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Venous thromboembolism risk among pediatric patients with traumatic brain injury: a nationwide study of 44,128 patients

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OBJECTIVE Venous thromboembolism (VTE) chemoprophylaxis in pediatric patients with traumatic brain injury (TBI) requires balancing the risk of progression of intracranial bleeding versus the risk of VTE. The identification of VTE risk factors requires analysis of a very large data set. This case-control study aimed to identify VTE risk factors in pediatric patients with TBI in order to develop a TBI-specific association model that can be used for VTE risk stratification in this population.

METHODS The study included patients (aged 1–17 years) from the 2013–2019 US National Trauma Data Bank who were admitted for TBI in order to identify risk factors for VTE. Stepwise logistic regression was used to develop an association model.

RESULTS Of 44,128 study participants, 257 (0.58%) developed VTE. Risk factors associated with VTE included age (OR 1.045, 95% CI 1.010–1.080), body mass index (OR 1.034, 95% CI 1.013–1.055), Injury Severity Score (OR 1.049, 95% CI 1.039–1.059), blood product administration (OR 1.436, 95% CI 1.008–2.046), presence of a central venous catheter (OR 3.333, 95% CI 2.431–4.571), and development of ventilator-associated pneumonia (OR 3.650, 95% CI 2.469–5.396). Based on this model, the predicted VTE risk in pediatric patients with TBI ranged from 0% to 16.8%.

CONCLUSIONS A model that includes age, body mass index, Injury Severity Score, blood transfusion, use of a central venous catheter, and ventilator-associated pneumonia can help to risk stratify pediatric patients with TBI from the standpoint of implementation of VTE chemoprophylaxis.

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KEYWORDS traumatic brain injury; TBI; venous thromboembolism; VTE; deep vein thrombosis; DVT; pulmonary embolism; PE; pediatric trauma

Venous thromboembolism (VTE) is a known complication after trauma, particularly in patients with traumatic brain injury (TBI) due to the presence of incremental risk factors such as need for mechanical ventilation (MV), protracted immobilization, central venous catheter (CVC) placement, and hyperosmotic therapy. The decision to implement VTE chemoprophylaxis in patients with TBI requires weighing the risks of progression of intracranial bleeding against the benefit of a decreased rate of VTE.

The best practices guidelines of the American College of Surgeons Trauma Quality Improvement Program (ACS TQIP) for managing adult TBI recommend VTE chemoprophylaxis depending on the risk of progression of traumatic intracranial bleeding, with risk assessed with the modified Berne-Norwood criteria.[1] Of note, the ACS-

ABBREVIATIONS ACS TQIP = American College of Surgeons Trauma Quality Improvement Program; AIS = Abbreviated Injury Scale; Blood Tx = blood product administration; CVC = central venous catheter; DVT = deep vein thrombosis; GCS = Glasgow Coma Scale; IQR = interquartile range; ISS = Injury Severity Score; MV = mechanical ventilation; PE = pulmonary embolism; ROC = receiver operating characteristic; TBI = traumatic brain injury; VAP = ventilator-associated pneumonia; VTE = venous thromboembolism.

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TQIP guidelines, and the recently updated guidelines for managing severe TBI in pediatric patients by the Brain Trauma Foundation, do not provide guidance regarding VTE prophylaxis in children with TBI.[1,2]

Most studies on VTE have included adult trauma patients. Few studies have assessed pediatric patients (age < 18 years) with TBI under the assumption that children are naturally protected against VTE due to endocrinological factors and a vascular endothelium that is less likely to be damaged by hypertension, diabetes, hypercholesterolemia, or smoking.[3] Lack of contrary evidence led the Eastern Association for the Surgery of Trauma and the Pediatric Trauma Society to conclude that routine VTE chemoprophylaxis is not recommended in prepubertal patients with trauma.[4]

However, recent studies point to a significant risk of VTE, even among prepubertal patients.[5] Additionally, VTE rates in the pediatric population have been rising for decades, leading to a potentially higher number of pulmonary embolisms (PEs) and increased morbidity from long-term complications of lower-extremity deep vein thrombosis (DVT).[6,7] Forty percent of pediatric patients with lower-extremity DVT develop a postthrombotic syndrome characterized by persisting pain, limb heaviness, paresthesia, and edema.[8,9]

In 2014, Harris and Lam studied VTE in the context of TBI-related hospital admissions among pediatric patients. Their study did not include information on injury severity, chemoprophylaxis, and other pertinent clinical information.[10] Given these limitations, in this study, we assessed the current VTE prevalence in pediatric patients with TBI and identified risk factors.

Methods

Patient Selection

The study included patients aged 1–17 years with TBI extracted from the National Trauma Data Bank, a product of the ACS TQIP, from January 1, 2013, to December 31, 2019. The study was approved by the Albert Einstein College of Medicine Institutional Review Board and qualified for exempted status.

