Original Investigation

Surgical Duration and Risk of Venous Thromboembolism

John Y. S. Kim, MD; Nima Khavanin, BS; Aksharananda Rambachan, BA; Robert J. McCarthy, DPharm; Alexei S. Mlodinow, BA; Gildasio S. De Oliveria Jr, MD; M. Christine Stock, MD; Madeleine J. Gust, MD; David M. Mahvi, MD

IMPORTANCE There is a paucity of data assessing the effect of increased surgical duration on the incidence of venous thromboembolism (VTE).

OBJECTIVE To examine the association between surgical duration and the incidence of VTE.

DESIGN, SETTINGS, AND PARTICIPANTS Retrospective cohort of 1 432 855 patients undergoing surgery under general anesthesia at 315 US hospitals participating in the American College of Surgeons National Surgical Quality Improvement Program from 2005 to 2011.

EXPOSURE Duration of surgery.

MAIN OUTCOMES AND MEASURES The rates of deep vein thrombosis (DVT), pulmonary embolism (PE), and VTE within 30 days of the index operation. Surgical duration was standardized across *Current Procedural Terminology* codes using a *z* score. Outcomes were compared across quintiles of the *z* score. Multiple logistic regression models were developed to examine the association while adjusting for patient demographics, clinical characteristics, and comorbidities.

RESULTS The overall VTE rate was 0.96% (n = 13 809); the rates of DVT and PE were 0.71% (n = 10 198) and 0.33% (n = 4772), respectively. The association between surgical duration and VTE increased in a stepwise fashion. Compared with a procedure of average duration, patients undergoing the longest procedures experienced a 1.27-fold (95% CI, 1.21-1.34; adjusted risk difference [ARD], 0.23%) increase in the odds of developing a VTE; the shortest procedures demonstrated an odds ratio of 0.86 (95% CI, 0.83-0.88; ARD, −0.12%). The robustness of these results was substantiated with several sensitivity analyses attempting to minimize the effect of outliers, concurrent complications, procedural differences, and unmeasured confounding variables.

CONCLUSIONS AND RELEVANCE Among patients undergoing surgery, an increase in surgical duration was directly associated with an increase in the risk for VTE. These findings may help inform preoperative and postoperative decision making related to surgery.

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Author Affiliations: Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Kim, Khavanin, Rambachan, Mlodinow, Gust, Mahvi); Department of Anesthesiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (McCarthy, De Oliveria, Stock).

Corresponding Author: John Y. S. Kim, MD, Department of Surgery, Feinberg School of Medicine, Northwestern University, 675 N St Clair St, Rm 19-250, Chicago, IL 60611 (jokim@nmh.org).

The putative association between longer surgical procedures and morbidity, including venous thromboembolism (VTE), has been examined.[1-11] Although this association is widely accepted, it has yet to be quantitatively assessed using a sufficiently powered, multi-institutional database. Our analysis seeks to address this critical question: Do longer operations increase the risk of VTE? With more than 500 000 hospitalizations and 100 000 deaths per year associated with VTEs, answering this question is of prime importance to policy makers, perioperative care physicians, surgeons, and anesthesiologists.[12-15] In turn, further assessing the link between surgical time and VTE will allow more informed medical and surgical decision making and concomitantly improve patient outcomes.[16-18] These findings can guide the decision to proceed with longer or combined procedures and, conversely, capitalize on technique advancements that shorten the time of operations.

We analyzed data from the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) database. The NSQIP was established as a quality improvement initiative to further our understanding of surgical outcomes through prospective data collection across the United States.[19] As of 2011, the NSQIP captures data on 240 patient variables from more than 300 institutions.[20] Furthermore, the absolute quality and interrater reliability of the data have been validated.[21] The NSQIP database includes information on more than 1.7 million patients from 2005 to 2011 across surgical disciplines. We hypothesized that increases in surgical duration, defined as the time from the induction of general anesthesia to emergence from the anesthesia, would be associated with an increase in the incidence of VTE even with adjustment for increased surgical and patient complexity.

Methods

Data Source and Population

Although the American College of Surgeons oversees the NSQIP database, we took sole responsibility for this study. The Northwestern University Institutional Review Board determined that this study does not constitute research with human participants and was thus exempt from formal approval.

