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Venous Thromboembolism Following Inpatient Pediatric Surgery: Analysis of 153,220 Patients

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Abstract

Purpose: To evaluate venous thromboembolism (VTE) rates and risk factors following inpatient pediatric surgery.

Methods: 153,220 inpatient pediatric surgical patients were selected from the 2012–2015 NSQIP-P database. Demographic and perioperative variables were documented. Primary outcome was VTE requiring treatment within 30 postoperative days. Secondary outcomes included length of stay (LOS) and 30-day mortality. Prediction models were generated using logistic regression. Mortality and time to VTE were assessed using Kaplan-Meier survival analysis.

Results: 305 patients (0.20%) developed 296 venous thromboses and 12 pulmonary emboli (3 cooccurrences). Median time to VTE was 9 days. Most VTEs (81%) occurred pre-discharge. Subspecialties with highest VTE rates were cardiothoracic (0.72%) and general surgery (0.28%). No differences were seen for elective vs. urgent/emergent procedures ($p=0.106$). All-cause mortality VTE patients was 1.2% vs. 0.2% in patients without VTE ($p<0.001$). After stratifying by American Society of Anesthesiologists (ASA) class, no mortality differences remained when ASA < 3. Preoperative, postoperative, and total LOS were longer for patients with VTE ($p<0.001$ for each). ASA 3, preoperative sepsis, ventilator dependence, enteral/parenteral feeding, steroid use, preoperative blood transfusion, gastrointestinal disease, hematologic disorders, operative time, and age were independent predictors (C-statistic=0.83).

Conclusions: Pediatric post-surgical patients have unique risk factors for developing VTE.

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Keywords

NSQIP; VTE; postoperative; risk factors; mortality; thrombosis Level of Evidence: Level II

1.1 INTRODUCTION

Venous thromboembolism (VTE) is a rare complication of pediatric surgery with significant associated morbidity and mortality.[1] VTE occurs in approximately 40 per 10,000 pediatric admissions.[2, 3] The risk of in-hospital death is significantly increased in pediatric patients with VTE, with an adjusted relative risk greater than 6 compared to children without VTE. [3] Furthermore, cost attributable to pediatric VTEs in the U.S. has been estimated at \$20,000 per event, or over \$90 million annually.[1]

Pediatric VTE has predominately been studied in the context of chronic illnesses (e.g., cancer) and known inciting events (e.g., central venous catheter [CVC] use, trauma). Studies investigating VTE following pediatric surgery have focused on the trauma surgery population and have identified older age and injury severity as risk factors for postoperative VTE development.[4–7] However, data on VTE following non-trauma inpatient surgery are lacking. Developing a better understanding of surgery-related VTE could identify patients at highest risk in order to improve guidelines on VTE prophylaxis, diagnosis, and treatment in children.

1.2 MATERIAL AND METHODS

1.2.1 Study Design and Data Source

This is a cohort study of data prospectively collected in The American College of Surgeons (ACS) National Surgical Quality Improvement Program-Pediatric (NSQIP-P) dataset. The Institutional Review Board at the authors' institution exempts NSQIP from IRB approval.[8]

Following alpha and beta phase testing,[9–11] NSQIP-P was officially expanded in 2012. Previous studies have demonstrated consistency between variables collected in NSQIP and NSQIP-P relative to medical record review.[12–14] The ACS trains Surgical Clinical Reviewers (SCRs) at each institution and completes inter-rater reliability (IRR) audits on collected data. Overall IRR disagreement rates are approximately 2% (confirmed in alpha phase testing).[9]

SCRs use an 8-day cycle to sample surgical cases from the hospital's operative log.[15–18] All cases under the NSQIP-P procedure list are included if they fall in the 8-day cycle, do not exceed the 35 consecutive case limit within an 8-day cycle, and do not violate the following exclusion criteria: patient age < 18 years, trauma surgery (except isolated long bone fractures), return to the operating room for complications related to a prior procedure, organ transplantation, and additional procedure performed by a different surgical team under the same anesthetic.[15–18]

1.2.2 Cohort Selection

NSQIP-P datasets from years 2012–2015 were combined yielding an initial cohort of 267,289 cases. Outpatient procedures were excluded, yielding 153,220 remaining inpatient surgeries. The following specialties/subspecialties are included in NSQIP-P: pediatric surgery/general surgery, orthopedics, cardiovascular/thoracic, neurosurgery, otolaryngology, urology, plastic surgery, and gynecology.

1.2.3 Primary and Secondary Outcomes

The primary outcome of interest was VTE requiring treatment (anticoagulation, placement of vena cava filter, or clipping of the vena cava) within 30 postoperative days. VTE includes venous thrombosis (VT) of the deep or superficial venous systems and pulmonary embolism (PE). The VT definition requires imaging confirmation by duplex ultrasound, venogram, or computed tomography (CT) scan. Internal jugular catheter clots, peripherally inserted central catheter (PICC) clots, and portal vein clots are all examples of VTE events that would be included in the NSQIP-P VT definition. The PE definition requires radiological confirmation of PE via a ventilation-perfusion scan interpreted as high probability of pulmonary embolism, a positive chest CT, trans-esophageal echocardiogram, pulmonary arteriogram, or CT angiogram. Timing to VTE was defined as the number of days from operation to diagnosis with zero days being a VTE that occurred the day of operation. Secondary outcomes included postoperative length of stay (LOS) and any-cause 30-day postoperative mortality.

