ORIGINAL ARTICLE

Duration of Anesthesia and Venous Thromboembolism After Hip and Knee Arthroplasty

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OBJECTIVE: **To determine whether longer duration of anesthesia predisposes patients undergoing orthopedic surgery to venous thromboembolism (VTE).**

PATIENTS AND METHODS: **We conducted a secondary analysis of a retrospective case-control study that examined risk factors for postoperative VTE in postmenopausal women. We matched women aged 50 years and older with radiographically confirmed postoperative VTE (cases) by age, surgeon, year of surgery, and surgical joint (knee vs hip) with women without postoperative VTE (controls). Duration of anesthesia, operative variables, demographic data, comorbid illnesses, and laboratory data were determined by medical record review.**

RESULTS: **Eighty-eight cases were matched with 181 controls. Duration of anesthesia of 3.5 hours or longer (corresponding to the upper tertile of patients) was strongly associated with postoperative VTE compared with a shorter duration of anesthesia (odds ratio, 3.58; 95% confidence interval, 2.11-6.16; *P*<.001). This relationship was maintained after controlling for multiple covariates with propensity score methods, including type of arthroplasty, route of anesthesia, type of antithrombotic prophylaxis, and surgical approach. In multivariate analysis, the important predictors of VTE included anesthesia duration of 3.5 hours or longer, type of antithrombotic prophylaxis, revision (vs primary) arthroplasty, and allogeneic blood transfusion.**

CONCLUSION: **We found a marked association between the duration of anesthesia and postoperative VTE in patients undergoing joint arthroplasty. Although it is possible that unmeasured intraoperative variables account for this relationship, we suggest that duration of anesthesia may be an important risk factor for postoperative VTE after orthopedic surgery.**

***Mayo Clin Proc.* 2005;80(6):732-738**

CCF = Cleveland Clinic Foundation; CI = confidence interval; DVT = deep venous thrombosis; IQR = interquartile range; OR = odds ratio; PE = pulmonary embolism; VTE = venous thromboembolism

Approximately 500,000 patients undergo total joint arthroplasty, either hip or knee, in the United States annually.[1] Major surgery, especially orthopedic surgery, is a powerful risk factor for venous thromboembolism (VTE). In the absence of prophylaxis, approximately half of the patients who undergo elective total hip or knee replacement develop VTE.[2] In the presence of appropriate antithrombotic prophylaxis, up to 38% of patients may still develop venographically apparent VTE.[3] Although most of these thrombi are small, asymptomatic, and confined to the deep veins of the calf, approximately 5% are symptomatic and proximal and can precipitate fatal pulmonary embolism (PE).[3-7] Therefore, further identification of risk factors for VTE in patients undergoing orthopedic surgery remains important.

Earlier studies have identified important risk factors associated with the development of VTE after hip surgery. These risk factors include a history of prior VTE, obesity, delay in ambulation after surgery, and female sex.[8] Factors associated with lower risk may include Asian/Pacific Islander ethnicity, use of pneumatic compression after surgery, and extended thromboprophylaxis after hospital discharge.[8] In addition, poor functional status (American Society of Anesthesiologists physical status classification ≥3) is associated with VTE after primary hip or knee replacement surgery.[9]

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Despite a low risk of trauma to the leg veins, there is a substantial risk of VTE after major general surgery (requiring general anesthesia for >30 minutes).[10,11] During anesthesia stasis occurs in the venous system, resulting from both the supine position and the effects of anesthesia. Venographic studies in supine patients have shown delayed clearing of venographic contrast media from the soleal sinuses of the calf muscles.[12,13] Additionally, the vasodilatory effect of anesthesia increases venous capacitance and decreases venous return from the lower extremities.[14,15] In this setting, venous thrombi may develop behind the venous valve cusps or the intramuscular sinuses of the calf. Therefore, it is conceivable that longer anesthesia time might predispose patients to postoperative VTE. This finding has been reported for gynecological surgery[16,17] but not for other surgical procedures.