Trained surgical nurses collect NSQIP data nationwide for 30 days following the primary operation. Data are collected in 8-day cycles and monitored on a weekly basis to ensure appropriate sampling. These data collection methods have been described in detail.[20] Effective training sessions for medical record reviewers have established the reliability of the data with a low (1.96%) rate of interobserver disagreement across the tracked variables.[21]

Primary Explanatory and Outcome Variables

Total surgical duration, defined as the duration of general anesthesia time, was the primary independent variable of interest. In an effort to standardize this measure across inherently shorter and longer procedures, a *z* score was calculated for each patient by dividing the difference between the anesthesia time and the mean for the patient's respective *Current Procedural Terminology* (*CPT*) code by its SD. Cases were divided into 5 quintiles (eTable 1 in the Supplement) based on this *z* score, with the first quintile (minimum to 20th percentile) representing the relatively shortest procedures, the third quintile representing procedures of average duration, and the fifth quintile representing the longest procedures. The primary outcome of interest was the development of a 30-day VTE, which included deep vein thrombosis (DVT) and pulmonary embolism (PE). Deep vein thrombosis is defined as a new clot or thrombus anywhere in the venous system and is confirmed via duplex ultrasonography, venogram, or computed tomography. Pulmonary embolism is diagnosed via computed tomography (spiral or angiogram), pulmonary arteriogram, or high-probability ventilation-perfusion scan.

Statistical Analysis

Patient demographic data included age, body mass index, sex, and race. Clinical characteristics included inpatient status, smoking status, American Society of Anesthesiologists class of 3 or greater, and surgical specialty. The surgical specialties in the analysis included general, urologic, gynecologic, orthopedic, vascular, cardiothoracic, otolaryngologic, plastic, and neurologic. Comorbidities of interest included diabetes mellitus, bleeding disorders (eg, vitamin K deficiency, hemophilia, thrombocytopenia, and chronic anticoagulation), hypertension, and prior stroke or transient ischemic attack. The logarithm of sum relative value units per procedure were included as a proxy for surgical complexity. Variables were selected using clinical judgment. Missing data were analyzed for patterns and handled using multiple imputation. Categorical variables were analyzed using χ^2 tests, and continuous variables were analyzed using 1-way analysis of variance tests.

Multiple logistic regression including the above covariates was used to examine the relationship between relatively short (first and second quintiles) and relatively long (fourth and fifth quintiles) operations and the risk for VTE compared with an average-length procedure for any given *CPT* codes (third quintile, or 41st-60th percentile). The influence of the *z* score of operative time as a continuous variable was also determined in a separate analysis. To assess the relative stability of our β coefficients across various populations, the relationship was observed using 1000 bootstrap samples taken with replacement, each with a population equal to 10% of our total cohort.

Several sensitivity analyses, including the relationship between operative time and development of PE and DVT, as well as subgroup analyses for the most common *CPT* codes and surgical specialties, were prespecified before initial data analysis to test the robustness of our results. The following post hoc sensitivity analyses were also performed. In an attempt to minimize the influence of uncommon *CPT* codes on our results, we first eliminated all *CPT* codes without a recorded VTE event and then eliminated all *CPT* codes with fewer than 1000 cases. Because of likely differences between inpatient and outpatient procedures, similar analyses were carried out for each of those subgroups. Multiple sensitivity analyses attempted to minimize the influence of outliers with respect to operative time on our results. Outliers were defined in 3 ways: *z* scores more than 3 SDs away from the mean, the top 10% of *z* scores, and the top 25% of *z* scores. To assess the influence of concomitant complications and generally sicker patients on our results, all patients who experienced any 30-day morbidity or mortality other than a VTE (or in addition to a VTE) were eliminated. Additional analyses included only VTEs that developed within 1 week of the primary procedure or a combination of 1 week postoperatively and no other complication. Finally, the relationships between operative time and DVT and PE were observed separately. To address the possibility of residual confounding by unmeasured variables, we used the array-approach sensitivity analysis described by Schneeweiss.[22]

The *C* statistics measured model discrimination, observed vs expected outcome graphs assessed calibration (eFigure 1 in the Supplement), and likelihood ratio tests assessed the influence of covariates on model fit. A threshold of .05 was used for statistical significance, and all *P* values were 2-sided. Bootstrap analysis was performed in R software (http://www.r-project.org/), using the rms package, and multiple imputation as well as all regression analyses were carried out in SPSS, version 20 (SPSS Inc).

