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A Clinical Tool for the Prediction of Venous Thromboembolism in Pediatric Trauma Patients

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IMPORTANCE Although rare, the incidence of venous thromboembolism (VTE) in pediatric trauma patients is increasing, and the consequences of VTE in children are significant. Studies have demonstrated increasing VTE risk in older pediatric trauma patients and improved VTE rates with institutional interventions. While national evidence-based guidelines for VTE screening and prevention are in place for adults, none exist for pediatric patients, to our knowledge.

OBJECTIVES To develop a risk prediction calculator for VTE in children admitted to the hospital after traumatic injury to assist efforts in developing screening and prophylaxis guidelines for this population.

DESIGN, SETTING, AND PARTICIPANTS Retrospective review of 536 423 pediatric patients 0 to 17 years old using the National Trauma Data Bank from January 1, 2007, to December 31, 2012. Five mixed-effects logistic regression models of varying complexity were fit on a training data set. Model validity was determined by comparison of the area under the receiver operating characteristic curve (AUROC) for the training and validation data sets from the original model fit. A clinical tool to predict the risk of VTE based on individual patient clinical characteristics was developed from the optimal model.

MAIN OUTCOME AND MEASURE Diagnosis of VTE during hospital admission.

RESULTS Venous thromboembolism was diagnosed in 1141 of 536 423 children (overall rate, 0.2%). The AUROCs in the training data set were high (range, 0.873-0.946) for each model, with minimal AUROC attenuation in the validation data set. A prediction tool was developed from a model that achieved a balance of high performance (AUROCs, 0.945 and 0.932 in the training and validation data sets, respectively; $P = .048$) and parsimony. Points are assigned to each variable considered (Glasgow Coma Scale score, age, sex, intensive care unit admission, intubation, transfusion of blood products, central venous catheter placement, presence of pelvic or lower extremity fractures, and major surgery), and the points total is converted to a VTE risk score. The predicted risk of VTE ranged from 0.0% to 14.4%.

CONCLUSIONS AND RELEVANCE We developed a simple clinical tool to predict the risk of developing VTE in pediatric trauma patients. It is based on a model created using a large national database and was internally validated. The clinical tool requires external validation but provides an initial step toward the development of the specific VTE protocols for pediatric trauma patients.

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Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) or pulmonary embolism (PE), is a major source of morbidity and mortality in the adult trauma population, with an estimated incidence as high as 20% to 58% in patients who do not receive appropriate thromboprophylaxis.[1-3] However, the incidence of VTE among pediatric trauma patients is considerably lower, occurring in less than 1% of patients.[4-7] Because of the low incidence in this population, no standardized VTE screening or thromboprophylaxis guidelines exist, to our knowledge.

Although rare, VTE in pediatric patients can have significant consequences, with a 20% to 25% estimated incidence of postthrombotic syndrome.[8,9] Independent of injury severity, VTE in pediatric trauma patients is associated with an increased length of stay and with higher hospitalization costs.[5] Furthermore, the VTE rate among all hospitalized pediatric patients is increasing.[10]

New evidence suggests a growing awareness of the importance of VTE in the pediatric trauma population. Prophylactic enoxaparin sodium use is increasing, and clinical guidelines have been implemented to successfully lower the rate of VTE in single-center pediatric intensive care units (ICUs).[11,12] Higher injury severity and older age are associated with an increased VTE risk in pediatric trauma patients.[6,7] A 2013 study[4] using the National Trauma Data Bank (NTDB) supported these findings. However, no standardized mechanism exists to estimate the risk of VTE among individual patients, to our knowledge.

The objective of this study was to develop a simple clinical tool to predict the risk of VTE among pediatric trauma patients. Such a tool would use readily obtainable and clinically relevant characteristics available early during hospital admission.

Methods

Data Source

Data were collected using the NTDB from January 1, 2007, to December 31, 2012. We received a human participants exemption by the Oregon Health & Science University Institutional Review Board.