Multiple surgical and perioperative variables may affect both duration of surgery and VTE risk. These variables include anesthesia route (spinal, epidural, and/or general), surgical approach of hip arthroplasty with anterior or posterior dislocation, transfusions, and use of cement. Some of these variables, such as use of general anesthesia, have been associated with increased postoperative VTE.[18] Use of cement in total knee arthroplasty may also be associated

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with increased risk of VTE,[19,20] but this has not been confirmed in other studies.[21] None of the studies specifically assessed whether the association between VTE and these surgical variables might be explained by longer duration of anesthesia. This study aimed to determine whether longer duration of anesthesia predisposes patients undergoing orthopedic surgery to VTE.

PATIENTS AND METHODS

Study Site

All case and control patients underwent surgery at the main campus of the Cleveland Clinic Foundation (CCF), a metropolitan academic hospital. The CCF Institutional Review Board approved the protocol.

Search Strategy

This study is a secondary analysis of a study that examined risk factors for postoperative VTE in postmenopausal women (≥50 years), particularly the relationship between hormone replacement therapy and postoperative VTE.[22] Cases were identified by searching the CCF *International Classification of Diseases, Ninth Revision* database for women older than 50 years who underwent hip or knee arthroplasty between January 1997 and July 2002. Total, partial, and revision elective arthroplasty were included for both joints. Bilateral total knee arthroplasty was included. Cases had also received a secondary or primary diagnosis of deep venous thrombosis (DVT) or PE during the initial hospitalization or within 45 days of surgery. Controls were identified in the same manner as cases, except these patients lacked the additional diagnosis of DVT or PE. All cases and controls underwent routine surveillance ultrasonography of the lower extremities postoperatively, as is the protocol at our institution. Controls were matched to cases in a 2:1 ratio by the following variables: year of surgery, surgeon, age, and surgical joint (hip or knee). When more than 2 possible controls were identified for a given case, 2 of these controls were chosen at random.

Data Acquisition

Data were obtained by review of the surgical and postoperative medical records. The presence of comorbid disease was ascertained by review of the documented relevant medical history and by review of patients' medication history. Laboratory test results were obtained by review of the electronic medical record. Duration of anesthesia was defined as the time when the anesthesiologist first made contact with the patient in the operating room to administer regional or general anesthesia until the time when the patient's surgery was completed and care transferred to the postanesthesia care unit. Degenerative joint disease and gout were not included as rheumatologic disease because these are not generally chronic inflammatory conditions. We defined DVT as proximal if it extended to the popliteal vein or above and distal if it involved the deep veins of the calf alone. Patients could be categorized as cases only if they had radiographically confirmed VTE (by duplex ultrasonography, angiography, helical computed tomography of the chest, or radionucleotide lung scan) and their thrombi were considered acute (not chronic) by the physicians involved in the patients' care.

Statistical Analyses

Univariate logistic regression was used (with cases vs controls as the dependent variable) to calculate odds ratios (ORs) with the following independent variables: type of arthroplasty, medical history, type of blood transfusion, surgical indication, anesthesia duration, anesthesia type, pharmacological VTE prophylaxis, enoxaparin-based VTE prophylaxis (30 mg subcutaneously twice daily), lateral surgical approach (hip only), and use of cement. Univariate logistic regression was also used with anesthesia duration of less than 3.5 hours vs 3.5 hours or longer as the dependent variable, using the same independent variables. (The cutoff of 3.5 hours corresponded to the upper tertile of anesthesia duration.) Furthermore, we examined the interaction between anesthesia duration and primary (vs revision) arthroplasty and VTE. Multiple logistic regression was used to determine adjusted ORs as appropriate. Two-sample unequal variance *t* tests or Wilcoxon rank sum tests were used to compare continuous data between cases and controls or between anesthesia duration of 3.5 hours or longer vs less than 3.5 hours. Because some surgical variables were confounded with respect to duration of surgery (including type of arthroplasty, anesthesia route, use of cement, and primary vs revision surgery), we used a propensity score method to adjust for confounding variables. To create propensity scores, we constructed a nonparsimonious multiple logistic regression model with anesthesia duration of less than 3.5 hours vs 3.5 hours or longer as the dependent variable. We incorporated all available clinical variables (except the presence or absence of VTE) into this propensity score model and then divided the propensity scores into deciles, assigning each patient a score (1 to 10), reflecting the likelihood of having an anesthesia duration of 3.5 hours or longer. This technique allowed us to adjust for all clinical variables associated with long anesthesia duration using a single covariable. We assessed the fit of the propensity model using the receiver operating characteristic curve–derived C-statistic, with the propensity score decile as the independent variable and anesthesia duration of 3.5 hours or longer vs less than 3.5 hours as the dependent variable. Multiple logistic regression was then used to