Subgroup Analyses

Two subgroup analyses were conducted to supplement our primary analysis. First, within each surgical subspecialty, pa-

Table 1. Preoperative Characteristics Across Surgical Time Groupings

Characteristic[a]	Quintile, %[b] 1st (0 to 20th Percentile)	2nd (21st to 40th Percentile)	3rd (41st to 60th Percentile)	4th (60th to 80th Percentile)	5th (81st to 100th Percentile)	No. Missing[c]
Age, mean (SD), y	55.9 (17.4)	54.8 (17.5)	54.7 (17.2)	54.9 (16.8)	55.3 (16.1)	2
BMI, mean (SD)	29.3 (8.0)	29.5 (8.0)	29.8 (8.2)	30.3 (8.5)	31.2 (9.1)	38 785
Male sex	38.8	41.2	42.6	44.0	45.6	3153
Race/ethnicity						
Asian	1.8	2.2	2.2	2.2	2.1	0
Black	7.3	9.1	10.2	11.3	12.3	
Other	13.3	12.3	12.0	12.1	11.8	
White	77.7	76.4	75.6	74.5	73.8	
Surgical specialty						
Cardiothoracic	1.5	1.2	1.3	1.5	1.7	0
General	70.7	72.3	71.5	71.1	69.6	
Gynecologic	3.7	3.7	3.4	3.4	3.6	
Neurologic	2.0	1.8	1.9	1.9	2.3	
Orthopedic	6.3	5.9	5.9	6.0	6.1	
Otolaryngologic	1.5	1.7	1.7	1.6	1.8	
Plastic	1.3	1.3	1.3	1.3	1.5	
Urologic	2.5	2.5	2.5	2.5	2.6	
Vascular	10.4	9.6	10.5	10.7	10.8	
Outpatient surgery	39.7	38.1	34.3	30.0	22.6	1
Diabetes mellitus	13.8	13.7	14.5	15.4	17.0	3
Smoking	21.1	20.7	20.5	20.4	20.4	22
Hypertension	44.9	43.8	44.5	46.1	48.3	13
Previous stroke or TIA	6.4	6.0	6.1	6.2	6.3	21 911
Bleeding disorder	5.4	5.3	5.4	5.6	5.8	13
ASA class 3, 4, or 5	42.3	41.6	43.4	45.9	50.6	1838
Sum of RVUs, mean (SD)	20.83 (14.40)	20.02 (14.89)	21.14 (16.28)	23.21 (18.22)	28.37 (23.64)	0

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); RVUs, relative value units; TIA, transient ischemic attack.

[a] Continuous variables are reported as mean (SD).

[b] All differences were significant at $P < .001$.

[c] Of 1 432 855 total cases, 65 741 values (0.4%) were missing across 64 996 patients (4.5%).

tients were stratified based on their *z* score for anesthesia time; the unadjusted incidence of VTE was calculated at each interval. Second, to eliminate interprocedural differences, the 3 most common *CPT* codes in the database were identified as laparoscopic cholecystectomy, appendectomy, and gastric bypass.

Results

Beginning with 1 777 035 surgical cases in the NSQIP database from 2005 to 2011, patients who did not receive general anesthesia (159 677) or received general anesthesia for an unspecified duration (184 503) were excluded, resulting in a sample of 1 432 855 patients. The patients were categorized into 5 quintiles based on the *z* score of their operative time (eTable 1 in the Supplement). Patient age; sex; body mass index; race; percentage as outpatients; sum relative value units; American Society of Anesthesiologists class 3, 4, or 5; and the rates of diabetes, smoking, hypertension, and a previous stroke or transient ischemic attack varied across quintiles (**Table 1**).

A total of 13 809 patients (0.96%) had a postoperative VTE, 10 198 patients (0.71%) experienced a DVT, and 4772 individuals (0.33%) developed a PE. Of these, 1161 patients (0.08%) had both a DVT and PE. The rates of each of these events consistently increased with the duration of the surgical procedure (eTable 2 in the Supplement).

The middle 20% of the procedures across all *CPT* codes demonstrated a VTE rate of 0.86% (95% CI, 0.83% to 0.90%). Compared with this third quintile, relatively short procedures (ie, first and second quintiles) carried odds ratios (ORs) of 0.86 (95% CI, 0.83 to 0.88; adjusted risk difference [ARD], −0.12%) and 0.98 (95% CI, 0.95 to 1.00; ARD, −0.02%), respectively. The fourth and fifth quintiles carried ORs of 1.10 (95% CI, 1.07 to 1.13; ARD, 0.09%) and 1.27 (95% CI, 1.21 to 1.34; ARD, 0.23%), respectively (**Table 2**). The association between VTE incidence and the longest procedures was significant in 82.0% of 1000 bootstrap samples (**Table 3** and eFigure 2 in the Supplement).