Study Population and Variables Considered

All patients 0 to 17 years old were included. Patients were excluded if they were not admitted because they died in the emergency department, were dead on arrival, or were discharged, transferred to another facility, or left against medical advice from the emergency department. The primary end point of interest was a diagnosis of VTE in pediatric trauma patients during the index hospitalization. We considered the relationship between VTE rates and baseline characteristics, comorbidities, mechanism of injury, characteristics and severity of injury, placement of a central venous catheter (CVC), transfusion of blood products, intubation, ICU admission, and major surgical procedures.

Risk factors were chosen based on known adult risk variables for VTE and those factors previously described in the pediatric literature. Demographic variables included age, sex, and race/ethnicity. Comorbidities included diabetes mellitus, cancer, bleeding disorder, and obesity. Injury severity was determined by the admission Injury Severity Score (ISS), Glasgow Coma Scale (GCS) score, and Abbreviated Injury Score (AIS) by body region. The mechanism of injury, presence of pelvic or lower extremity fractures, and ICU admission were also included (eTable in the Supplement).

Based on previously established criteria, major surgery was categorized by organ system using *International Classification of Diseases, Ninth Revision* (*ICD-9*) operation codes, including neurologic, thoracic, cardiovascular, hematologic or spleen, gastrointestinal, and genitourinary. Musculoskeletal operations were defined as spine or nonspine. We examined *ICD-9* codes for CVC placement and transfusion of blood products. Intubation was defined by *ICD-9* codes or the presence of at least 1 ventilator day (eTable in the Supplement).[4]

Age was categorized into the following groups: 0, 1 to 9, 10 to 12, 13 to 15, or 16 to 17 years. Adolescent groupings were determined by presumed physiologic changes, previously observed transition points in VTE rates by age, and varying thromboprophylaxis policies among patients 13 to 17 years old.[4] The admission GCS score was categorized as mild (13-15), moderate (9-12), or severe (3-8). The ISS was similarly categorized as mild (0-8), moderate (9-15), severe (16-24), or very severe (25-75). All variables were coded as present or absent. The analysis was performed based on the set of patients with complete information for all variables in a given model.

Statistical Analysis

The characteristics of patients with and without VTE were compared using *t* test or Mann-Whitney test for continuous variables and χ^2 test or Fisher exact test for categorical variables, as appropriate. The models were developed on a training data set and were validated using a validation data set. The training data set consisted of half of the VTE cases and half of the noncases from the original data set, selected randomly, and the validation data set consisted of the other half. Mixed-effects logistic regression with robust SEs was used to evaluate the independent associations of VTE occurrence with explanatory variables. A random intercept for facility was used to account for potential within-facility correlation. A set of models of varying complexity was considered. The ability of each model to distinguish between VTE cases was assessed and then validated. Specifically, mixed-effects logistic regression was performed for each model on the training data set, and the corresponding area under the receiver operating characteristic curve (AUROC) was calculated. The estimates of the fixed effects and random intercepts from each model were used to generate the AUROC from the validation data set. The equality of the AUROCs from the training and validation data sets was tested. Minimal attenuation of the AUROC between the training and validation data sets was evidence of validity. The model fit was assessed via the Bayesian information criterion, which penalizes the models for the inclusion of additional terms.

Because almost all patients who are intubated require ICU admission, a sensitivity analysis that included an interaction

term between intubation and ICU admission was performed. Given the possibility for interaction between the GCS score and ICU admission, as well as CVC placement and transfusion of blood products, a sensitivity analysis was also performed for these terms. Statistical software (Stata, version 13; StataCorp LP) was used for all analyses.[13]

Creation of a Clinical Tool

To create a clinical tool using an additive points scale to provide a VTE prediction score, points were calculated as log odds ratios (ORs) from each variable considered and multiplied by 100. To account for facility random effect, the predicted probability from the clinical tool was averaged over facilities and is presented with a 95% CI band for the variance component.

Results

Baseline Characteristics

In total, 536 423 pediatric patients were identified among 856 trauma centers. Venous thromboembolism was diagnosed in 1141 patients (0.2%), of which 926 (0.2%) had DVT only, 164 (0.03%) had PE only, and 51 (0.0001%) had both DVT and PE.