calculate adjusted ORs using the propensity score decile as an independent (adjuster) variable. We did not use any other variables as adjusters in the propensity score–adjusted models. Data were analyzed using JMP 5.1 statistical software (SAS Institute Inc, Cary, NC).

RESULTS

Searches for Cases and Controls

A total of 4075 women aged 50 years and older underwent joint arthroplasty at CCF between January 1997 and July 2002. Of these patients, 130 (3.2%) were identified as having a concurrent diagnosis of VTE within 45 days of surgery. These patients were each matched with 2 controls (as stated previously). Because the original goal of the study was to assess the relationship between hormone replacement use and postoperative VTE,[22] we excluded patients who lacked documentation of hormone replacement use and those who lacked objective radiographic testing for VTE (22 potential cases and 50 potential controls); we then excluded an additional 20 potential cases and 29 potential controls who lacked documentation of anesthesia duration. A total of 88 cases and 181 controls remained for analysis.

Classification of VTE

Of the 88 cases with VTE, 36 (40.1%) had distal DVTs, 48 (54.5%) had proximal DVTs, and 4 (4.5%) had PEs. Most of these episodes of VTE were diagnosed within 7 days of surgery, usually by surveillance ultrasonography of the lower extremities on day 2 or 3 postoperatively.

Types of Surgery

Of the 269 patients, 130 (48.2%) underwent unilateral hip arthroplasty, 97 (36.1%) underwent unilateral knee arthroplasty, and 42 (15.6%) underwent bilateral knee arthroplasty. Of these surgical procedures, 42 (15.6%) were revision arthroplasties. Table 1 gives the number of each type of procedure performed in cases and controls.

Clinical Features of Cases and Controls

Table 1 compares clinical characteristics of cases and controls. Although we matched for surgical joint (hip vs knee), we did not match for number of surgical joints; there were more bilateral knee arthroplasties performed in the cases than in the controls (P=.004). Baseline characteristics of cases and controls were otherwise similar except that cases were more likely to have had a medical history of congestive heart failure (P=.01) or rheumatologic disease (P=.03).

Cases were also less likely than controls to have received pharmacological VTE prophylaxis; in some cases in which no pharmacological prophylaxis was administered, contraindications to anticoagulation were documented (such as recent intracranial hemorrhage or history of adverse reactions to anticoagulants). The use of low-molecular-weight heparin (enoxaparin) was associated with lower VTE risk (P<.001).[23] The use of spinal anesthesia (vs general anesthesia) appeared to be protective (P=.03). Allogeneic blood transfusion was associated with VTE (P=.01).

Duration of Anesthesia

The overall median duration of anesthesia was 185 minutes (interquartile range [IQR], 144-234 minutes). For hip arthroplasty, the median duration of anesthesia was 178 minutes (IQR, 135-230 minutes); for unilateral knee arthroplasty and bilateral knee arthroplasty, median durations of anesthesia were 169 minutes (IQR, 140-216 minutes) and 225 minutes (IQR, 205-251 minutes), respectively. The anesthesia duration for unilateral knee arthroplasty and for hip arthroplasty was not significantly different (P=.63). Median anesthesia duration for bilateral knee replacement was longer than that for unilateral hip or knee arthroplasty (P<.001). Duration of revision arthroplasty was longer than that for primary arthroplasty: 252 minutes (IQR, 184-295 minutes) vs 175 minutes (IQR range, 140-216 minutes) (P<.001).

