Risk Factors for Venous Thromboembolism in Pediatric Trauma Patients and Validation of a Novel Scoring System: The Risk of Clots in Kids With Trauma Score*

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Objectives: Identify risk factors for venous thromboembolism and develop venous thromboembolism risk assessment models for pediatric trauma patients.

Design: Single institution and national registry retrospective cohort studies.

Setting: John Hopkins level 1 adult and pediatric trauma center and National Trauma Data Bank.

Patients: Patients 21 years and younger hospitalized following traumatic injuries at John Hopkins (1987–2011). Patients 21 years and younger in the National Trauma Data Bank (2008–2010 and 2011–2012).

Interventions: None.

Measurements and Main Results: Clinical characteristics of Johns Hopkins patients with and without venous thromboembolism were compared, and multivariable logistic regression analysis was used to identify independent venous thromboembolism risk factors. Weighted risk assessment scoring systems were developed based on these and previously identified factors from National Trauma Data Bank patients (2008–2010); the scoring systems were validated in this cohort from Johns Hopkins and a cohort from the National Trauma Data Bank (2011–2012). Forty-nine of 17,366 pediatric trauma patients (0.28%) were diagnosed with venous thromboembolism after admission to our trauma center. After adjusting for

potential confounders, venous thromboembolism was independently associated with older age, surgery, blood transfusion, higher Injury Severity Score, and lower Glasgow Coma Scale score. These and additional factors were identified in 402,329 pediatric patients from the National Trauma Data Bank from 2008 to 2010; independent risk factors from the logistic regression analysis of this National Trauma Data Bank cohort were selected and incorporated into weighted risk assessment scoring systems. Two models were developed and were cross-validated in two separate pediatric trauma cohorts: 1) 282,535 patients in the National Trauma Data Bank from 2011 to 2012 and 2) 17,366 patients from Johns Hopkins. The receiver operating curve using these models in the validation cohorts had area under the curves that ranged 90–94%.

Conclusions: Venous thromboembolism is infrequent after trauma in pediatric patients. We developed weighted scoring systems to stratify pediatric trauma patients at risk for venous thromboembolism. These systems may have potential to guide risk-appropriate venous thromboembolism prophylaxis in children after trauma. (*Pediatr Crit Care Med* 2016; 17:391–399)

Key Words: pediatric; thromboprophylaxis; trauma; Risk of Clots in Kids in Trauma score; venous thromboembolism

Trauma is an independent risk factor for venous thromboembolism (VTE) in adults, with a reported incidence from less than 1% to 7.6% (1, 2). In trauma patients 21 years and younger, the incidence is considerably lower, in the range of 0.1–0.6% (3–5). Although VTE is much less common in children compared with adults, the overall incidence of hospitalized pediatric patients diagnosed with VTE has increased by 70% in the past decade (6). In the subset of pediatric patients with hospital-associated VTE, trauma is one of the most frequent diagnoses (4). Although evidence-based guidelines are available to guide VTE thromboprophylaxis in adults with trauma (7), no consensus recommendations are available for children.

In adults, the use of pharmacologic prophylaxis with low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH) is a well-established practice after major trauma in the absence of contraindications. However, the widespread use of pharmacologic prophylaxis in children may be inappropriate due to the relatively low prevalence of VTE and potential bleeding risk. On the other hand, failure to implement VTE prophylaxis in the subset of the pediatric patients at high risk may result in significant VTE-related morbidity. Several studies have found that older age, central venous catheters (CVCs), and increased Injury Severity Score (ISS) were risk factors for VTE (3, 5, 8–10). In addition, the presence of multiple simultaneous risk factors has been demonstrated to increase the odds of VTE in trauma patients (2, 8) as well as in medical patients (4, 11, 12). Based on the patient's age and the presence of multiple risk factors, Hanson et al (13) developed a local hospital-based guideline for the use of VTE prophylaxis in pediatric trauma patients. The incidence of VTE decreased after implementation of this guideline. Risk assessment models that incorporate multiple weighted risks have been used to stratify adult patients into high-risk groups who may benefit most from VTE prophylaxis and identify low-risk groups in whom the risks of prophylaxis may not be warranted. Several of these models have been developed for adult trauma (14), medical (15–17), and surgical patients (18, 19). However, few have been validated, and none had existed for pediatric trauma patients until a recent publication of a clinical prediction tool by Connelly et al (20).

The aim of this study were 1) to identify risk factors for VTE in a large population of pediatric and young adult trauma patients at a level 1 trauma center and 2) based on upon risks identified in this cohort and from the previously published National Trauma Data Bank (NTDB 2008–2010) (3), to develop a weighted risk assessment model for VTE after pediatric trauma. We validated models in a cohort from the NTDB (2011–2012) and the Johns Hopkins Trauma Registry to assess its potential to capture pediatric trauma patients at risk for VTE.

METHODS

Low molecular weight heparin is not approved by the U.S. Food and Drug Administration for use in pediatrics.