1.2.4 Variables of Interest

Demographic, comorbidity, operative, and postoperative variables of interest were selected for analysis. For more specific variable details including definitions for each NSQIP-P variable referenced herein, please reference the NSQIP-P user guides. [15–18]

1.2.5 Statistical Analysis

Descriptive statistics of overall VTE frequency and frequency by variable of interest were generated. Contingency tables were generated for categorical variables with corresponding unadjusted odds ratios (OR), 95% confidence intervals (CI), and p values using univariate logistic regression. Univariate binary logistic regression was used to analyze VTE risk for continuous and LOS variables with calculation of corresponding unadjusted ORs, 95% CIs, and p values. Median (with interquartile range [IQR]) time from surgery to VTE event was calculated. Survival analyses were performed for VTE and mortality using Kaplan Meier estimates and log-rank tests. Statistical significance within univariate tests was set at $p < 0.05$. All tests for statistical significance were 2-tailed.

Multivariate binary logistic regression models were fitted using variables deemed significant on univariate testing ($p < 0.05$) with calculation of corresponding adjusted ORs, 95% CIs, and p values. Adjusted models were generated for the following sub-stratified analyses: overall cohort, patient age < 3 years, age > 15 years, pre-discharge VTE, and post-discharge VTE. Patients were only included in the models if all independent variables in the model existed for that patient. A receiver operating characteristic (ROC) curve was generated for each adjusted model with subsequent calculation of the area under the curve (AUC) or C-statistic,

95% CI for the AUC, and p values. Statistical significance for the adjusted models was set at $p < 0.05$. All statistical analyses were performed using IBM SPSS v. 23.

1.3 RESULTS

1.3.1 Overall VTE Rates

Of 153,220 unique inpatient pediatric patients, 305 (0.20%) had a VTE requiring treatment within 30 postoperative days (Table 1). VT occurred after 296 cases, and PE occurred after 12 cases. Three patients had VT with subsequent PE. No patient had multiple VTs or PEs. There was no significant difference in VTE rate between years of operation.

1.3.2 Surgical Subspecialty

The four specialties with the highest VTE rates were cardiothoracic, general/pediatric surgery, otolaryngology, and neurosurgery (Table 2). The specialties with the lowest VTE rates were plastic surgery, urology, and orthopedics. Gynecology had no VTEs. General/pediatric surgery had both the greatest number of surgical cases (74,446) and the greatest number of VTEs (211) of any specialty.

1.3.3 Time to VTE

Median time from surgery to VTE was 9 (IQR: 4–16) days. Median time to VT was 9 (IQR: 4–16) days, whereas median time to PE was 5 (IQR: 2.25–9) days. Seventy percent of VTEs occurred within the first two weeks postoperatively. Fifty (16.4%) VTE events occurred post-discharge, and post-discharge VTE events differed significantly from pre-discharge VTE in timing to event ($p < 0.001$).

1.3.4 Individual Procedures

Of 640 CPT codes in the NSQIP-P dataset, the top procedures by VTE rate are predominately general/pediatric surgery or cardiovascular-thoracic procedures (Table 3). Approximately 70% of the procedures in Table 3 are gastrointestinal or thoracic procedures. The procedures listed in Table 3 account for 128 VTEs (42% of total).

1.3.5 Demographics

Patient age was significantly associated with VTE on univariate analysis (Table 4). VTE risk was greatest in patients < 3 years or > 15 years of age at surgery (Fig. 1A). No differences were seen between sexes. Black race was the only race significantly associated with VTE on univariate analysis.

1.3.6 Operative Variables

Longer operative time, ASA classification, and prior operation in 30 days were all significantly associated with higher VTE rate (Table 4, Fig. 1B). Procedures lasting > 5 hours had over three times the VTE rate vs. procedures < 1 hour (0.41% vs. 0.12%). Greater ASA classification corresponded to higher VTE risk, with ASA 3 being the first classification to surpass the general study population VTE rate. Prior operation within 30 days was significantly associated with VTE; however, 87,061 cases (57%) had no data on

prior operations. Therefore, this variable was excluded from the multivariate models. Case status (elective vs. urgent or emergent procedure) VTE rate was no different between groups.

1.3.7 Comorbidities

The strongest effect sizes (unadjusted OR>5) among comorbidities were observed for preoperative blood transfusion, ventilator dependence, steroid use, nutritional support, and hematologic comorbidities (Table 5). Comorbidities that were not significantly associated with VTE were neuromuscular disorder, cerebral palsy, and weight for age z-score.

1.3.8 All-Cause Mortality and Length of Stay

Of the 305 children with VTE, eleven (1.2%) died of any cause within 30 postoperative days. Median time from VTE to death was 6 (IQR: 3–11) days. All 11 children with VTE who died had a VT, not PE. Children with VTE had a significant increase in mortality vs. children without VTE (1.2% vs. 0.2%, $p<0.001$, OR 6.3, 95% CI 3.5–11.6) (Fig. 2A). No mortality differences were observed for pre- vs. post-discharge VTE (Fig. 2B). For children with ASA class <3, no mortality differences were seen when comparing VTE status (Fig. 2C and 2D).