Duration of Anesthesia and Risk of VTE

Analysis of the data suggested that there was a threshold of approximately 3.5 hours (210 minutes) above which the odds for VTE increased substantially. Values above this cutoff corresponded to the upper tertile of anesthesia duration. No difference occurred in VTE prevalence between the first and second tertiles (OR, 1.3; 95% confidence interval [CI], 0.6-2.7; P=.48).

Patients with anesthesia duration of 3.5 hours or longer were more likely to have received general and/or epidural (vs spinal) anesthesia (P<.001), to have undergone bilateral knee surgery (vs unilateral knee surgery or hip surgery) (P<.001), to have undergone revision arthroplasty (vs primary arthroplasty) (P<.001), and to have had cement used (P=.007) (Table 2).

The unadjusted OR for VTE for patients with anesthesia duration of 3.5 hours or longer compared with those with duration of less than 3.5 hours was 3.58 (95% CI, 2.11-6.16; P<.001). This relationship persisted after patients with distal DVT were excluded from the analysis (Table 3).

Propensity Score

The propensity score decile predicted duration of anesthesia of 3.5 hours or longer with excellent accuracy (C-statistic = 0.88). Additionally, adjustment for the propensity score effectively eliminated the association among most of the surgical variables (type of surgery, type of anesthesia, and use of cement) and anesthesia duration of

TABLE 1. **Characteristics of Cases (With VTE) and Controls (Without VTE)***

Characteristic	Cases (n=88)	Controls (n=181)	Unadjusted OR (95% CI)	*P* value (2-tailed)
Type of arthroplasty				
Unilateral knee	24/88 (27.3)	73/181 (40.3)	1.0 (referent)	NA
Hip	43/88 (48.9)	87/181 (48.1)	1.50 (0.84-2.73)	.17
Bilateral knee	21/88 (23.9)	21/181 (11.6)	3.04 (1.43-6.57)	.004
Median (IQR) age, y	74 (67-78)	73 (64-77)	NA	.12
Median (IQR) body mass index† (kg/m^2)	29 (25-32)	29 (25-34)	NA	.86
Medical history				
Diabetes mellitus	7/88 (8.0)	19/181 (10.5)	0.74 (0.28-1.75)	.50
Hypertension	51/88 (58.0)	101/181 (55.8)	1.09 (0.65-1.83)	.74
Congestive heart failure	6/88 (6.8)	2/181 (1.1)	6.55 (1.47-45.3)	.01
Coronary artery disease	15/88 (17.1)	27/181 (14.9)	1.17 (0.58-2.31)	.65
Prior VTE	12/88 (13.6)	18/181 (9.9)	1.43 (0.64-3.09)	.37
COPD	3/88 (3.4)	9/181 (5.0)	0.67 (0.15-2.33)	.56
Active malignancy	7/88 (8.0)	6/181 (3.3)	2.52 (0.81-8.06)	.11
Stroke or TIA	10/88 (11.4)	11/181 (6.1)	1.98 (0.79-4.89)	.13
Rheumatologic disease	15/87 (17.2)	15/181 (8.3)	2.31 (10.6-5.00)	.03
Smoking (>10 pack-years)	20/78 (25.6)	45/166 (27.1)	1.08 (0.59-2.02)	.81
Median (IQR) laboratory values				
Preoperative creatinine (mg/dL)	0.8 (0.7-1.0)	0.8 (0.7-0.9)	NA	.60
Preoperative hemoglobin (g/dL)	12.3 (11.3-13.5)	12.3 (11.5-13.3)	NA	.96
Preoperative platelets ($\times 10^3/\mu L$)	261 (217-320)	259 (216-305)	NA	.69
Decrease in hemoglobin (g/dL)	3.0 (1.9-4.1)	2.9 (2.0-3.8)	NA	.65
Decrease in platelets ($\times 10^3/\mu L$)	76 (45-100)	59 (36-92)	NA	.12
Transfusion				
Autologous	15/75 (20.0)	51/164 (31.1)	0.55 (0.28-1.06)	.09
Allogeneic	42/75 (56.0)	61/162 (37.7)	2.11 (1.21-3.69)	.01
Surgical variables				
Revision arthroplasty (vs primary)	25/85 (29.4)	17/172 (9.9)	3.80 (1.93-7.64)	<.001
Duration of anesthesia				
Median (IQR) minutes	216 (156-253)	175 (140-210)	NA	<.001
Anesthesia duration ≥3.5 h	49/88 (55.7)	47/181 (26.0)	3.58 (2.11-6.16)	<.001
Anesthesia types‡				
General	19/84 (22.6)	23/172 (13.4)	1.86 (0.96-3.71)	.07
Epidural	11/84 (13.1)	23/172 (13.3)	1.02 (0.48-2.29)	>.99
Spinal	60/84 (71.4)	144/172 (83.7)	0.48 (0.26-0.91)	.03
Enoxaparin-based prophylaxis[23]	55/81 (67.9)	173/181 (96.7)	0.10 (0.04-0.22)	<.001
Lateral approach (hip only)	19/34 (55.9)	47/71 (62.9)	0.65 (0.27-1.50)	.39
Cement used	67/81 (82.7)	133/168 (79.2)	1.26 (0.65-2.67)	.61