Patients younger than 12 months of age were excluded because of distinct VTE risk factors beyond the scope of this study. Figure 1 shows the selection criteria. Patients subjected to interfacility transfer, arrival without signs of life, or death in the emergency department were excluded from the analysis. TBI was identified using ICD-9 and ICD-10 codes. The data set was limited to patients with an Abbreviated Injury Scale (AIS) score of the head or face of 2 or higher, which served as a validated parameter of TBI severity,[11] and an AIS score of less than 4 in other body regions to exclude confounding from other severe injuries. VTE was captured using ICD-9 and ICD-10 codes and database-specific variables for DVT and PE reported as hospital complications. To avoid selection bias, we did not exclude patients with VTE chemoprophylaxis from the analysis.

Variables and Outcomes of Interest

The primary outcome was the development of VTE. Clinical variables were selected on the basis of their previously reported association with risk of VTE.[4–6,10,12–16] The following independent variables were investigated: age, sex, race, ethnicity, weight, BMI, AIS score, Glasgow Coma Scale (GCS) score, midline shift (> 5 mm), pupillary response, Injury Severity Score (ISS), volume of blood products transfused in the first 4 hours, occurrence of ventilator-associated pneumonia (VAP), and presence of a CVC (identified through ICD-9 and ICD-10 procedure codes). ICD-10 procedure codes allowed identification of the anatomical CVC placement site. The frequencies of comorbid conditions, such as diabetes mellitus, steroid use, smoking, chronic obstructive pulmonary disease, alcoholism, substance abuse, and anticoagulation, were analyzed to assess their roles as possible confounders. Because the study focused on patients with TBI without severe accompanying injuries, we did not analyze injuries other than TBI as risk factors.

The patients were categorized into three age groups—1–6 years of age (toddlers), 7–14 years (school-aged children), and 15–17 years (adolescents)—to determine the impact of age category on the risk of VTE based on the notion that the first two groups are distinct from adults in terms of their anatomy and physiology, while the third represents a group similar to adults from the standpoint of risk for VTE.[12] To assess the impact of BMI and ISS on the rate of VTE, BMI-for-age percentiles (as described by the Centers for Disease Control and Prevention[17]) and ISS were used to group the patients into four BMI quartiles (0th–25th, 26th–50th, 51st–75th, 76th–100th percentiles) and four ISS groups (scores 1–10, 11–15, 16–25, and > 25), respectively. The utilization of VTE chemoprophylaxis was analyzed to estimate its impact on the actual VTE rate in our study.

Statistical Analysis

The distribution of patient characteristics was summarized using descriptive statistics. Categorical variables are presented as number (percentage) and continuous variables as mean ± SD or median (interquartile range [IQR]), depending on the type of distribution. The prevalence of VTE and its corresponding 95% Clopper-Pearson exact confidence interval were estimated. Univariate analysis, with parametric and nonparametric tests, was used to identify group differences concerning VTE. Variables statistically significant at $p < 0.2$ in the univariable analysis were considered for multivariable analysis. Multivariable logistic regression models were fitted to estimate the adjusted OR (95% CI) and p values. Poisson regression modeling with robust variance was performed to confirm stable results. Overdispersion was excluded using influence diagnostics. The group rates for ISS and BMI (in 10,000 person-days) were calculated using Poisson regression models with hospital stay in days as an offset. The threshold for statistical significance was set at 5% for all the models. Variables were assessed for multicollinearity. In the case of collinearity, the most clinically relevant variable was used in the risk factor model. The analysis was performed using SAS version 9.4 (SAS Institute).[18]