Preoperative LOS (12.5 ± 29.2 days for VTE vs. 4.2 ± 19.6 days for no VTE; OR 1.008, 95% CI 1.005–1.010, $p<0.001$), postoperative LOS (26.8 ± 24.1 days vs. 5.6 ± 11.1 days; OR 1.039, 95% CI 1.036–1.043, $p<0.001$), and total LOS (33.9 ± 30.2 days vs. 7.8 ± 17.3 days; OR 1.016, 95% CI 1.015–1.018, $p<0.001$) were all significantly longer in children with VTE.

1.3.9 Multivariate Logistic Regression

In the overall cohort model, the predictors with greatest effect size (adjusted OR>2) included ASA classification 3, preoperative sepsis/SIRS/septic shock, ventilator dependence, and parenteral/enteral nutrition (Table 6). Other significant VTE risk factors in the overall cohort model included preoperative blood transfusion, patient age, and operative time. Prematurity history, although associated with VTE on univariate analysis, was associated with lower VTE rate multivariate analysis. No differences were observed for current malignancy, chronic seizure disorder, preoperative length of stay, or tracheostomy.

In the subgroup analyses, several differences were observed between age groups (age 3 years vs. age 15 years) and between pre- vs. post-discharge VTE (Supplement S1). Generally, the statistical models were not as accurate at predicting VTEs in the older patient group and in the post-discharge VTE group, nor were there as many independently significant variables identified in these groups. All subgroup analyses had C-statistics > 0.75.

1.4 DISCUSSION

We report VTE rates following inpatient pediatric surgery using a validated national database. Procedures and subspecialties with the highest VTE rates were identified. We have

also identified risk factors that are associated with increased VTE risk. We report that VTE-associated mortality, although small, is significantly greater than patients without VTE.

1.4.1 Overall VTE Rates and Timing to VTE

The overall VTE rate is low and consistent with prior literature on pediatric VTE. [2, 3, 19, 20] Several publications have reported VTE rates in the hospitalized pediatric population [2, 3, 21–23] and in the intensive care population.[20, 24, 25] To date, no study has investigated the pediatric inpatient surgical population as a whole while comparing rates between procedures and subspecialties.

Several studies have reported increasing incidence of pediatric VTE over time, likely owing to the increased burden of intervention and higher screening rates. [1, 6, 26] We observed a slight increase over the years evaluated (2012–2015), however this difference was insignificant. We speculate that inpatient pediatric VTE is a multi-hit problem: patients who are already critically ill (e.g., septic, intubated, with central lines placed, etc.) who also have a surgical procedure are at increased risk for VTE vs. those who are only critically ill or are only having a procedure without underlying critical illness. Although NSQIP itself cannot be used to examine this hypothesis since inpatients not undergoing surgery are excluded, this idea is supported by the literature showing that inpatient pediatric inpatients who are critically ill are at higher risk for VTE vs. the general inpatient population and by studies showing that postoperative pediatric patients are at increased risk for VTE vs. patients who did not undergo a procedure. [1, 3, 23, 26, 28, 31]

Median time to VTE was nine days postoperatively, seventy percent of VTE events occurred within two weeks, PE typically occurred before VT, and nearly one in five VTEs occurred post-discharge. Collectively, these data are unsurprising and consistent with prior literature discussing timing to pediatric VTE.

1.4.2 VTE Rates by Surgical Subspecialty and Procedure

We report that the VTE rate is highest in cardiothoracic procedures followed by general surgery, otolaryngology, and neurosurgery. We suspect our findings partially result from the acuity of the patient population since sicker patients require longer LOS, often require long-term CVCs, and have reduced mobility, all of which have been implicated as VTE risk factors.[2, 20, 21, 27–29]

Patients with congenital heart disease have been reported as having high VTE rates in the literature, owing to the need for surgical intervention, alterations in blood flow, and need for CVCs.[30, 31] VTE rates after congenital cardiac surgery have been reported from 3.9% to 31%, much higher than most other surgical subspecialties in our database and in the literature.[32, 33] Four of the top procedures in the present analysis were colectomies, although the gastrointestinal procedure with the highest VTE rate was first stage omphalocele repair. Gonzalez-Hernandez et al. discuss the relationship between gastrointestinal disease, CVC usage, and VTE.[34] Necrotizing enterocolitis and gastroschisis were the most common diagnoses associated with CVC-related VTE in that analysis, and no patients diagnosed with omphalocele were included.[34] Antiel et al. noted 4% incidence of

VTE in pediatric patients with ulcerative colitis undergoing colectomy, similar to our observed rate for complete colectomy (4.1%).[35]

Pediatric neurosurgical procedures in the present analysis had a VTE incidence of 0.17%. Sherrod et al. noted a slightly higher 0.4% incidence in 30-day readmission in a cohort of pediatric neurosurgical patients.[36] In one case series of 14 pediatric neurosurgical patients with VTE,[37] all had significant comorbidities, and over half had a history of trauma. Ventriculoatrial shunts had the second highest VTE rate in our dataset. This procedure involves placement of an intracardiac catheter, and many of the patients are the neonatal and premature population. This population, has a large comorbidity burden and have been noted to have a higher VTE rate than other age groups.[6, 23, 25, 29]