Patients with VTE were older, were more severely injured, more frequently were intubated or underwent major surgery, and more often received a CVC or transfusion of blood products. Patients with VTE were often admitted to the ICU; among those admitted to the ICU, patients with VTE tended to have longer stays. Patients with VTE were also more likely to be obese, have diabetes mellitus, or manifest a bleeding disorder, although these outcomes were uncommon (**Table 1**). These observed differences are consistent with previous findings in this population using the NTDB.[4]

Development of the Risk Prediction Model

Five models of varying complexity were developed to predict VTE. The simplest included the GCS score alone, and more complex models included additional characteristics of the patient, injuries, and treatment. The results of the models fitted to the training data set are listed as estimated ORs that correspond to each covariate (**Table 2**). The GCS score was strongly associated with the risk of VTE, but other clinical factors absorb this effect in more complex models. Age category and ICU admission were strongly associated with the risk of VTE in models 2 through 5. Major surgery was strongly associated with VTE risk. Cardiovascular surgery was associated with the highest risk, while other types of surgery were associated with only moderate risk.

For each model, the AUROCs that correspond to the training and validation data sets are listed in **Table 3**. Because all prior studies list injury severity as strongly associated with VTE, we first evaluated the ISS as an independent predictor of VTE (AUROC, 0.896; 95% CI, 0.883-0.909). However, we elected to use admission GCS in model 1 because the ISS is not calculated until discharge; the AIS was also omitted for the same reason. The GCS score provided reasonable distinction between VTE cases and noncases (model 1 AUROC, 0.873). The inclusion of a modest set of patient characteristics provided excellent discrimination between groups (model 2 AUROC, 0.936), and the presence or absence of major surgery further improved performance (model 3 AUROC, 0.945). However, the inclusion of the mechanism of injury and the specific type of major surgery performed added little to performance of models 4 and 5 (AUROC, 0.946 for both). On validation, the AUROC attenuated by a moderate amount for model 1 and by a small amount for models 2 through 5. The drop in the AUROC reflects slight overfitting of the estimated coefficients and facility random effect in the training data set.

Model 3 was selected to develop our risk prediction tool because it achieves the optimal balance among performance in distinguishing VTE cases and noncases, the minimal Bayesian information criterion of all models considered, and ease of use in a clinical setting. Its performance was validated with similar ROC curves (**Figure 1**) and an excellent validation AUROC of 0.932. There was moderate within-facility correlation in this model, with an estimated intracluster correlation of 0.12 (range, 0.09-0.18). In sensitivity analyses, there was a significant negative interaction between intubation and ICU admission (OR, 0.396; $P = .008$), and a negative interaction was observed between ICU admission and a GCS severe score relative to a mild score (OR, 0.333; $P = .01$). No significant interaction was found between CVC placement and transfusion of blood products (OR, 0.776; $P = .29$). Therefore, model 3 may overestimate the risk of VTE for patients who are intubated and admitted to the ICU and may underestimate the risk for patients who have only one of these characteristics. Similarly, it may overestimate the risk of VTE for patients who are admitted to the ICU and have a severe GCS score and may underestimate the risk for those who have only one of these variables.

Development of the Clinical Tool

The results of our prediction model are presented as a score that can be translated into a measure of VTE risk. Using model 3, the points are calculated and totaled (**Figure 2**A). The total score is translated into a predicted risk. Because of moderate within-facility correlation, the predicted probability of VTE per individual will vary by facility. Therefore, we demonstrate the mean predicted risk for a given score and 95% CI band (Figure 2B). The maximum total number of points is 797, corresponding to a 14.4% predicted risk of VTE. For example, consider a 13-year-old male motor vehicle crash patient with a femur fracture and chest injuries causing respiratory distress. His GCS score is 11, and he is admitted to the ICU, intubated, and requires a CVC, transfusion of blood products, and operative fixation of his femur. Using Figure 2A, we calculate his points total as 733, yielding a 7.6% (95% CI, 4.3%-12.8%) risk of VTE.