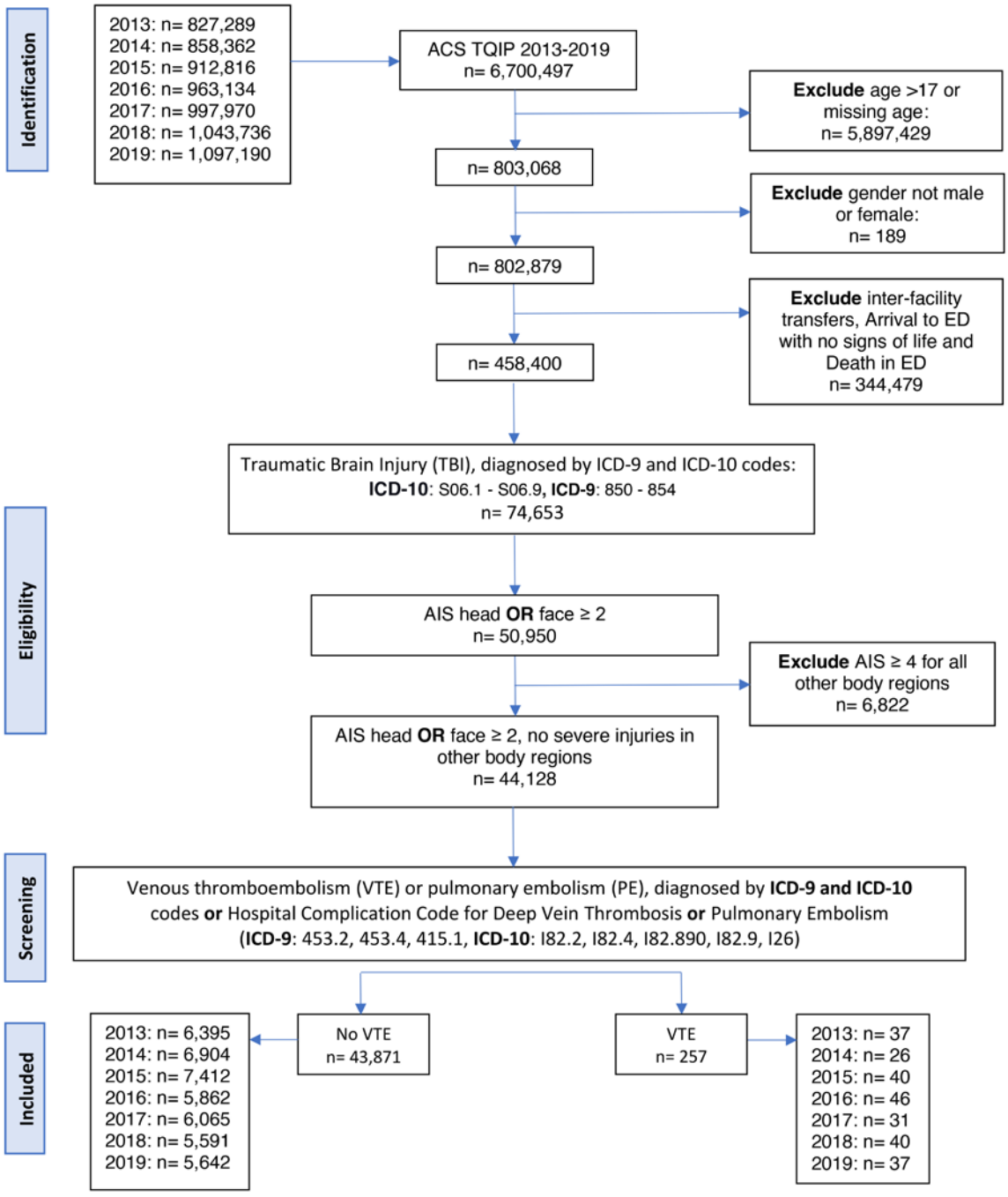

FIG. 1. Study selection process using the ACS TQIP data set, 2013–2019. ED = emergency department. Figure is available in color online only

Results

Overall VTE Prevalence

Of 50,950 pediatric patients with TBI, 0.55% (95% CI 0.49%–0.62%) (n = 279) developed VTE. Among those with VTE, 44 (16%) had unprovoked PEs, defined as PE without DVT. The prevalence ranged from 0.35% in 2014 to 0.75% in 2016, without a trendline over the 7-year observation period (Fig. 2). After exclusion of patients with severe accompanying injuries (AIS score in other body regions of 4 or greater), the prevalence of VTE in the 44,128 remaining patients was 0.58% (257 VTEs, 222 DVTs, and 39 PEs).

Patient Demographic Characteristics

Table 1 shows the demographic and clinical variables by VTE status. The groups did not differ in terms of race, eth-

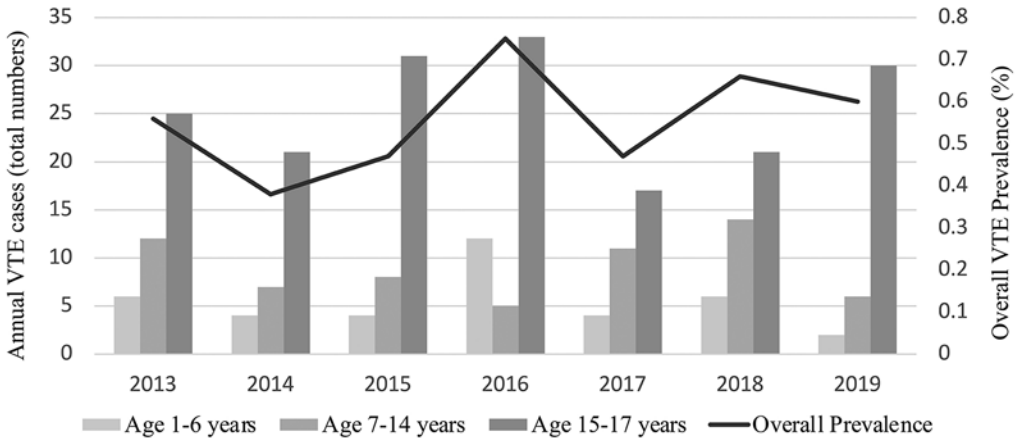

FIG. 2. Observed overall VTE prevalence (%) per year and annual VTE cases per age group from 2013 to 2019.

nicity, and comorbid conditions. The median (range) age of patients was 13.0 (1–17) years. Patients who developed VTE were older (13.4 ± 4.9 vs 11.0 ± 5.4 years, $p < 0.0001$), with an increased VTE rate after 14 years. The increase in relative risk of VTE was 63% in the group aged 15–17 years compared with the group aged 7–14 years. Figure 2 shows age-specific VTE prevalence over the reporting years. Sixty-six percent of patients were male. Although sex did not show an association with VTE overall, females older than 14 years had a higher rate of VTE (Fig. 3).