Similar trends were noted across multiple sensitivity analyses (eTables 3-12 in the Supplement), for DVTs (eTable 13 in the Supplement), and for PEs (eTable 14 in the Supplement). The

Table 2. VTE Event Rates and Multiple Logistic Regression Results for Surgical Time

Surgical Time[a]	No. of VTE Events	Absolute Proportion, %	Adjusted (95% CI)[b]			P Value
			Proportion	Risk Difference	OR[c]	
Quintile						
1st (0 to 20th Percentile)	2033	0.71	0.74 (0.72 to 0.76)	−0.12 (−0.14 to −0.10)	0.86 (0.83 to 0.88)	<.001
2nd (21st to 40th Percentile)	2278	0.80	0.84 (0.82 to 0.87)	−0.02 (−0.04 to 0.00)	0.98 (0.95 to 1.00)	.39
3rd (41st to 60th Percentile)	2478	0.87	0.865 (0.831 to 0.899)	1 [Reference]	1 [Reference]	
4th (61st to 80th Percentile)	2960	1.03	0.95 (0.93 to 0.98)	0.09 (0.06 to 0.11)	1.10 (1.07 to 1.13)	<.001
5th (81st to 100th Percentile)	4060	1.42	1.11 (1.04 to 1.15)	0.23 (0.18 to 0.29)	1.27 (1.21 to 1.34)	<.001
z Score[d]					1.12 (1.10 to 1.13)	<.001

Abbreviations: OR, odds ratio; VTE, venous thromboembolism.

[a] Total of 1 432 855 patients; includes 13 809 VTEs.

[b] Adjusted for sex; race; surgical specialty; diabetes mellitus; smoking; hypertension; bleeding disorder; American Society of Anesthesiologists class 3, 4, or 5; previous stroke or transient ischemic attack; body mass index; and relative value units for concurrent procedures.

[c] C statistic: 0.76 (0.76 to 0.77); −2 log likelihood for a model: without quintiles, 143 317.57; with quintiles, 143 080.51.

[d] The z score value represents the OR for each SD from the mean from our z score analysis; every SD above the mean was associated with an OR of 1.12.

Table 3. Bootstrap Analysis

Variable	β	OR (95% CI)	P Value	Significant Bootstrap Samples, % (n = 1000)
z Score, quintile[a]				
1st	−0.16	0.86 (−0.21 to −0.10)	<.001	37.1
2nd	−0.03	0.97 (−0.08 to 0.03)	.37	4.3
4th	0.10	1.10 (0.04 to 0.15)	.001	19.0
5th	0.24	1.27 (0.19 to 0.29)	<.001	82.0
Surgical specialty[b]				
Cardiothoracic	−0.02	0.98 (−0.13 to 0.08)	.65	2.9
Gynecologic	−0.38	0.68 (−0.52 to −0.23)	<.001	34.7
Neurologic	0.21	1.24 (0.12 to 0.31)	<.001	32.2
Orthopedic	0.08	1.08 (0.00 to 0.15)	.045	10.7
Otolaryngologic	−1.08	0.34 (−1.48 to −0.69)	<.001	77.7
Plastic	−0.30	0.74 (−0.62 to 0.01)	.06	2.6
Urologic	−0.31	0.74 (−0.43 to −0.18)	<.001	29.1
Vascular	−0.42	0.66 (−0.48) to −0.36)	<.001	99.6
Male sex	0.19	1.20 (0.15 to 0.22)	<.001	90.6
Race/ethnicity[c]				
Asian	−0.54	0.58 (−0.71 to −0.37)	<.001	52.6
Black	0.21	1.24 (0.16 to 0.27)	<.001	69.9
Other	−0.11	0.89 (−0.17 to −0.05)	<.001	19.4
Outpatient	−1.47	0.23 (−1.54 to −1.39)	<.001	100.0
Age	0.02	1.02 (0.02 to 0.02)	<.001	100.0
Diabetes mellitus	−0.13	0.88 (−0.17 to −0.08)	<.001	39.6
Smoking	−0.08	0.92 (−0.13 to −0.04)	<.001	20.0
Hypertension	−0.07	0.93 (−0.11 to −0.03)	<.001	21.4
Bleeding disorder	0.44	1.56 (0.39 to 0.50)	<.001	99.6
ASA class 3, 4, or 5	0.72	2.06 (0.68 to 0.77)	<.001	100.0
Previous stroke or TIA	0.01	1.01 (−0.06 to 0.07)	.88	4.1
BMI	−0.001	0.10 (−0.003 to 0.001)	.33	5.7
Sum of RVUs	0.01	1.01 (0.01 to 0.01)	<.001	100.0

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; OR, odds ratio; RVU, relative value units; TIA, transient ischemic attack.