Model 3I is a revised tool showing the results of the sensitivity analysis with the inclusion of interaction terms (Figure 2A). The correspondence between the points total and the predicted risk corresponds closely to model 3. This modified tool is unwieldy, and the benefit of the correction is outweighed by the difficulty of use. Therefore, we advocate the use of model 3.

Table 1. Characteristics of the Study Population by Diagnosis of Venous Thromboembolism (VTE) During the Hospital Stay[a]

Variable	No VTE (n = 535 282)	VTE (n = 1141)	*P* Value[b]
Demographic Characteristics			
Age, median (IQR), y	9 (4-15)	15 (11-17)	<.001
Age category, y, No. (%)			
0	209 997 (39.2)	146 (12.8)	<.001
1-9	58 922 (11.0)	105 (9.2)	
10-12	64 853 (12.1)	70 (6.1)	
13-15	99 829 (18.7)	256 (22.4)	
16-17	101 681 (19.0)	564 (49.4)	
Male sex, No. (%)	351 375 (65.9)	763 (66.9)	.50
Race/ethnicity, No. (%)			
American Indian	4651 (1.0)	14 (1.3)	<.001
Asian	8549 (1.8)	19 (1.8)	
Black or African American	85 026 (17.4)	224 (20.7)	
Native Hawaiian or Pacific Islander	1100 (0.2)	9 (0.8)	
White	319 578 (65.4)	680 (62.9)	
Other	69 516 (14.2)	136 (12.6)	
Clinical Characteristics of Trauma			
ISS, No. (%)			
Mild, 0-8	282 367 (55.3)	83 (7.6)	<.001
Moderate, 9-15	151 462 (30.0)	212 (19.5)	
Severe, 16-24	49 182 (9.6)	262 (24.0)	
Very severe, 25-75	27 567 (5.4)	533 (48.9)	
AIS location, No. (%)			
Head	11 292 (4.0)	25 (6.2)	.03
Face	68 254 (16.7)	190 (23.4)	<.001
Neck	4530 (1.0)	19 (2.1)	.002
Spine	7018 (1.7)	14 (2.0)	.55
Thorax	11 107 (2.8)	32 (6.2)	<.001
Abdomen	17 760 (4.5)	53 (8.3)	<.001
Upper extremity	32 059 (9.8)	84 (11.7)	.09
Lower extremity	28 711 (8.4)	70 (12.5)	<.001
Unspecified	42 435 (9.9)	117 (12.7)	.004
Mechanism of injury, No. (%)			
Blunt	434 091 (81.3)	840 (73.8)	<.001
Penetrating	31 084 (5.8)	158 (13.9)	
Burn	23 456 (4.4)	29 (2.6)	
Other	45 151 (8.5)	112 (9.8)	
GCS score, No. (%)			
Mild, 13-15	449 256 (92.1)	478 (44.6)	<.001
Moderate, 9-12	9948 (2.0)	76 (7.1)	
Severe, 3-8	28 460 (5.8)	517 (48.3)	
Intubation, No. (%)	42 032 (7.9)	765 (67.1)	<.001
Central venous catheter placement, No. (%)	30 139 (5.6)	457 (40.1)	<.001
Transfusion of blood products, No. (%)	11 683 (2.2)	318 (27.9)	<.001
Major surgery, No. (%)	136 325 (25.5)	969 (84.9)	<.001
ICU admission and length of stay			
Admission to ICU, No. (%)	129 646 (24.2)	985 (86.3)	<.001
Length among admitted, median (IQR), d	2 (1-3)	13 (6-23)	<.001

(continued)

Table 1. Characteristics of the Study Population by Diagnosis of Venous Thromboembolism (VTE) During the Hospital Stay[a] (continued)