Weight and BMI

Patients who developed VTE were heavier with larger BMI (Table 1). The VTE rate (calculated with Poisson regression) among those with BMI between the second and third quartiles was more than double that of the patients with BMI below the first quartile (OR 2.17, 95% CI 1.19–3.96, $p = 0.01$). When stratified into four groups based on BMI quartile, the rates of VTE per 10,000 person-days from the first to the fourth quartile group were 1.9, 3.3, 4.1, and 4.1, respectively.

VTE Chemoprophylaxis

Data regarding pharmacological VTE prophylaxis were available for 32,505 patients; of these, 4823 (14.8%) received chemoprophylaxis. Patients who received prophylaxis had a higher BMI (23.5 ± 6.3 vs 20.9 ± 6.1 kg/m^2, $p < 0.0001$). When stratified by VTE status, 14.4% of patients in the no-VTE group received prophylaxis, whereas 80.6% of the VTE group received chemoprophylaxis.

Injury Severity

Patients with VTE had more severe TBI according to the following measures compared to those without VTE: lower GCS score (10.8 ± 4.4 vs 14.2 ± 2.5), higher AIS-head score (3.1 ± 0.7 vs 2.6 ± 0.7), more frequent midline shift > 5 mm (28% vs 10%), and bilateral unresponsive pupils (27% vs 10%) ($p < 0.0001$ for all measures). Additionally, patients with VTE had higher AIS scores in the other body regions: abdomen (2.0 ± 0.8 vs 1.7 ± 0.7), thorax (2.3 ± 0.6 vs 2.1 ± 0.7), upper extremities (1.6 ± 0.5 vs 1.4 ± 0.5), lower extremities (1.8 ± 0.6 vs 1.6 ± 0.7), and face (1.3 ± 0.5 vs 1.2 ± 0.4) (all $p < 0.05$). Consequently, mean ISS was greater in the VTE group (30.6 ± 11.9 vs 15.1 ± 10.7, $p < 0.0001$). A comparison of the VTE rates (calculated with Poisson regression) within the four ISS groups showed lower rates of VTE in the groups with ISS ≤ 25. The rate ratio was 0.45 (95% CI 0.22–0.94, $p = 0.03$) between the 11–15 ISS and > 25 ISS groups and 0.62 (95% CI 0.44–0.87, $p = 0.006$) between the 16–25 ISS and > 25 ISS groups.

Additional VTE Risk Factors

The presence of a CVC was associated with increased risk of VTE: thromboembolic complications occurred in 123/4906 (2.5%) patients with a CVC compared to 0.3% in those without it ($p < 0.0001$). CVCs were present in 123/257 (48%) patients in the VTE group. The anatomical site of CVC placement was available for 1879 patients between 2016 and 2019: 58%, 32%, and 9% of CVCs were placed in the femoral, subclavian, and jugular veins, respectively. The proportion of patients with a femoral CVC did not change during the 4 observation years. Patients with VAP had a 10-fold higher VTE rate than those without VAP: 6.5% (46/703) versus 0.58%, respectively. Additionally, the volume of transfused blood products of the VTE group was greater. Although there were no statistically significant differences in the volumes of fresh frozen plasma, platelets, and cryoprecipitate received between groups, patients who developed VTE received more packed red blood cells (94.8 ± 395 ml vs 18.8 ± 202 ml, $p = 0.006$).

Association Model

Table 2 shows the results of the binary logistic regression. Age, ISS, GCS score, VAP, BMI, presence of CVC, and blood product administration (Blood Tx) were predictive of VTE. CVC and VAP were the most important risk factors, each leading to more than 3-fold increased odds of VTE. Multicollinearity was detected for ISS and GCS score. ISS was ultimately selected for the model because