Pediatric orthopedic postoperative VTE rates range from 0.05–0.1%, similar to our findings of 0.1%. [38–40] Orthopedic procedures were not the procedures with the highest VTE rate, but they were among the procedures with the highest overall VTE number (CPT code 22804, posterior arthrodesis of 13 or more vertebral segments, had 10 reported VTE events). However, NSQIP excludes trauma with the exception of isolated long bone fractures. Therefore the database may be missing important information about VTE rates in children with polytrauma undergoing the orthopedic procedures. We were unable to find published VTE rates in pediatric otolaryngology, but our VTE incidence of 0.18% be explained by VTE rates after tracheostomies (2.2%), and prolonged mechanical ventilation is a known VTE risk factor.[6, 25, 41] No data has been published on VTE rates after pediatric plastic or urological surgical procedures, however VTE incidence in renal tumor patients is low (0.1%).[42]

1.4.3 VTE-associated Mortality

VTE was associated with increased mortality. Previous pediatric VTE studies have reported similar findings.[3, 25] However, the effect size of the mortality difference was small (1.2% vs. 0.2%), particularly when accounting for the denominator in the non-VTE group. Our data on survival by ASA classification support that patients with higher comorbidity burden are more likely to die postoperatively. Importantly, no patient with VTE and ASA < 3 died in 30 days postoperatively (see Figure 1D).

Surprisingly, all eleven patients with VTE who died had a VT. Prior literature suggests that PEs have greater mortality risk than VTs; [28, 43, 44] however, this was not observed here.

1.4.4 VTE Risk Factors

Many of the risk factors reported here are well-known. Longer operative times have been associated with increased postoperative VTE risk.[45, 46] Younger and older pediatric patients in a bimodal distribution have the highest VTE risk in the literature relative to the early teen years similar to our findings.[28, 47] Ventilator dependence,[48] steroid use,[49] nutritional support,[34] seizure disorders,[50] and preoperative blood transfusions[5] have all been previously reported as VTE risk factors.

There were several pertinent negative results within the risk factor analysis. One surprising finding was a lack of difference observed for emergent/urgent vs. elective procedures since

this has been reported as a VTE risk factor.[51] The following comorbidities were not independently associated with VTE despite previous studies implicating them as risk factors: neuromuscular disease,[52] cerebral palsy,[52] obesity,[53] and current malignancy/current treatment for malignancy.[54]

History of prematurity was independently associated with lower VTE rates despite being associated with higher VTE rates on univariate testing. One explanation for this finding is that accounting for patient age and comorbidities in the multivariable analysis attenuates the effect of prematurity on VTE risk.

1.4.5 Limitations

Limitations of the NSQIP-P dataset include limited follow up for capturing postoperative events including VTE and later VTE-associated complications. The NSQIP-P definition of VTE includes superficial and deep VTs, which may lead to an overestimation of clinically relevant VTEs in the current study due to inclusion of superficial VTs that may be insignificant but nevertheless present on imaging modalities that meet the NSQIP-P criteria for diagnosis. Only VTEs requiring treatment and VTEs meeting other previously mentioned guidelines are captured, potentially decreasing VTE capture sensitivity. Many VTEs are likely related to PICC lines and CVCs;[55] importantly, NSQIP-P does not capture whether these are used within a separate variable, limiting analysis of the contribution of PICC lines and CVCs to the VTEs observed in NSQIP. Binary categorical variables limit analysis of comorbidity severity (e.g., “hematologic disorder” variable), and certain conditions known to increase VTE risk are not included (e.g., pregnancy). Perioperative medication data is lacking, preventing analysis of anticoagulation used either prophylactically or therapeutically. VTE-related morbidity such as post-thrombotic syndrome is not captured. Individual hospital identifiers are removed, precluding analysis of hospital outliers or hospitals implementing routine VTE prophylaxis. The large number of patients lacking prior operation data (over 50%) precludes analysis of what may be a significant VTE risk factor. Traumatic cases (except long bone fractures) are excluded, which are known to have high VTE rates.

Limitations in the authors’ own analyses should be recognized. Our results may be too generalized to be applicable within subspecialties or within particular procedures given lack of stratified analyses by specialty/procedure. However, we attempted to overcome this to a degree by reporting VTE rates by subspecialty and procedure. Our statistical analysis risks type I error (observing a difference that doesn’t truly exist) due to multivariable analysis including a relatively high number of variables.

1.4.6 Future Directions

The most complete, evidenced-based clinical guideline on pediatric VTE treatment and prophylaxis to date comes from the American College of Chest Physicians (ACCP).[56] However this guideline is focused more on a general pediatric population and is lacking in recommendations for perioperative patients.

While no national guidelines exist currently for post-surgical patients, there are institutional guidelines and consensus statements published to aid decision-making. Jackson et al

published an institutional guideline in 2008.[57] They considered orthopedic procedures to have the highest risk and used a cutoff of < or > 30 minutes for procedure length.[57] Our own analysis is inconsistent with orthopedic procedures being at greatest VTE risk and suggests operative times longer than 30 minutes are likely necessary to be concerning for VTE development.

Cincinnati Children's Hospital published an institutional guideline for VTE prophylaxis in 2014.[58] A scoring system based on risk factors and immobility following surgery dictates prophylactic intervention. Similar to the Jackson et al. guideline, the only surgical procedures mentioned as risk factors are orthopedic.[58]

Clearly, future research should be directed at VTE risk associated with post-surgical pediatric patients. Our own analysis suggests that findings in the adult literature on postoperative VTE rates may not be applicable in the pediatric population and that the existing guidelines on pediatric VTE prophylaxis are limited in their utility.