Variable	No VTE (n = 535 282)	VTE (n = 1141)	*P* Value[b]
Mechanical ventilation and duration			
Received mechanical ventilation, No. (%)	145 029 (27.1)	848 (74.3)	<.001
Duration among ventilated, median (IQR), d	2 (1-5)	11 (5-19)	<.001
Total length of hospital stay, median (IQR), d	2 (1-3)	20 (11-32)	<.001
Disease Characteristics, No. (%)			
Obesity	2726 (0.51)	25 (2.19)	<.001[c]
Diabetes mellitus	1433 (0.27)	9 (0.79)	.004[c]
Bleeding disorder	1028 (0.19)	15 (1.31)	<.001[c]
Cancer	117 (0.02)	1 (0.09)	.22[c]

Abbreviations: AIS, Abbreviated Injury Score; GCS, Glasgow Coma Score; ICU, intensive care unit; IQR, interquartile range; ISS, Injury Severity Score.

[a] The statistics in the table are based on the number of participants who had a nonmissing value for that variable.

[b] By Welch *t* test, χ^2 test of independence, or Mann-Whitney test, as appropriate, unless otherwise indicated.

[c] By Fisher exact test.

Table 2. Association Between Venous Thromboembolism and Various Characteristics From the Models Under Consideration

Variable	Odds Ratio (95% CI)				
	Model 1 (n = 245 062)	Model 2 (n = 244 106)	Model 3 (n = 244 106)	Model 4 (n = 243 541)	Model 5 (n = 243 541)
GCS score					
Mild, 13-15	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Moderate, 9-12	7.01 (4.93-9.95)	1.39 (0.96-2.03)	1.49 (1.04-2.15)	1.53 (1.06-2.21)	1.66 (1.14-2.42)
Severe, 3-8	14.90 (12.19-18.22)	1.34 (0.99-1.80)	1.40 (1.05-1.86)	1.43 (1.08-1.89)	1.36 (1.01-1.84)
Age category, y					
0		1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
1-9		0.43 (0.28-0.65)	0.39 (0.26-0.59)	0.42 (0.28-0.63)	0.42 (0.28-0.64)
10-12		1.02 (0.61-1.69)	0.85 (0.51-1.42)	0.93 (0.57-1.50)	0.94 (0.58-1.52)
13-15		1.63 (1.14-2.32)	1.30 (0.91-1.85)	1.37 (0.98-1.94)	1.36 (0.98-1.90)
16-17		2.26 (1.56-3.26)	1.69 (1.18-2.44)	1.81 (1.27-2.57)	1.65 (1.16-2.34)
Male sex		0.99 (0.82-1.20)	0.96 (0.80-1.16)	0.95 (0.78-1.14)	0.92 (0.75-1.11)
Intubation		3.61 (2.54-5.13)	2.63 (1.87-3.68)	2.63 (1.88-3.67)	2.50 (1.77-3.55)
Admission to ICU		6.25 (4.53-8.62)	5.53 (3.99-7.67)	5.57 (4.01-7.73)	5.50 (3.97-7.61)
Transfusion of blood products		2.15 (1.61-2.89)	1.79 (1.37-2.33)	1.77 (1.36-2.30)	1.59 (1.20-2.12)
Central venous catheter placement		2.30 (1.79-2.96)	1.85 (1.45-2.35)	1.82 (1.43-2.31)	1.58 (1.22-2.05)
Pelvic fracture		1.50 (1.13-2.00)	1.39 (1.06-1.83)	1.46 (1.11-1.93)	1.23 (0.90-1.67)
Lower extremity fracture		1.80 (1.42-2.27)	1.43 (1.13-1.81)	1.48 (1.16-1.88)	1.51 (1.16-1.96)
Major surgery			4.46 (3.36-5.93)	4.33 (3.25-5.75)	
Mechanism of injury					
Blunt				1 [Reference]	1 [Reference]
Penetrating				1.28 (0.98-1.68)	1.14 (0.86-1.52)
Burn				1.36 (0.74-2.50)	1.46 (0.79-2.70)
Other				1.22 (0.89-1.68)	1.43 (1.03-1.98)
Neurosurgery					2.13 (1.69-2.69)
Thoracic surgery					1.38 (1.08-1.77)
Cardiovascular surgery					3.30 (2.55-4.27)
Heme or spleen surgery					1.24 (0.78-1.95)
Gastrointestinal surgery					1.83 (1.42-2.35)
Genitourinary surgery					0.73 (0.55-0.96)
Musculoskeletal surgery					1.56 (1.21-2.00)
Spine surgery					0.95 (0.64-1.43)

Abbreviations: GCS, Glasgow Coma Scale; ICU, intensive care unit.