*Data are presented as number (percentage) of patients unless indicated otherwise. Because some medical records failed to document the presence or absence of particular variables, not all denominators equal the total number of cases or controls. CI = confidence interval; COPD = chronic obstructive pulmonary disease; IQR = interquartile range; NA = not applicable; OR = odds ratio; TIA = transient ischemic attack; VTE = venous thromboembolism.

†Defined as a measure of weight in kilograms divided by the square of height in meters.

‡Some patients had multiple types of anesthesia.

3.5 hours or longer (Table 2). However, it did not eliminate the relationship between anesthesia duration and primary vs revision arthroplasty; the propensity score–adjusted OR was 2.58 (95% CI, 1.07-6.04; *P*=.03) for revision arthroplasty (vs primary arthroplasty).

Multivariate and Subgroup Analysis

A significant interaction occurred between anesthesia duration of 3.5 hours or longer and revision arthroplasty (*P*=.002); specifically, in patients who underwent revision arthroplasty, the duration of anesthesia did not predict VTE (unadjusted OR, 0.39; 95% CI, 0.09-1.47; *P*=.17), whereas the duration of anesthesia strongly predicted VTE in the patients who underwent primary arthroplasty (unadjusted OR, 4.57; 95% CI, 2.42-8.77; *P*<.001). Table 3 gives the propensity score–adjusted ORs that relate VTE to anesthesia duration of 3.5 hours or longer. Despite adjustment, anesthesia duration of 3.5 hours or longer continued to predict VTE in our patients. This relationship persisted when patients with distal DVTs were excluded.

Other Predictors of VTE

After adjusting for anesthesia duration of 3.5 hours or longer and for type of VTE prophylaxis, VTE was still associated with allogeneic blood transfusion (OR, 2.45; 95% CI, 1.29-4.95; *P*=.007) and with revision arthroplasty (OR, 3.21; 95% CI, 1.48-7.03; *P*=.003) (Table 4). No other variables significantly predicted VTE after adjustment for

TABLE 2. **Characteristics of Patients With Anesthesia Duration of 3.5 Hours or Longer Compared With Those With Shorter Anesthesia Duration***