1.5 CONCLUSION

This study successfully reports VTE risk in the pediatric inpatient surgical population with analyses of contributing comorbidities and VTE-associated mortality. We report VTE rates across surgical subspecialties. Individual surgical procedures with the highest VTE rates are reported here as well. These data may be used to identify pediatric patients at highest postoperative VTE risk and for developing guidelines on VTE prophylaxis and therapeutic intervention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations List:

VTE	venous thromboembolism
VT	venous thrombosis
PE	pulmonary embolism
CVC	central venous catheter

ACS	American College of Surgeons
NSQIP	National Surgical Quality Improvement Program
NSQIP-P	National Surgical Quality Improvement Program-Pediatric
SCR	surgical clinical reviewer
CT	computed tomography
PICC	peripherally inserted central catheter
CDC	Centers for Disease Control and Prevention
SIRS	systemic inflammatory response syndrome
CPT	current procedural terminology
ASA	American Society of Anesthesiologists
CI	confidence interval
ROC	receiver operating characteristic
AUC	area under the curve
OR	odds ratio
DVT	deep venous thrombosis
CSF	cerebrospinal fluid
SD	standard deviation
TPN	total parenteral nutrition
NG	nasogastric
PRBC	packed red blood cells
LOS	length of stay
ACCP	American College of Chest Physicians

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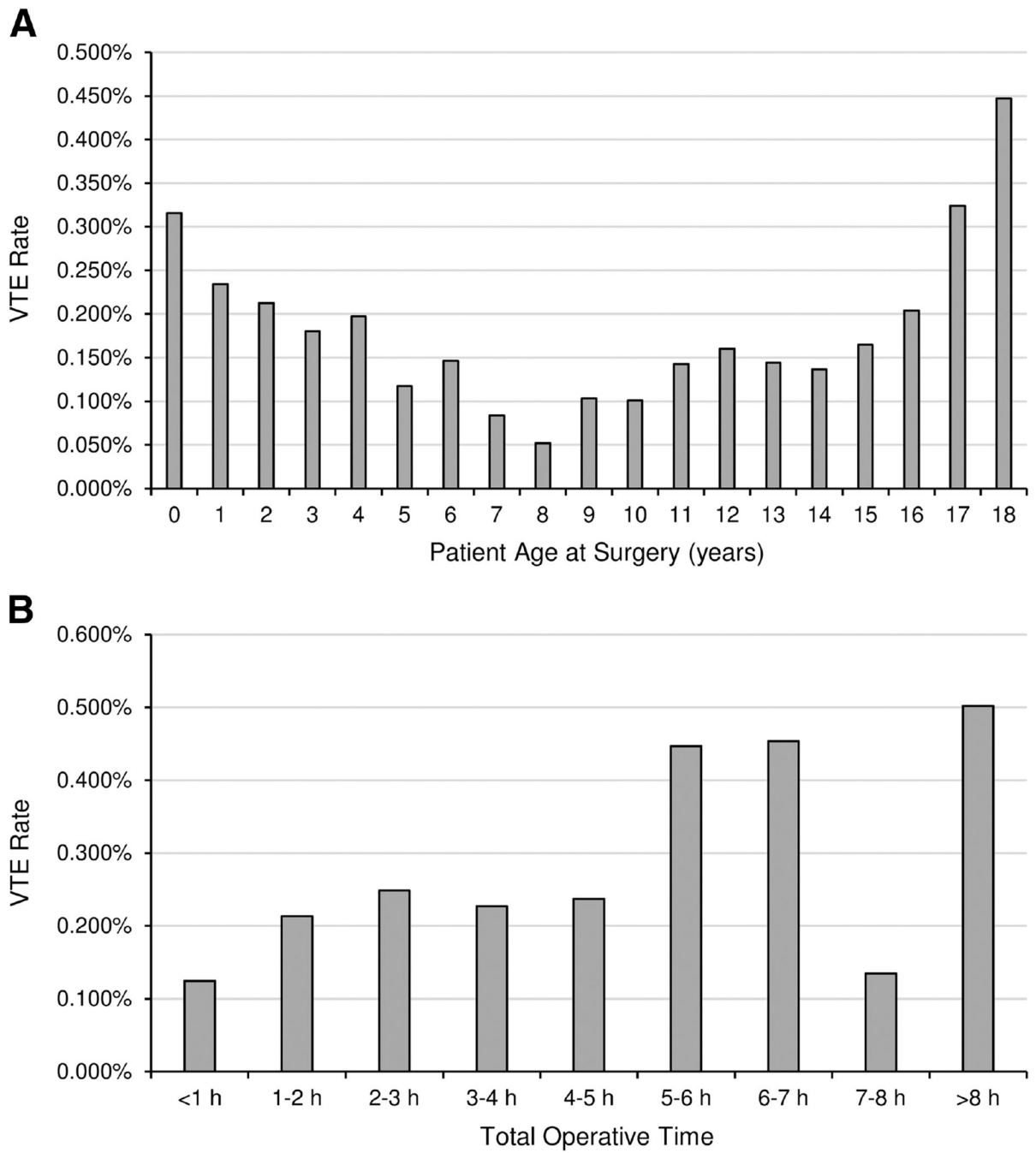


Figure 1.
VTE rate by (A) patient age at surgery and (B) total operative time.