Discussion

This study is the first to develop a simple and validated bedside prediction tool to assess VTE risk in pediatric trauma patients, to our knowledge. Because the NTDB is the largest consolidated data repository for trauma patients, it provides adequate power to capture a rare clinical outcome and information about associated risks. Using readily available clinical information, we developed a simple tool to help

Table 3. Estimated Area Under the Receiver Operating Characteristic Curve (AUROC) From the Model Fit on the Training Data Set and Tested on the Validation Data Set

Model	AUROC, 95% CI		P Value[a]
	Training Data Set	Validation Data Set	
1	0.873 (0.860-0.887)	0.806 (0.785-0.828)	<.001
2	0.936 (0.927-0.945)	0.919 (0.907-0.931)	.03
3	0.945 (0.937-0.953)	0.932 (0.922-0.943)	.048
4	0.946 (0.938-0.953)	0.932 (0.922-0.943)	.045
5	0.946 (0.938-0.954)	0.930 (0.918-0.941)	.03

[a] By test of equality of the AUROCs.

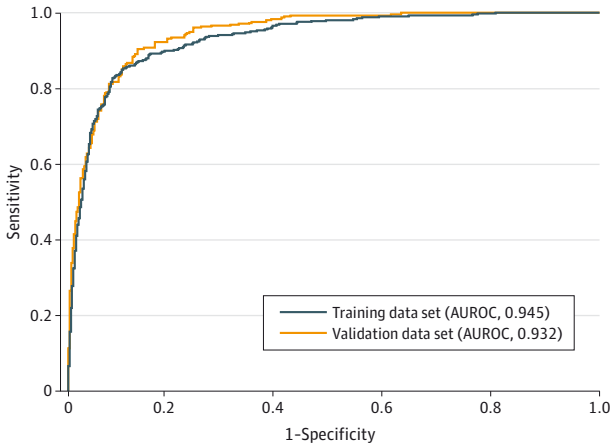
guide clinical decision making when treating critically injured children.

Prevention of VTE has been identified as a high priority in surgical and trauma patients and has become an important quality improvement metric across institutions.[14,15] Among adult trauma patients, there exists strong consensus that thromboprophylaxis is an essential intervention that leads to a dramatic decrease in VTE.[1] However, controversy exists as to the appropriate approach to pediatric trauma patients. Because of its rarity among young children, authors have argued that withholding VTE prophylaxis is safe.[16,17] An increased incidence of pediatric VTE has been associated with older age in other studies,[4,6] which is consistent with our data. Despite evidence for an increased risk among adolescent patients, considerable variability exists in VTE prophylaxis across institutions. Deep vein thrombosis prophylaxis patterns were assessed in a survey of 133 trauma centers published in 2008, which found that the use of thromboprophylaxis is rare among patients 0 to 11 years old, that 13% of centers regularly prescribe enoxaparin in those 11 to 15 years old, and that 57% of centers regularly use enoxaparin in those 16 to 20 years old.[18] At our institution, all patients 15 years or older are treated using our adult VTE screening and prophylaxis protocol. Given this variability in practice, it was our aim to create a risk prediction tool to guide clinical practice in any pediatric trauma patient regardless of age.