Characteristic	Anesthesia duration ≥3.5 h† (n=96)	Anesthesia duration <3.5 h (n=173)	Unadjusted OR (95% CI)	Unadjusted *P* value (2-tailed)	Propensity score adjusted OR	Propensity score adjusted *P* value
Type of arthroplasty						
Unilateral knee	27/96 (28.1)	70/173 (40.4)	1.00 (referent)	NA	1.00	NA
Hip	40/96 (41.7)	90/173 (52.0)	1.15 (0.36-2.07)	.63	1.02	.95
Bilateral knee	29/96 (30.2)	13/173 (7.5)	5.78 (2.67-13.1)	<.001	1.07	.89
Median (IQR) age, y	74 (63-78)	74 (67-77)	NA	.99	NA	.89
Median (IQR) body mass index‡ (kg/m^2)	30 (26-35)	29 (24-33)	NA	.13	NA	.87
Medical history						
Diabetes mellitus	10/96 (10.4)	16/173 (9.3)	1.14 (0.48-2.59)	.76	0.90	.86
Hypertension	50/96 (52.1)	102/173 (59.0)	0.76 (0.46-1.25)	.28	0.99	.98
Congestive heart failure	5/96 (5.2)	3/173 (1.7)	3.11 (0.74-15.4)	.14	1.32	.74
Coronary artery disease	17/96 (17.7)	25/173 (14.5)	1.27 (0.64-2.49)	.48	1.04	.93
Prior VTE	12/96 (12.5)	18/173 (10.4)	1.23 (0.55-2.65)	.60	1.05	.92
COPD	4/96 (4.2)	8/173 (4.6)	0.90 (0.23-2.93)	.86	1.07	.94
Active malignancy	6/96 (6.3)	7/173 (4.1)	1.58 (0.50-4.90)	.42	0.89	.88
Stroke or TIA	4/96 (4.2)	17/173 (9.8)	0.40 (0.11-1.12)	.10	1.09	.91
Rheumatologic disease	12/95 (12.6)	18/173 (10.4)	1.24 (0.56-2.69)	.58	0.87	.82
Smoking (>10 pack-years)	23/88 (26.1)	42/156 (26.9)	0.96 (0.53-1.73)	.89	1.03	.93
Median (IQR) laboratory values						
Preoperative creatinine (mg/dL)	0.8 (0.7-0.9)	0.8 (0.7-0.9)	NA	.34	NA	.69
Preoperative hemoglobin (g/dL)	12.1 (11.3-13.2)	12.5 (11.6-13.6)	NA	.03	NA	.97
Preoperative platelets (× 10^3/μL)	255 (213-304)	262 (223-318)	NA	.48	NA	.98
Decrease in hemoglobin (g/dL)	2.8 (1.7-3.9)	3.0 (2.2-4.0)	NA	.23	NA	.96
Transfusion						
Autologous	21/87 (24.1)	45/152 (29.6)	0.76 (0.41-1.37)	.45	1.10	.83
Allogeneic	39/86 (45.4)	64/151 (42.4)	1.13 (0.66-1.92)	.68	0.98	.95
Surgical variables						
Revision arthroplasty (vs primary)	27/90 (30.0)	15/167 (9.0)	4.35 (2.19-8.90)	<.001	2.58	.03
Anesthesia types§						
General	27/90 (30.0)	15/166 (9.0)	4.31 (2.18-8.84)	<.001	1.06	.89
Epidural	23/90 (25.6)	11/166 (6.6)	4.84 (2.28-10.9)	<.001	1.07	.89
Spinal	60/90 (66.7)	144/166 (86.8)	0.31 (0.16-0.57)	<.001	1.00	>.99
Enoxaparin-based prophylaxis	74/91 (81.3)	154/171 (90.1)	0.48 (0.23-1.00)	.05	0.95	.92
Lateral approach (hip only)	19/34 (55.9)	47/71 (66.2)	0.65 (0.28-1.50)	.39	0.89	.86
Cement used	78/87 (89.7)	122/162 (75.3)	2.84 (1.36-6.54)	.007	1.04	.94

*Data are presented as number (percentage) of patients unless indicated otherwise. Because some medical records failed to document the presence or absence of particular variables, not all denominators equal the total number of cases or controls. CI = confidence interval; COPD = chronic obstructive pulmonary disease; IQR = interquartile range; NA = not applicable; OR = odds ratio; TIA = transient ischemic attack; VTE = venous thromboembolism.

†Propensity score for anesthesia duration ≥3.5 hours includes all clinical variables presented in Table 1 and Table 2 except for the presence or absence of VTE.