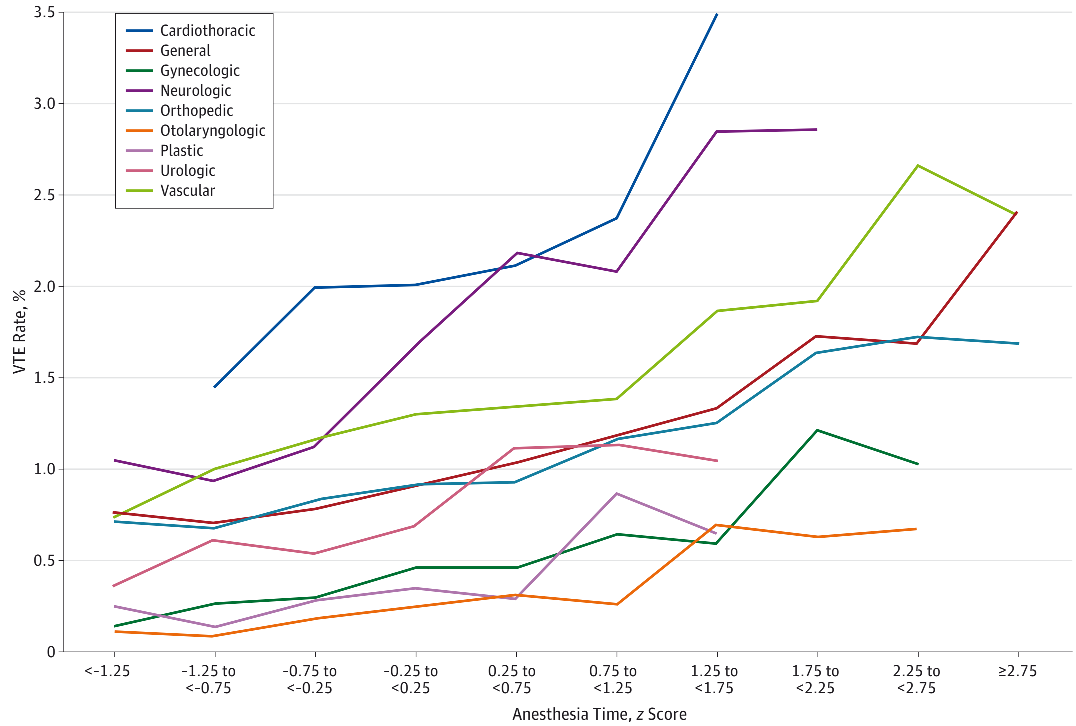
[a] Reference group was the third quintile of the operative time z score.

[b] Reference group was general surgery.

[c] Reference group was white race.

first array-based sensitivity analyses demonstrated that, for these findings to lose significance, an unmeasured confounder that carries a 0.50 relative risk of VTE must differ in prevalence by 40% between the fifth quintile and the average case (eTable 15 in the Supplement). Conversely, the second sensitivity analysis revealed that an unmeasured confounder with a relative risk of 2.0 would have to differ in prevalence by at least 30% between the fifth quintile and the average case (eTable 16 in the Supplement). Both of these differences in prevalence would have to be even larger to eliminate the significance of the difference between the first and fifth quintiles. Bootstrap analysis revealed an aggregate OR in the high-