Multiple studies have been conducted to identify risk factors for VTE in children. Although overall risk factors are similar to those in adults, the risk conferred by each factor is different in children. Among all patients, admission to the pediatric ICU, mechanical ventilation, and CVC placement have been strongly associated with VTE development. Further risk factors include the presence of chronic complex comorbidities or preexisting malignancy.[10,19,20] In pediatric trauma patients, older age and higher injury severity are consistently identified as important risk factors associated with VTE.[6,7,17] In addition, the most comprehensive study[4] available has identified intubation, ICU admission, blood transfusion of blood products, major surgery, CVC placement, and longer length of ICU and hospital stay as associated with an increased risk of VTE. We constructed our risk prediction tool using risk factors previously associated with VTE, and our models are consistent with published results.

Our VTE risk calculator for pediatric trauma patients uses clinical information typically available to the physician early in the course of the hospital stay. We constructed increasingly complex risk prediction models using additional known risk factors for VTE. Given its strong prediction value and ease of use, we based our prediction tool on model 3. There are only 10 clinical variables in this model, all of which are objectively measurable and are generally available early after hospital admission. Models 4 and 5 provide marginal improvements; however, they introduce additional complexity to the prediction calculator, with little justifiable benefit. We did not include the comorbidities of obesity, diabetes mellitus, cancer, or bleeding disorder because their incidence was low, and they are likely underreported in the NTDB. Finally, we did not include ICU or overall length of stay in our models because they are unknown until discharge.

Figure 1. Area Under the Receiver Operating Characteristic Curve (AUROC) for Model 3 on the Training and Validation Data Sets



This model, developed on the training data set, maintained its performance on the validation data set.

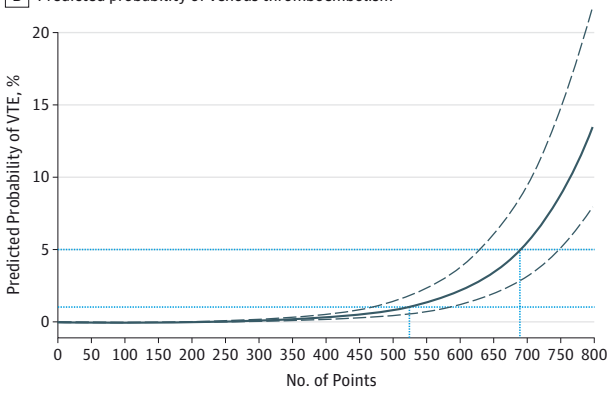
While risk factors associated with VTE in pediatric trauma patients have been well described, there have been few attempts to develop a cohesive approach to screening and thromboprophylaxis. In 2010, risk factors associated with VTE in pediatric trauma patients admitted to the pediatric ICU of a single institution were published and demonstrated that VTE occurred in 6% of their critically injured children and was associated with poor perfusion, immobility, and CVC placement.[21] Using these risk factors, the authors developed and implemented clinical guidelines for screening and thromboprophylaxis. Patients were divided into the following 3 groups: (1) those with a high VTE and bleeding risk, who received sequential compression devices (SCDs) only and screening ultrasonography on pediatric ICU day 7; (2) those with a high VTE risk

Figure 2. Calculation of a Patient's Points Total and the Predicted Probability of Venous Thromboembolism (VTE) Given the Points Total

A Calculation of a patient's points total

Characteristic	Points	
	Model 3	Model 3I
GCS score		
Mild, 13-15	+0	+0
Moderate, 9-12	+40	+29
Severe, 3-8	+34	+101
Age category, y		
0	+94	+94
1-9	+0	+0
10-12	+78	+78
13-15	+120	+120
16-17	+147	+146
Female sex	+4	+4
Male sex	+0	+0
Intubation	+97	+143
Admission to ICU	+171	+186
Transfusion of blood products	+58	+57
Central venous catheter placement	+61	+61
Pelvic fracture	+33	+32
Lower-extremity fracture	+36	+37
Major surgery	+150	+149
Intubation AND admission to ICU	NA	-51
GCS category moderate AND admission to ICU	NA	+10
GCS category severe AND admission to ICU	NA	-70