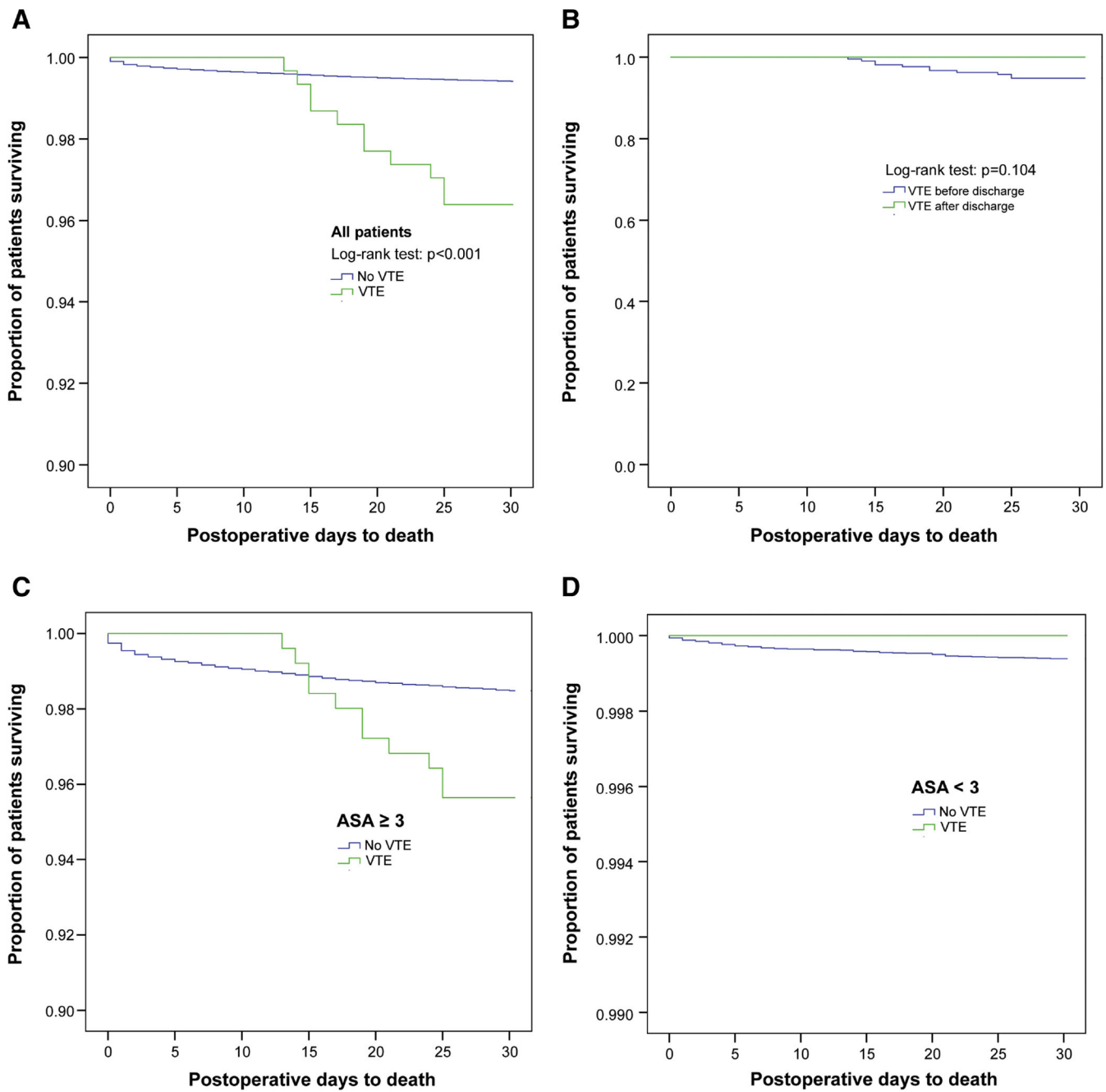


Figure 2. Mortality-free survival curves for (A) all patients, (B) pre- vs. post- discharge VTE, (C) patients with ASA class ≥ 3 , and (D) patients with ASA class < 3 . Survival analyses were performed using Kaplan-Meier estimates and log-rank tests.

Table 1.

Overall 30-day VTE frequencies within NSQIP-P by year of operation

Year	N Hospitals	N Inpatient Cases	N VT	N PE	N VTE*	% VTE per procedure	VTE Rate 95% CI (lower-upper)
2012	50	29,620	55	3	57	0.19%	0.14–0.24%
2013	56	36,539	63	5	68	0.19%	0.14–0.23%
2014	64	37,718	68	2	69	0.18%	0.14–0.23%
2015	80	49,343	110	2	111	0.22%	0.18–0.27%
TOTAL		153,220	296	12	305	0.20%	0.18–0.22%

* 3 patients had co-occurrences of VT with subsequent PE. There was no significant difference between years (p=0.3).

VTE = venous thromboembolism; NSQIP-P = National Surgical Quality Improvement Program-Pediatric; VT = venous thrombosis; PE = pulmonary embolism; CI = confidence interval

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Table 2.

VTE rate sorted by surgical subspecialty.