‡Defined as a measure of weight in kilograms divided by the square of height in meters.

§Some patients had multiple types of anesthesia.

anesthesia duration and type of VTE prophylaxis, including (1) route of anesthesia (*P*>.15 for all types); (2) use of cement (*P*=.89); (3) anterior vs posterior hip dislocation (*P*=.69); (4) any comorbid diseases (*P*≥.05 for all); and (5) any laboratory parameter (*P*>.15 for all).

DISCUSSION

Our study shows that anesthesia duration of 3.5 hours or longer strongly predicted the occurrence of postoperative VTE in postmenopausal women undergoing primary major joint replacement. This relationship was maintained after controlling for multiple covariates, including type of arthroplasty, route of anesthesia (general vs epidural vs spinal), type of antithrombotic prophylaxis, use of cement, age, type of blood transfusion (autologous vs allogeneic), history of congestive heart failure, rheumatologic disease, and preoperative hemoglobin level. This finding has relevance for patients undergoing major joint replacement and for surgeons who perform these procedures. Because duration of anesthesia is usually related to how long it takes an orthopedic surgeon to perform a major joint replacement, longer surgical procedures may expose patients to a higher risk of VTE. This makes sense because during anesthesia there is stasis from the supine position and pooling of blood.

Long anesthesia duration did not predict VTE in our patients who underwent revision arthroplasty, which may be due to several factors. One possibility is that the trauma

TABLE 3. **ORs Associating VTE With Duration of Anesthesia of 3.5 Hours or Longer***

Model	All patients		Excluding revision arthroplasty		Excluding revision arthroplasty and bilateral arthroplasty	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Any VTE						
Unadjusted	3.58 (2.11-6.16)	<.001	4.58 (2.42-8.77)	<.001	5.09 (2.37-11.1)	<.001
Propensity score adjusted	2.70 (1.35-5.48)	.005	4.42 (1.96-10.4)	<.001	4.96 (1.96-13.1)	<.001
Proximal DVT or PE						
Unadjusted	4.21 (2.22-8.10)	<.001	5.33 (2.47-11.8)	<.001	6.11 (2.52-15.0)	<.001
Propensity score adjusted	3.83 (1.64-9.27)	.002	6.55 (2.37-19.6)	<.001	6.74 (2.22-22.0)	<.001

*CI = confidence interval; DVT = deep venous thrombosis; OR = odds ratio; PE = pulmonary embolism; VTE = venous thromboembolism.

related to the joint and adjacent venous circulation during the revision might increase the patient's risk of VTE to such a level that the additional risk of a duration of anesthesia longer than 3.5 hours has little further impact on the overall risk of VTE. Another possibility is that the median time of revision arthroplasty (252 minutes in our patients) is long enough to maximally increase the risk of VTE in susceptible patients. However, because only 42 of our patients underwent revision arthroplasty, it is difficult to draw firm conclusions.

The most important limitation of our study is its retrospective case-control design. Although cases and controls were generally well matched for baseline age and comorbid diseases, we cannot exclude the possibility that they were systematically different in some unmeasured way. Similarly, although we attempted to identify and adjust for factors that are associated with duration of anesthesia, unmeasured surgical factors, such as anatomical difficulties in disarticulating a joint, may lead to longer anesthesia duration and simultaneously predispose a patient to VTE via more tissue trauma. The potential for residual confounding makes it impossible to conclude that longer duration of anesthesia is a causal factor for VTE; it may just be a marker for any number of complexities or complications that might occur in the operating room and that simultaneously lengthen duration of surgery and contribute to postoperative VTE risk.

Our definition of anesthesia duration may have included a few minutes before induction of anesthesia. Conversely, many patients may have been taken to the postanesthesia care unit while their legs were still paralyzed by regional anesthesia. Nevertheless, we believe our definition is a reasonable estimate of the true time under anesthesia. Furthermore, any inaccuracies created by our definition of anesthesia duration would be expected to affect cases and controls similarly.