TABLE 1. Characteristics of patients with and without VTE

Variable	All Patients (n = 44,128)	No VTE (n = 43,871)	VTE (n = 257)	p Value
Demographic characteristic				
Age, median (IQR), yrs	13.0 (10.0)	13.0 (10.0)	16.0 (5.0)	<0.0001*
Male sex, no. (%)	29,189 (66.1)	29,019 (66.1)	170 (66.1)	0.99
Race, no. (%)				0.59
White	28,187 (63.9)	28,015 (63.9)	172 (66.9)	
African American	7,780 (17.6)	7,739 (17.6)	41 (16.0)	
Other	8,161 (18.5)	8,117 (18.5)	44 (17.1)	
Ethnicity, no. (%)				0.89
Not Hispanic or Latino	35,755 (81.0)	35,549 (82.6)	206 (80.8)	
Hispanic or Latino	7,529 (17.1)	7,480 (17.4)	49 (19.2)	
Weight & BMI				
Weight, median (IQR), kg	50.0 (45.0)	50.0 (44.8)	65.0 (29.0)	<0.0001*
1–35 kg, no. (%)	14,688 (36.3)	14,644 (36.5)	44 (18.1)	
35–75 kg, no. (%)	19,297 (47.8)	19,170 (47.7)	127 (52.3)	
≥75 kg, no. (%)	6,424 (15.9)	6,352 (15.8)	72 (29.6)	
BMI, median (IQR), kg/m^2	20.4 (7.0)	21.3 (6.2)	22.6 (8.1)	<0.0001*
VTE chemoprophylaxis, no. (%)				
Yes	4,823 (14.8)	4,657 (14.4)	166 (80.6)	<0.0001*
No	27,682 (85.2)	27,642 (85.6)	40 (19.4)	
Injury severity				
AIS-head score, median (IQR)	2.4 (1.0)	2.4 (1.0)	3.0 (0.9)	<0.0001*
ISS, median (IQR)	12.0 (12.0)	11.0 (13.0)	29.0 (17.0)	<0.0001*
GCS score, median (IQR)	15.0 (0.0)	15.0 (0.0)	12.0 (8.0)	<0.0001*
No pupillary response, no. (%)	2,059 (10.1)	2,021 (10.0)	38 (27.3)	<0.0001*
Midline shift, no. (%)	2,176 (10.5)	2,134 (10.3)	42 (28.0)	<0.0001*
Additional risk factors				
VAP, no. (%)	703 (1.6)	657 (1.5)	46 (17.9)	<0.0001*
CVC, no. (%)	4,906 (11.1)	4,783 (10.9)	123 (47.9)	<0.0001*
Blood products in first 4 hrs				
PRBC, mean (SD), ml	19.3 (203.4)	18.8 (201.6)	94.8 (395.1)	0.006*
Plasma, mean (SD), ml	51.0 (272.9)	49.8 (269.0)	120.3 (443.9)	0.1385
Platelets, mean (SD), ml	14.2 (84.3)	14.0 (83.8)	26.6 (106.2)	0.2667
Cryo, mean (SD), ml	2.9 (34.5)	2.6 (30.2)	20.2 (131.3)	0.2101

Cryo = cryoprecipitate; PRBC = packed red blood cells.
Continuous variables were compared with the t-test (mean [SD]) or Wilcoxon test (median [IQR]); categorical variables were compared with the chi-square test. Data were missing for some variables, and the percentages were calculated accordingly.
* Indicates statistical significance.

it reflects the injury severity of several body regions and because of the advantages of AIS-head score over GCS as a parameter of TBI severity in epidemiological research. The final model yielded excellent discriminatory ability, with an area under the receiver operating characteristic (ROC) curve of 87%.

The probability of VTE was calculated with the following equation: $p = 1/1 + e^{-z}$, where $z = -7.822 + 0.0436$ (age) + 0.0334 (BMI) + 0.0477 (ISS) + 1.2947 (0 or 1 for VAP presence) + 1.2039 (0 or 1 for CVC presence) + 0.3621 (0 or 1 for Blood Tx). Based on the model, the predicted risk of VTE in a 6-year-old child increased from a low risk of 0.003 in the absence of risk factors to 0.104 (10.4%) with the presence of all predictors.

Discussion

The prevalence of VTE in pediatric trauma patients reportedly ranges from 0.02% to 1.2%, rising to 10% in patients requiring ICU treatment.[6] The VTE prevalence in our study was 0.58% and comparable to the rate of 0.46% reported by Harris and Lam.[10] Based on the variables included in our TBI-specific association model, pediatric patients with TBI and all risk factors present had a maximum risk of VTE of 16.8%; this is higher than the risks