Subspecialty	N Procedures	N VTE	% VTE	VTE Rate 95% CI (lower-upper)
Cardiothoracic surgery	277	2	0.72%	0.00–1.72%
General/pediatric surgery	74446	211	0.28%	0.25–0.32%
Otolaryngology	8297	15	0.18%	0.09–0.27%
Neurosurgery	22385	38	0.17%	0.12–0.22%
Orthopedics	29285	30	0.10%	0.07–0.14%
Urology	9711	7	0.07%	0.02–0.13%
Plastic surgery	8514	2	0.02%	0.00–0.06%
Gynecology	305	0	0.00%	NA
TOTAL	153,220	305	0.20%	0.18–0.22%

VTE = venous thromboembolism; CI = confidence interval; NA = not applicable

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Table 3.

Top individual procedures sorted by VTE rate.

CPT Code	Description	N Cases	N (%) VTE*
49610	First stage repair of omphalocele	30	2 (6.7)
62220	Creation of CSF shunt; ventriculo-atrial, -jugular, or -auricular	48	2 (4.2)
44150	Complete colectomy with ileostomy by abdominal approach	97	4 (4.1)
32607	Unilateral thoracoscopy with biopsy of lung infiltrate	122	4 (3.3)
44143	Partial colectomy with end colostomy and closure of distal segment	167	5 (3.0)
47600	Cholecystectomy	105	3 (2.9)
32601	Diagnostic thoracoscopy of mediastinal space	106	3 (2.8)
44187	Surgical laparoscopy with jejunostomy or ileostomy	106	3 (2.8)
44020	Enterotomy of small intestine for biopsy or foreign body removal	75	2 (2.7)
31600	Tracheostomy	180	4 (2.2)
32652	Surgical thoracoscopy with complete pulmonary decortication	251	5 (2.0)
44211	Surgical laparoscopy with complete colectomy, proctectomy, ileoanal anastomosis, creation of ileal reservoir, and loop ileostomy	151	3 (2.0)
44210	Surgical laparoscopy with complete colectomy and ileostomy	209	4 (1.9)
49421	Open insertion of tunneled intraperitoneal catheter for dialysis	259	4 (1.5)
27030	Arthrotomy of hip with drainage for infection	340	5 (1.5)
38510	Open biopsy or excision of cervical lymph nodes	210	3 (1.4)
44120	Resection and anastomosis of small intestine	1283	18 (1.4)
47100	Wedge biopsy of liver	240	3 (1.3)
39503	Repair of hernia of diaphragm with creation of ventral hernia	729	9 (1.2)
44160	Partial colectomy with removal of terminal ileum and ileocolostomy	459	5 (1.1)
44125	Resection of small intestine with enterostomy	603	5 (0.8)
32480	Single lobe lobectomy	390	3 (0.8)
49000	Exploratory celiotomy	925	7 (0.8)
44126	Enterectomy, resection of small intestine for congenital atresia	310	2 (0.6)
31601	Tracheostomy, under 2 years of age	787	5 (0.6)
38120	Laparoscopy with splenectomy	488	3 (0.6)
44055	Correction of malrotation by lysis of duodenal band	1262	7 (0.6)
44050	Laparotomy and reduction of intussusception or volvulus	543	3 (0.6)
44130	Anastomosis of intestine with cutaneous enterostomy	374	2 (0.5)

* Minimum 2 VTEs per individual procedure were required to be included in this table. Procedures were included if the VTE rate was greater than or equal to 0.5%.

VTE = venous thromboembolism; CPT = current procedural terminology; CSF = cerebrospinal fluid

Table 4.

Patient demographic and operative variables corresponding univariate analyses via binary logistic regression.

Demographic Variable	VTE Group (n=305)	No VTE Group (n=152,915)	p value	Unadjusted OR	95% CI (Lower-Upper)
Age at surgery, n (%)					
<1 year	115 (0.28)	40463 (99.72)	<0.001	2.59	1.83–3.65
1–3 years	39 (0.25)	15681 (99.75)	<0.001	2.26	1.47–3.48
3–10 years	45 (0.11)	40925 (99.89)		Reference cate;	gory
10–15 years	53 (0.15)	35816(99.85)	0.14	1.35	0.91–2.00
15–18 years	53 (0.26)	20030 (99.74)	<0.001	2.40	1.62–3.58
Gender, n (%)					
Male	155 (0.19)	83370(99.81)	0.21	0.86	0.69–1.08
Female	150 (0.22)	69545 (99.78)		Reference category	
Race, n (%)					
White	208 (0.19)	107168(99.81)		Reference category	
Black	54 (0.26)	20586 (99.74)	0.05	1.35	1.00–1.82
Other*	6 (0.11)	5670 (99.89)	0.14	0.55	0.24–1.23
Unknown or not reported	40 (0.20)	19510(99.80)	0.75	1.06	0.75–1.48
Operative time in hours**, n (%)					
Less than 1 hour	70 (0.12)	58543 (99.88)		Reference	
1 hour – 5 hours	191 (0.23)	83683 (99.77)	<0.001	1.91	1.45–2.51
Greater than 5 hours	44 (0.41)	10689 (99.59)	<0.001	3.44	2.36–5.02
Emergent or urgent operation§, n (%)					
	122 (0.23)	54078 (99.77)	0.09	1.22	0.97–1.53
Prior operation in 30 days prior to index surgery†, n (%)					
	17 (1.02)	1652 (98.98)	<0.001	6.14	3.67–10.25
ASA Class, n (%)					
ASA 1 (Normal healthy patient)	7 (0.02)	31854(99.98)		Reference	
ASA 2 (Mild systemic disease)	44 (0.07)	65757 (99.93)	0.01	3.04	1.37–6.76
ASA 3 (Severe systemic disease)	153 (0.32)	47364 (99.68)	<0.001	14.7	6.89–31.4
ASA 4 (Severe, life-threatening systemic disease)	89 (1.21)	7259 (98.79)	<0.001	55.8	25.8–120.5
ASA 5 (Moribund)	10 (2.66)	366 (97.34)	<0.001	124.3	47.1–328.4