An additional limitation of our study is the mode of VTE diagnosis. Routine surveillance ultrasonography after arthroplasty is not performed in many centers, and some authors have cautioned against this practice because it is of unproven benefit,[24] whereas others advocate this practice.[25] The accuracy of ultrasonography (particularly the sensitivity) may be lower in the postarthroplasty setting, especially when used as a routine screening tool in patients without symptoms of VTE.[26,27] It is possible that our classification of cases and controls was compromised by reliance on routine postoperative ultrasonography as a means of diagnosis. Moreover, because postarthroplasty ultrasonography is performed routinely at our institution, there is less need

TABLE 4. **Associations Between Clinical Variables and VTE After Adjustment for Type of VTE Prophylaxis (Enoxaparin Based vs Other) and Duration of Anesthesia of 3.5 Hours or Longer (vs <3.5 Hours)***

Characteristic	Adjusted OR (95% CI)	*P* value (2-tailed)
Type of arthroplasty		
Unilateral knee	1.0 (referent)	NA
Hip	1.39 (0.71-2.74)	.34
Bilateral knee	1.78 (0.70-4.45)	.22
Medical history		
Diabetes mellitus	0.66 (0.22-1.78)	.44
Hypertension	1.21 (0.67-2.21)	.53
Congestive heart failure	5.50 (0.94-43.3)	.07
Coronary artery disease	0.76 (0.32-1.70)	.52
Prior VTE	1.08 (0.42-2.61)	.87
COPD	0.42 (0.07-1.98)	.32
Active malignancy	3.14 (0.94-10.7)	.06
Stroke or TIA	2.82 (1.00-7.77)	.05
Rheumatologic disease	2.04 (0.84-4.85)	.11
Smoking (>10 pack-years)	0.90 (0.45-1.84)	.77
Transfusion		
Autologous	0.45 (0.20-1.00)	.05
Allogeneic	2.45 (1.29-4.95)	.007
Surgical variables		
Revision arthroplasty (vs primary)	3.21 (1.48-7.03)	.003
Anesthesia types†		
General	1.27 (0.56-2.78)	.56
Epidural	0.54 (0.20-1.33)	.20
Spinal	0.71 (0.34-1.49)	.35
Lateral approach (hip only)	1.24 (0.45-3.73)	.69
Cement used	0.95 (0.44-2.14)	.89

*CI = confidence interval; COPD = chronic obstructive pulmonary disease; NA = not applicable; OR = odds ratio; TIA = transient ischemic attack; VTE = venous thromboembolism.
†Some patients had multiple types of anesthesia.

for a systematic clinical assessment of symptoms (such as swelling and pain in the entire limb vs focal edema and pain at the arthroplasty site) to identify patients who might benefit from postoperative ultrasonography. Therefore, we cannot comment on how many of the cases in our study had symptoms related to their VTE and how many were asymptomatic because this clinical information was not recorded reliably in the medical records. It is also possible that some patients developed VTE after discharge from the hospital and either sought care at other hospitals or never had objective diagnostic testing; we suspect that the number of such patients was small. Regardless of these limitations, however, there is no reason to suspect that the accuracy of ultrasonography or follow-up patterns should vary based on duration of anesthesia. Furthermore, if the use of ultrasonography led to some false-positive and false-negative diagnoses of DVT, we would expect this to attenuate the OR relating to duration of anesthesia to VTE, not to magnify it. Finally, our study was performed in a select group of postmenopausal women—a group that may be at particularly high risk of VTE after hip replacement[8]; therefore, our results may not apply to men or younger women.

CONCLUSION

Our data suggest that extended duration of anesthesia is a strong risk factor for VTE after orthopedic surgery. This finding may apply to other types of surgical procedures as well. We suggest that all future studies that examine risk factors for (or prevention of) postoperative VTE examine anesthesia duration as an important, and potentially confounding, clinical variable.

We thank Debbie L. Knack, John J. Smetanko, Gerald A. Roberson, Michael A. Dombrowski, Denise Sassanno, Sherrie L. Grams, and Laurie E. Hyer for their help in obtaining medical records and facilitating data entry.

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