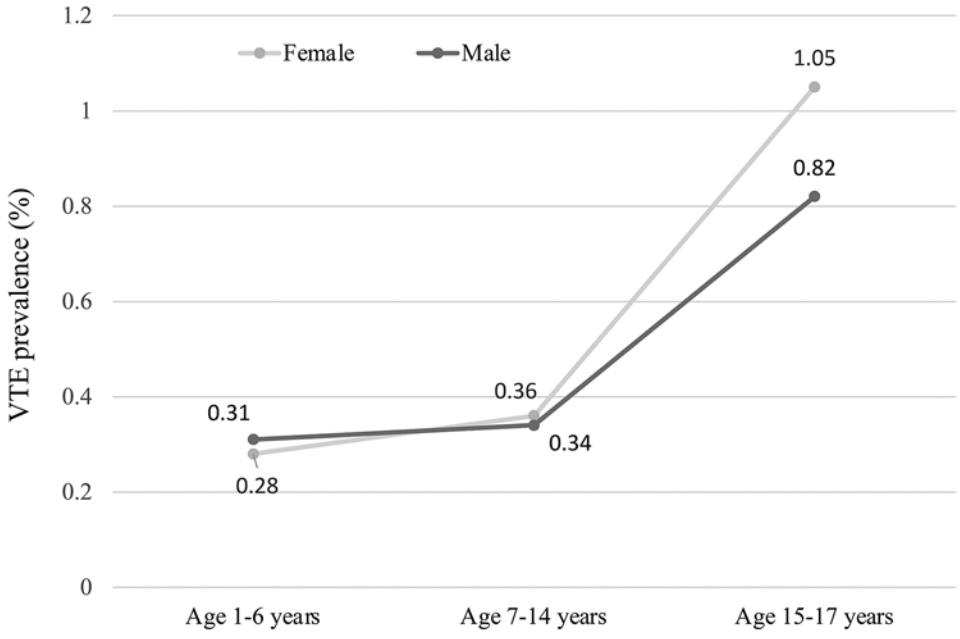

FIG. 3. VTE prevalence (%) by sex and age group.

of 14.4% and 9.0% for VTE in pediatric trauma patients estimated with the predictive models of Connelly et al. and Yen et al., respectively.[13,15]

Figure 4 shows a comparison of maximum VTE risk according to the three different models. The higher risk of VTE in our model can be attributed to the presence of many incremental risk factors in patients with TBI, including the high proportion of ICU admissions, need for protracted MV, longer immobilization, and use of a CVC. In conjunction with the development of acute posttraumatic inflammatory syndrome, these factors are among the most impactful risk factors used in all available pediatric VTE risk assessment models.[13,15,16,19,20] Furthermore, the presence of severe TBI in isolation has been shown to increase the risk of VTE.[10,21,22] Because our tool was derived from a cohort of patients with TBI, it can presumably be applied better to this patient group. The existing VTE risk models for the pediatric trauma population underestimate VTE risk in young patients with isolated TBI because the models focus on age and major surgery, in addition to injury severity, and they omit VAP as a variable, which indicates evolving complications and occurs very frequently in patients with severe TBI (prevalence 35%[23]).

Due to limited laboratory data regarding the coagulation system available in the National Trauma Data Bank, we could not assess the impact of early posttraumatic coagulopathy on the rate of VTE; early posttraumatic coagulopathy is reportedly present in both patients with isolated TBI and those with multiple trauma.[24–26]

The predicted risk of VTE of 16.8% in the patients with all risk factors is lower than the VTE rate of 25% confirmed with ultrasound surveillance on day 7 of ICU stay in a high-risk group of patients not receiving prophylaxis.[27] The absence of data on VTE surveillance in our data set, as well as the VTE chemoprophylaxis rate of 15%, underestimated the true incidence of VTE and limited validation of the performance of our predictive model despite an area under the ROC curve of 0.87. The predicted risk of 16.8% remains theoretical in the absence of confirmation of the diagnoses.

The risk of VTE increases with age, with an inflection point at 15 years of age. Age is a well-established risk factor of VTE, with a lower risk in prepubertal children and an increased risk in patients aged 13 to 16 years.[15,28] Of note, prepubertal children with higher BMI and ISS and who require a CVC and Blood Tx are at significant risk for VTE. The association model developed shows that a 7-year-old obese child with TBI, ISS 30, and CVC and requiring Blood Tx during the first 4 hours of treatment could have a 3% risk of VTE. The impact of sex on risk of VTE was observed in only postpubertal patients. Adolescent females had a higher risk of VTE than their male counterparts (Fig. 3). This finding is consistent with female sex previously identified as a VTE risk factor in patients who are of fertile age.[29]

TABLE 2. Stepwise logistic regression

Variable	OR	95% CI	p Value	Beta Coefficient
Age	1.045	1.010–1.080	0.0106	0.0436
ISS	1.049	1.039–1.059	<0.001	0.0477
Blood Tx in first 4 hrs	1.436	1.008–2.046	0.0449	0.3621
CVC	3.333	2.431–4.571	<0.0001	1.2039
VAP	3.650	2.469–5.396	<0.0001	1.2947
BMI	1.034	1.013–1.055	0.0012	0.0334
Constant	–7.8220		0	0