* Includes Native American, Native Hawaiian/Pacific Islander, and Asian

** Unadjusted odds ratio is with respect to per hour increase in operative time.

§ vs. elective operations

† Data on prior surgery unavailable for 87,061 cases (only available for 66,159 cases). This variable was not included in the multivariate model.

VTE = venous thromboembolism; ASA = American Society of Anesthesiologists; SD = standard deviation; OR = odds ratio; CI = confidence interval

Table 5.

Patient pre-existing comorbidities with corresponding univariate analyses via Chi-square tests.

Comorbidity*, n (%)	VTE group (n=305)	Non VTE Group (n=152,915)	P value	Unadjusted OR	95% CI (Lower-Upper)
Ventilator dependent in 48 hours before surgery	88(1.17)	7421 (98.83)	<0.001	7.95	6.20–10.20
Hematologic disorder	63 (0.84)	7481 (99.16)	<0.001	5.06	3.83–6.68
Neuromuscular disorder	27 (0.27)	9994 (99.73)	0.10	1.39	0.94–2.06
Cerebral palsy	21 (0.28)	7591 (99.72)	0.14	1.42	0.91–2.21
Parenteral or enteral nutrition required at surgery	140 (0.70)	19848 (99.30)	<0.001	5.69	4.54–7.13
Prematurity history (gestational age at birth <37 weeks gestation)	77 (0.32)	23988 (99.68)	<0.001	1.83	1.41–2.38
Current malignancy or current treatment for malignancy	33 (0.57)	5779 (99.43)	<0.001	3.09	2.15–4.44
Weight-for-age z-score > 2 (categorical)	18(0.17)	10847 (99.83)	0.50	0.82	0.51–1.33
Gastrointestinal disease	159 (0.41)	39018(99.59)	<0.001	3.18	2.54–3.98
Tracheostomy present at time of surgery	13 (0.54)	2403 (99.46)	0.001	2.79	1.60–4.87
Sepsis, SIRS, or septic shock in 48 h preoperatively	64 (0.40)	16094 (99.60)	<0.001	2.26	1.71–2.98
Blood transfusion in 48 h preoperatively	38(1.41)	2664 (98.59)	<0.001	8.03	5.70–11.30
Chronic seizure disorder	52 (0.46)	11234(99.54)	<0.001	2.59	1.92–3.50
Oral or parenteral steroid course in 30 d preoperatively	61 (1.04)	5795 (98.96)	<0.001	6.35	4.79–8.41

* For all binary predictor variables, the “no” or null state is the reference category for the given unadjusted odds ratios. Please refer to Supplement S1 and the NSQIP-P user guides for specifics of comorbidity variable descriptions.

VTE = venous thromboembolism; OR = odds ratio; CI = confidence interval; SIRS=systemic inflammatory response syndrome

Table 6.

Multivariate binary logistic regression analysis for the overall cohort.[‡]

Variable	Model C-Statistic (95% CI)	p value	Adjusted OR	95% CI lower bound	95% CI upper bound
Entire Cohort Analysis (N=135,964; 273 VTEs)	0.83 (0.81–0.86)				
ASA Class 3 (vs. ASA <3)		0.001	4.09	2.83	5.91
Sepsis, SIRS, or septic shock in 48 h preoperatively		0.001	2.72	1.97	3.76
Ventilator dependent in 48 h preoperatively		0.001	2.33	1.68	3.24
Parenteral or enteral nutrition required at surgery		0.001	2.01	1.48	2.74
Oral or parenteral steroid course in 30 d preoperatively		0.001	1.92	1.39	2.67
Blood transfusion in 48 h preoperatively		0.02	1.64	1.09	2.47
Gastrointestinal disease		0.003	1.51	1.15	1.98
Hematologic disorder		0.02	1.50	1.08	2.09
Operative time (h)		0.001	1.14	1.08	1.20
Patient age squared (y)		0.03	1.002	1.000	1.003
Prematurity history (gestational age <37 wks at birth)		0.03	0.72	0.54	0.97

[‡] Only independently significant (p<0.05 in multivariate logistic regression) variables are shown. Only variables significant on univariate analyses (p<0.05) were included in the multivariate models. Patients were only included for analysis if all variables in the model were present for that patient. No model had more than 20 total predictor variables analyzed.

* Adjusted odds ratio with respect to per hour increase in operative time.

VTE = venous thromboembolism; OR = odds ratio; CI = confidence interval; ASA = American Society of Anesthesiologists; SIRS = systemic inflammatory response syndrome

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