Figure. The Influence of Surgical Duration on Venous Thromboembolism (VTE) Rates



Specialty	No.	<-1.25	-1.25 to <-0.75	-0.75 to -0.25	<-0.25 to 0.25	<0.25 to <0.75	0.75 to <1.25	1.25 to <1.75	1.75 to <2.25	2.25 to <2.75	≥2.75	Total
Cardiothoracic	VTE	0	61	98	90	66	44	80	0	0	0	**439**
	Cases	0	4214	4905	4479	3118	1854	2294	0	0	0	**20 864**
General	VTE	208	1207	2217	2061	1450	928	552	376	199	391	**9589**
	Cases	27 203	172 302	283 938	225 205	140 236	77 978	41 359	21 828	11 832	16 239	**1 018 120**
Gynecologic	VTE	2	24	42	49	31	25	13	15	16	0	**217**
	Cases	1408	9278	14 030	10 678	6669	3875	2179	1238	1558	0	**50 913**
Neurologic	VTE	10	44	81	102	85	52	39	49	0	0	**462**
	Cases	961	4710	7226	6079	3902	2499	1371	1711	0	0	**28 459**
Orthopedic	VTE	24	99	191	175	109	78	46	32	18	25	**797**
	Cases	3346	14 533	23 133	19 023	11 671	6726	3671	1944	1046	1478	**86 571**
Otolaryngologic	VTE	1	3	12	13	10	5	8	4	6	0	**62**
	Cases	873	3431	6603	5339	3210	1870	1147	637	892	0	**24 002**
Plastic	VTE	2	4	14	14	8	14	14	0	0	0	**70**
	Cases	809	2920	5008	4044	2727	1613	2155	0	0	0	**19 276**
Urologic	VTE	5	34	52	55	56	32	35	0	0	0	**269**
	Cases	1384	5615	9678	7976	5006	2828	3346	0	0	0	**35 833**
Vascular	VTE	45	231	442	439	285	167	121	66	51	57	**1904**
	Cases	6056	23 170	38 122	33 890	21 346	12 016	6479	3441	1911	2386	**148 817**

The relationship between the *z* score of anesthesia time and the incidence of VTE is shown across 9 surgical specialties. The table details the numbers of cases and VTEs at each point estimate.

est quintile of 1.27 (*P* < .001), with this quintile reaching significance in 82.0% of the 1000 iterations.

For every 1-SD increase in surgical time, the OR for VTE was 1.12 (95% CI, 1.10 to 1.13) across all *CPT* codes. The median *z* score was −0.19 (interquartile range, 1.08). The exclusion of outliers did not significantly affect this result (OR, 1.15; 95% CI, 1.13 to 1.17).

The incidence of VTE increased with increasing quintiles of surgical duration in all 9 surgical specialties in the subgroup analyses (*P* < .05) (**Figure**). The basal incidence of VTE varied across the specialties. Otolaryngologic procedures had the lowest incidence of VTE (0.11% in the shortest operations; 0.67% in the longest procedures). Cardiothoracic and neurologic surgical procedures had the greatest incidence of VTE (1.44% and 3.49%, and 1.04% and 2.86%, respectively). Interaction terms between operative time and surgical subspecialty were not statistically significant (eTable 17 in the Supplement).

In each of the 3 most common procedures (ie, laparoscopic cholecystectomy, appendectomy, and gastric bypass), surgical time was a significant independent risk factor for VTE (**Table 4**). A 1-hour increase in surgical time carried an OR of 1.18 (95% CI, 1.06-1.30) for laparoscopic cholecystectomy, 1.18 (95% CI, 1.08-1.29) for laparoscopic appendectomy, and 1.26 (95% CI, 1.15-1.40) for laparoscopic gastric bypass (all *P* < .05). Similar trends were noted for a 1-unit increase in the *z* score of operative time (Table 4).

Table 4. Risk of VTE by Surgical Duration for the Most Common Surgical Procedures

Laparoscopic Procedure	*CPT* Code	No. of Patients	No. of VTEs	Surgical Time, Mean (SD), min	OR (95% CI) per Hour[a,b]	*P* Value[c]	OR (95% CI) per 1-SD Increase[a,b]	*P* Value[c]
Cholecystectomy	47562	87 491	203	107.7 (45.1)	1.18 (1.06-1.30)	.005	1.13 (1.04-1.22)	.003
Appendectomy	44970	76 235	140	91.8 (42.3)	1.18 (1.08-1.29)	<.001	1.12 (1.05-1.19)	<.001
Gastric bypass	43644	43 260	180	192.0 (65.0)	1.26 (1.15-1.40)	<.001	1.29 (1.16-1.44)	<.001

Abbreviations: *CPT*, *Current Procedural Terminology*; OR, odds ratio; VTE, venous thromboembolism.