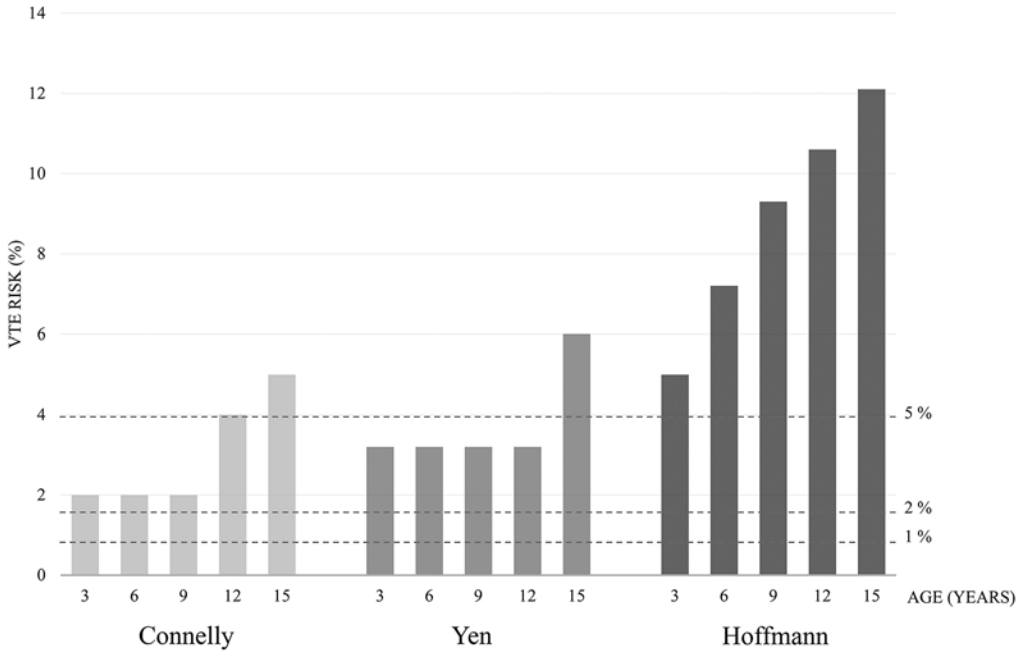

FIG. 4. Three models were used to predict the risk of VTE and to estimate a patient's maximum VTE risk (i.e., for a patient who has all the risk factors that are relevant to the employed model). Risks are presented by age. The underlying assumptions for risk determination included the following: isolated severe TBI (GCS score 3–8, AIS-head score 5, and ISS 25), obesity, (30 kg/m^2 BMI), admitted to ICU, mechanically ventilated, positive for blood transfusion, CVC placement, major surgery, and VAP.

The effect of weight-corrected age on VTE risk was examined using BMI-for-age percentiles. BMI between the 85th and 95th percentile defines overweight, whereas BMI greater than the 95th percentile identifies obesity.[17] The risk of VTE increased with BMI up to but not after the 50th percentile. This finding does not corroborate previous reports showing that the risk of VTE continues to rise linearly without a weight threshold.[30] The threshold BMI for VTE in our study can be explained by the chemoprophylaxis data: patients with higher BMI were more likely to receive prophylaxis and were presumably better protected against VTE. Several studies have shown an association between obesity and VTE in pediatric patients.[3,31–33] Van Arendonk et al. found a 3-fold increased risk of VTE in obese patients aged ≤ 21 years.[28] Despite its proven association with VTE, obesity is not commonly used in the predictive models presently used for VTE risk stratification of pediatric trauma patients because of its low beta coefficient value. However, obesity remains an important risk factor for VTE because of its effect on the inflammatory response after trauma, and because of its aggravated effect in combination with oral contraception in postpubertal females.[34] Moreover, obesity may contribute to increased risk of VTE because it can cause endothelial dysfunction and can inhibit fibrinolysis in childhood.[3]

Our results corroborate the association between injury severity based on GCS score and AIS-head score, and in aggregate based on ISS, in addition to presence of a CVC as risk factors for VTE.[4–6,10,12–16,19,35,36] In total, 123/4906 (2.5%) patients with a CVC developed VTE. A CVC, particularly in the femoral vein position, has been identified as a significant risk factor for VTE, with a reported incidence of catheter-related thrombosis as high as 70%, particularly in young children because of their small vessel diameter in relation to the diameter of the catheter.[3,14,22,37] Based on these findings, there have been recommendations to abandon the use of CVCs in children or to shorten their duration of use.

VAP was identified as a strong risk factor for VTE. VAP reportedly occurs in 35% of children with TBI who require MV for 2 days or longer. It is commonly diagnosed on day 4 of MV, earlier than day 7 when VTE is typically diagnosed.[23,37] One may question retaining VAP, which does not occur until day 2 or later, as a predictor variable in our model that included time-insensitive and pathophysiologically reasonable predictors of VTE such as age, BMI, ISS, and CVC present on admission. The occurrence of VAP may predispose patients with TBI to increased risk from protracted positive-pressure MV and its effect on mean systemic venous pressure, protracted immobilization, and upregulated inflammatory infectious response. Based on these findings, pediatric patients with VAP should be classified as a high-risk group for VTE, regardless of age and other risk factors. To our knowledge, this is the first study that has identified VAP as a risk factor as important as presence of CVC for the development of VTE.

