylaxis. Further studies must be done to validate the PE risk stratification criteria presented here. These criteria, together with similar risk stratification for postoperative bleeding risk, ultimately can help to determine the appropriate postoperative PE prophylaxis on an individualized basis for patients undergoing TJAs.

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