[a] *C* statistics for *CPT* code 47562, 0.78 (0.75-0.81); *CPT* code 44970, 0.74 (0.70-0.78); *CPT* code 43644, 0.70 (0.66-0.74) -2 log likelihood; *CPT* code 47562, 2537.03 without operative time, 2630.68 with operative time; *CPT* code 44970, 19221.98 without operative time, 1915.44 with operative time; and *CPT* code, 43644, 2248.03 without operative time, and 2230.91 with operative time.

[b] Adjusted for sex; race; surgical specialty; diabetes mellitus; smoking; hypertension; bleeding disorder; American Society of Anesthesiologists class 3, 4, or 5; previous stroke or transient ischemic attack; body mass index; and relative value units for concurrent procedures.

[c] Differences were considered significant at $P < .05$.

Discussion

Further understanding of the relationship between VTE and surgical duration could help direct surgical planning and management. Such risk stratification could help target chemoprophylaxis strategies for perioperative care physicians, surgeons, and anesthesiologists and better inform patients and clinicians of the potential hazards associated with prolonged surgery. We performed a systematic search of PubMed using all permutations of the search terms *pulmonary embolism, deep venous thrombosis, and venous thromboembolism*, the search terms *operative, surgical, and anesthesia*, and the search terms *time and duration* and identified 11 relevant articles from 2003 to 2013.[1-11] Several insightful studies examined the effect of surgical duration on individual procedures within specialties or institutions. However, to our knowledge, a comprehensive analysis across specialties and institutions using a generalizable database has not been performed to date. By accessing more than 1.4 million surgical cases through the NSQIP database, we hoped to more rigorously address the issue of surgical duration and VTE risk.

Although we found increasing rates of DVT, PE, and VTE with increasing surgical duration (eTable 2 in the Supplement), cohort characteristics varied across these time intervals (Table 1). After adjustment for these differences, surgical duration was independently associated with an increased likelihood of DVT, PE, and VTE development. Compared with average-length procedures of any kind, the odds of developing a postoperative VTE was significantly increased within the longest procedures and decreased within the shortest procedures (Table 2). Similar trends were observed for DVTs and PEs (eTables 13 and 14 in the Supplement).

This finding of an association between surgical duration and the odds of VTE was corroborated by the rising unadjusted incidence of VTE across all surgical specialties (Figure). When compared with general surgery procedures, the baseline risk of a VTE differed across many surgical procedures (Figure and Table 3). However, interaction terms between z score quintiles and the various subspecialties were nonsignificant (eTable 15 in the Supplement), suggesting that the association (represented by the slope of each line) is similar across all 9 specialties (Figure).

The explanation linking surgical duration to VTE is multifactorial. The pathophysiologic basis of a VTE was described more than 100 years ago and is now known as "Virchow's triad."[23] Immobility resulting from long surgical procedures can lead to the simultaneous presence of blood stasis, increased coagulation, and endothelial damage caused by vessel wall distension.[24-29] Patients undergoing longer surgical procedures are more likely to experience blood stasis, hypercoagulability, and vascular trauma causing endothelial damage that together can contribute to the formation of a VTE.[26,30] Venous stasis and ischemia can promote DVT formation via the upregulation of P-selectin and local prothrombotic microparticles.[28,30] The hypercoagulable state as well as the inflammation and endothelial damage brought about by surgery can similarly trigger the clotting cascade and contribute to thrombus formation.

Clinically, this relationship between operative time and the incidence of VTE suggests an important role of surgical duration in the postoperative assessment of VTE risk. Currently, the 2 common risk stratification methods for VTE are the Caprini[31] and Rogers[7] scores. The Rogers score does not take surgical duration into account, whereas the Caprini score distinguishes only between operations shorter or longer than 45 minutes for the sake of defining "major surgery."

Our findings suggest that risk assessment should factor in the length of surgery more thoroughly. With such a large volume of procedures performed annually, the ARDs of 0.23% among the longest procedures and −0.12% among the shortest (Table 2) translate into a substantial burden of VTEs attributable to surgical duration. Nonetheless, the development of strict criteria for risk stratification based on surgical duration is difficult given the inherent differences across procedures. The use of quintiles presents an intuitive approach whereby a surgeon can adjust the risk assessment based on whether the procedure was relatively long, short, or of average duration. Furthermore, these data give us pause when deciding to couple operations or proceed with longer operations. Technical advancements that shorten procedures, particularly in a VTE-prone surgical milieu, are indicated.