The effect of Blood Tx on the risk of developing VTE, documented in previous studies, was corroborated: children who received packed red blood cells during the first 4 hours of admission had higher VTE rates compared with those who did not require transfusion.[13–15]

The developed association model includes easily assessable parameters and is designed for bedside use. It should be used daily because the diagnosis of the time-

sensitive predictive variable VAP may increase the risk of VTE and provide useful information to estimate the benefit of chemoprophylaxis in children at intermediate-high risk of progression of intracranial bleeding. Furthermore, in contrast to the assumption that prepubertal children do not need a VTE risk assessment because of their low propensity for VTE, our association model demonstrated that even very young patients with TBI may be at higher risk for VTE due to their BMI, ISS, and presence of CVCs, VAP, and Blood Tx.

Although our VTE risk stratification tool is different from previously published VTE prediction tools for the pediatric population, it has similarities to the Trauma Embolic Scoring System, a VTE risk prediction tool developed for adult trauma patients that uses data obtained between 2000 and 2009 from one US trauma center. This model found that obesity, ventilator duration longer than 3 days, lower-extremity trauma, age, and ISS were predictive of VTE. The utilization of this scoring system for VTE risk stratification in adults was recently recommended by the American Association for the Surgery of Trauma and the American College of Surgeons Committee on Trauma.[38,39]

Although the overall rate of VTE in our study was low at 0.58%, a subset of pediatric patients were at much higher risk based on their age, BMI, ISS, presence of CVC, Blood Tx, and development of VAP. The rate of chemoprophylaxis was low, and a relevant proportion of patients in the VTE group were without chemoprophylaxis. Based on our findings, pediatric patients should have a daily VTE risk assessment, regardless of their age, to identify those at higher risk for VTE. Ideally, CVC placement should be avoided unless absolutely necessary for the treatment of severe TBI. Patients at a high risk of VTE should be assessed for risk of progression of intracranial bleeding due to chemoprophylaxis by using the modified Berne-Norwood criteria.[1,40]

This study had several limitations. First, the National Trauma Data Bank data set is limited by its retrospective nature and the level of detailed clinical information available for each patient, including data on coagulation parameters and detailed cerebral imaging. Second, the extraction of VTE (DVT/PE) is reported as a complication, without information about whether DVT was identified through the screening surveillance protocols used by the reporting hospitals. Therefore, we cannot exclude surveillance bias and underestimation of the true VTE prevalence. Third, as it is common with databases, a percentage of patients had missing data, which may have caused selection bias. Fourth, for comparison of the results of our study with those reported by other authors, it is important to underline our inclusion criteria. We chose an AIS-head score of at least 2 as a requirement for study inclusion, whereas other studies have used GCS score. The average GCS score of our control group was 14.2, which suggests that our data set had a smaller proportion of patients with severe TBI. This may have led to an underestimation of the VTE prevalence among patients with moderate to severe TBI. Fifth, the rate of VTE prophylaxis of 15% of the patients in our study could have affected the overall rate of VTE. In addition, a previous study found that registry data may underreport VTE chemoprophylaxis by 50%, meaning that the VTE prophylaxis effect in our study may have been larger than that estimated on the basis of the documented chemoprophylaxis rate.[37]

Conclusions

Based on our results, we conclude that the risk of VTE in pediatric patients with TBI can be estimated by a model with an area under the ROC curve of 87% that includes age, BMI, ISS, presence of a CVC, Blood Tx, and development of VAP. Based on this model, the risk of VTE in our data set ranged from 0% to 16.8% on the basis of increasing age, age-adjusted obesity, ISS, presence of a CVC, Blood Tx, and development of VAP. The utilization of this model to risk stratify pediatric patients with TBI in order to evaluate the risk-benefit ratio of VTE chemoprophylaxis in clinical practice requires additional internal validation from a larger data set followed by external validation.

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Disclosures

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Conception and design: Hoffmann, Marini, McNelis, Viswanathan, Lowery Wilson. Acquisition of data: Lewis. Analysis and interpretation of data: Hoffmann, Lewis, Marini, McNelis, Viswanathan, Lieb, Lowery Wilson. Drafting the article: Hoffmann, Lewis, Posti. Critically revising the article: all authors. Reviewed submitted version of manuscript: Hoffmann, Lewis, Marini, McNelis, Posti, Lieb, Lowery Wilson. Approved the final version of the manuscript on behalf of all authors: Hoffmann. Statistical analysis: Hoffmann, Lewis, Marini. Administrative/technical/material support: McNelis. Study supervision: McNelis, Viswanathan.

Supplemental Information

Previous Presentations

The abstract of this study was presented orally at the Winter Scientific Session of the New York Surgical Society, New York, NY, February 8, 2023. The objective, methods, and results of the univariate analysis were briefly explained. No details regarding the developed association model were disclosed.

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