B Predicted probability of venous thromboembolism



Averaged over facilities, model 3 scores of 0 to 523 correspond to low risk (<1%) of VTE, scores of 524 to 688 correspond to medium risk (1%-5%), and scores of 689 to 797 correspond to high risk (>5%). The predicted probability averaged over facilities (ie, zero intercept) is shown as a dark blue line. The 95% CI band, shown as a set of solid light blue lines, represents variability in the predicted probabilities over facilities. Cutoff values for risk categories averaged over facilities are shown as dashed lines. GCS indicates Glasgow Coma Scale; ICU, intensive care unit; and NA, not applicable.

and a low bleeding risk, who received prophylactic anticoagulation and SCDs; and (3) those with a low VTE risk, who received no intervention. Patients in the last 2 groups underwent duplex ultrasonography only for symptoms. This intervention substantially lowered the rate of VTE from 5.2% to 1.8%.[12] Our risk prediction calculator could be used to implement a similar screening and prophylaxis program. One possible approach would be to categorize patients based on the predicted risk of VTE as those with less than 1% risk (86.8% of patients in our data set) as low risk, those with 1% to 5% risk (3.5% of our patients) as intermediate risk, and those with greater than 5% risk (9.8% of our patients) as high risk. A potential therapeutic strategy would be to provide no intervention to the low-risk group, a screening protocol and SCDs to the intermediate-risk group, and a screening protocol, SCDs, and pharmacologic thromboprophylaxis to the patients at high VTE risk but with a low bleeding risk. For those patients with high VTE risk who are deemed to have a high bleeding risk, only a screening protocol and SCDs should be provided.

This study has several limitations. One commonly cited pitfall in using the NTDB is the presence of surveillance bias, largely because of the significant variation in VTE screening protocols across institutions. It is generally accepted that the NTDB underreports complications,[22] so the actual rate of VTE may be higher than we reported. In our study, we demonstrated moderate within-facility clustering of VTEs, likely because of variable screening and reporting. Furthermore, considerable variation exists in the approach to thromboprophylaxis in pediatric patients, especially among adolescents.[18] Information about thromboprophylaxis is not available in the NTDB. Underreporting, in combination with variable prophylaxis patterns, likely results in a higher actual VTE rate than was observed in this study. Consequently, our model and the prediction tool likely underestimate VTE risk because they assume a lower rate of VTE than its actual incidence. Finally, the temporal relationship between the occurrence of clinical risk factors and a VTE is variable and difficult to define in our data set. Therefore, VTE may have occurred before some clinical risk factors for some patients in the data set, possibly overestimating the risk of these factors. Also, when using our clinical tool for an individual, it should be recognized that all possible risk factors for VTE may not yet have occurred, resulting in an underestimation of the associated VTE risk when used at that particular time. The effect of this limitation is minimized by our selection of risk factors that typically occur early during admission.

Conclusions

Using the NTDB, we developed a VTE prediction tool for pediatric trauma patients. This tool is unique in that it provides a risk assessment for pediatric patients of any age and relies on clinical characteristics that should be available early during hospital admission. It has been internally validated but requires external validation using existing institutional databases and a prospective evaluation before broad application. If successful, this tool may be a useful clinical guide in the treatment of critically injured children.

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Statistical analysis: Connelly, Laird, Fischer, Zonies.
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Invited Commentary

Pediatric Venous Thromboembolism—Like Adult Clots, Only Smaller

Matthew J. Martin, MD

To say that we are "operating in the dark" when it comes to venous thromboembolism (VTE) screening and prophylaxis in children is an understatement. In this issue of *JAMA Surgery*, Connelly and colleagues[1] have published a technically well-done statistical analysis of the National Trauma Data Bank (NTDB) to develop a VTE risk prediction score for pediatric trauma patients. They ran a variety of permutations of clinical risk factors to develop the most accurate yet parsimonious risk prediction system from a training data set, and then they validated the accuracy using a validation data set. Their final best prediction model demonstrated an area under the receiver operating characteristic curve of 0.932, generating a simple scoring system that predicted deep vein thrombosis risk ranging from 0% to 14%. To their credit, the authors avoided using in their risk prediction calculator standard injury characterization variables such as the Injury Severity Score or the Abbreviated Injury Score, which

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