The recent implementation of the Patient Protection and Affordable Care Act continues to pressure physicians to reduce postoperative complications that drive readmissions and contribute to high health care costs. Because VTE is responsible for more than 500 000 hospitalizations annually, quantifying its risk is valuable to both improving the quality and reducing the cost of patient care. The importance of this quantification is emphasized by major insurers and organizations, including the Joint Commission, the Agency for Healthcare Research and Quality, and the National Quality Forum, which have mandated VTE risk reduction and prophylactic measures.[13,32] In addition to playing a role in postoperative risk assessment, our findings can provide a useful benchmark for VTE rates, helping to assess the efficacy of future risk-reduction initiatives.

Our study has several limitations. The NSQIP database samples more procedures from a greater number of institutions with every iteration, and it is not possible to determine the completeness of sampling year to year for any given procedure or any given hospital. In addition, although the definition of DVT and PE is explicit in the NSQIP user guide, the characteristics of each event are not tracked by the database. For example, there is no information regarding whether the event was symptomatic or the diagnosis was incidental, neither is there information regarding which imaging modality was used to make the diagnosis. However, the NSQIP database is based on a review of medical records—it is not a screening program targeted specifically to VTE. Thus, it is reasonable to assume that most VTE events at participating hospitals were found because they were high probability or symptomatic and thus prompted postoperative imaging for diagnosis. Another limitation of the present study is that the risk for VTE may remain elevated for 90 days postoperatively, and the NSQIP database captures complications only within 30 days of the primary operation.[33] However, it has been shown[34] that the highest risk for VTE occurs within 19 days after surgery, and our trends are not likely to vary greatly over longer follow-up periods. In addition, multiple logistic regression is susceptible to statistical overfitting, which we attempted to control for by careful selection of the variables included.

Finally, a limitation of the retrospective design is the inability to include some information that would have been useful additions to the model. For example, although we assumed fairly high rates of chemoprophylaxis use in quality-seeking NSQIP centers, we recognize that NSQIP does not explicitly track chemoprophylactic measures or institution type, and the inability to control for variation of those measures across surgical specialties or across hospitals represents a limitation. In addition, NSQIP does not track the history of VTE or known thrombophilia. However, guidelines and consensus statements[7,31,35,36] for chemoprophylaxis vary among surgical specialties—and even by procedure—and do not include surgical duration. We attempted to account for this inherent discrepancy by controlling for *CPT* code and analyzing our data at the specialty and procedural level. Moreover, given that longer procedures outside of the consensus guidelines will tend to be considered for heparin prophylaxis, the strength of the relationship between surgical duration and VTE may be artificially dampened.

A distinct advantage of the NSQIP is that a wealth of data is prospectively collected from various clinicians across the country with a low rate of interobserver disagreement.[21] Specifically, DVT was found to have the highest concordance of any complication between NSQIP and other databases, such as the Agency for Healthcare Research and Quality ($\kappa = 0.60$) and the Cardiovascular Information Registry ($\kappa = 0.51$).[37] Our overall rates of DVT, PE, and VTE are confirmed by the rates noted in other large-scale studies.[14,37,38]

Given the observational design of our study, it is not possible to definitively conclude that the observed relationship between surgical duration and VTE incidence reflects a strict cause-and-effect relationship. However, even if additional unquantifiable confounders, including surgeon skill and the extent of disease, continue to bias our results, surgical time would be a surrogate for these immeasurable potential risk factors when assessing a patient's risk for VTE.

Conclusions

Through a multiple logistic regression of more than 1.4 million patients from 315 hospitals across the United States, we found surgical duration to be an independent risk factor for VTE. Subgroup analyses substantiated this finding accounting for variation across surgical specialties, procedures, and cases and controlling for confounding to the extent afforded by the NSQIP database. This study provides quantitative validation of the widely held, but not previously substantiated, belief that longer operations are associated with a higher risk of VTE. These findings may improve VTE risk modeling, enhance existing prophylaxis guidelines, and better inform surgical decision making.

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Study concept and design: Kim, Khavanin, Rambachan, Mlodinow, De Oliveria, Gust, Mahvi.
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Drafting of the manuscript: Kim, Khavanin, Rambachan, Mlodinow, De Oliveria, Stock, Gust.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Khavanin, Rambachan, McCarthy, Mlodinow, De Oliveria.
Administrative, technical, or material support: McCarthy Mlodinow, Gust, Mahvi.
Study supervision: Kim, De Oliveria, Gust.

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