The Johns Hopkins Hospital and Johns Hopkins Children's Center adult and pediatric trauma registries include all patients who are evaluated after presentation with traumatic injury. Patient demographics, admission and discharge dates, VTE diagnoses (including deep vein thrombosis [DVT] and pulmonary embolism [PE]), injury type and ISS, operations, blood transfusions administered, and complications during hospitalization, and other clinical characteristics are recorded in the registry. Dedicated full-time registrars enter data into the clinical trauma registry as required by the state of Maryland. Johns Hopkins University is a verified level 1 adult and pediatric trauma center; we are required submit these data to the state. The data entry registrars have specific training in medical coding with a trauma focus. We reviewed records from the adult registry from 1987 to 2011, and we reviewed records from the pediatric registry from 1990 to 2011. The total number of patients 21 years old or younger in the registries was 17,366. Major surgery was defined as having operations on the nervous system (*International Classification of Diseases,* 9th Edition, codes 01.xx to 05.xx), respiratory system (30.xx to 34.xx), cardiovascular system (35. xx to 39.xx), hematopoietic and lymphatic system (i.e., spleen operations) (40.xx to 41.xx), digestive system (42.xx to 54.xx), urinary system (55.xx to 59.xx), or musculoskeletal system (77. xx to 78.xx, 79.20 to 79.39, 79.50 to 79.69, 79.80 to 79.99, 81.xx, and 83.xx to 84.xx) as previously described (3).

Patients 21 years old or younger in the adult and pediatric registries were included in the study if they were admitted to the hospital following trauma evaluation. Clinical data were extracted from the registry, and additional data were gathered through detailed chart review for only patients diagnosed with VTE. All VTE diagnoses were confirmed by review of radiology reports and deemed line-associated if a central line was located in the same anatomic location as the VTE.

Patients diagnosed with VTE were compared with patients without VTE in the Johns Hopkins registries using Wilcoxon rank-sum tests for continuous variables and chi-square tests for categorical variables. We then examined 402,329 patients registered in the NTDB from 2008 to 2010 (3). Initially, univariate

logistic regression models were created to determine which variables were statistically associated with the outcome of VTE in the NTDB. Those variables that were found to be statistically associated with VTE in the NTDB and in the Johns Hopkins registries were then chosen to be incorporated into a multivariable logistic regression model. A severity scoring system was then created based on the coefficient estimates of multivariable model, normalized by the lowest coefficient, and rounded to the nearest whole number. We considered two systems of scores, one that included and one that excluded intubation. The fit of this scoring system to the data was determined by the area under the curve (AUC) from receiver operating characteristic (ROC) analyses, the Hosmer–Lemeshow goodness of fit test, and cross-validation of the score using data from a separate cohort of 282,535 patients in the NTDB from 2011 to 2012, and the Johns Hopkins trauma cohort. A ROC curve was generated using the GraphPad Prism statistical software (San Diego, CA). Other analyses were performed using STATA 12.1/SE (College Station, TX). The study was approved by the Johns Hopkins Institutional Review Board.

RESULTS

Study Population

A total of 17,366 patients 21 years or younger were admitted to the Johns Hopkins pediatric and adult trauma centers with traumatic injury during the study period. VTE was diagnosed in 49 patients for a prevalence of 0.28%. Twelve of the 49 were from the pediatric database, and 37 from the adult database. Forty-two patients had DVT, 11 had PE, and 4 had both. The majority of patients were African American males in both groups. The median age of patients with VTE was significantly higher than that of those without VTE (18 vs 11 yr; $p < 0.001$). As patient age increased, the frequency of VTE also increased, especially after the age of 15 years. The frequency of VTE for ages 0–12 years was 9 per 10,000, compared with 27 and 73 per 10,000 for ages 13–15 and 16–21 years, respectively.

Clinical Characteristics

The clinical characteristics of the patients with VTE are outlined in **Table 1**. Seventy-one percent of patients underwent surgery that lasted over 2 hours, and 67% were intubated for over 72 hours. Seventy-one percent of patients with VTE were intubated with an average number of 9.5 days (± 8.0 SD). The most common body regions injured were abdomen and head, followed by chest, long bone, and vascular injuries. Eight percent of patients with VTE suffered other orthopedic injuries, and one patient experienced a burn injury. Many patients were injured in more than one body region. The majority of patients with VTE (62%) had a central line during some point of their hospitalization. Thirty-seven percent did not have a CVC placed; of those, the most common site of DVT was the lower extremity. Five had PE and only two had upper extremity DVT. Of the 31 patients with CVCs, 65% were diagnosed with lower extremity DVT, 23% had upper extremity DVT, and a total of 12% had PE. The majority of DVTs in patients with CVCs were in the same vessel as the catheter, or line-associated (64%, 20 of 31). Most of the upper extremity DVTs were CVC-associated (67%, six of nine total upper extremity DVTs); in contrast, most lower extremity DVTs were not CVC-associated (58%, 19 of 33 total lower extremity DVTs).

TABLE 1. Clinical Characteristics of Pediatric Trauma Patients With Venous Thromboembolism

Clinical Characteristics	Patients (*n*)	%
Surgery > 2 hr	35	71
Immobilized > 72 hr	33	67
Intubated	35	71
Days intubated, mean (SD)	9.5 (8.0)	45
Site of injury		
Abdomen	22	45
Head	22	45
Chest	14	29
Long bone	14	29
Vascular	11	22
Other orthopedic	4	8
Burn	1	2
Central lines	31	63 (% of total with lines)
LE DVT	20	65
UE DVT	7	23
PE	2	6
LE DVT + PE	2	6
No central line	18	37 (% of total without lines)
LE DVT	11	61
UE DVT	2	11
PE	5	28
Prophylaxis		
Pharmacologic	21	43 (% of total pharmacologic)
UFH	10	48
LMWH	7	29
UFH + LMWH	4	19
Mechanical	33	67 (% of total mechanical)
Thromboembolic disease compression stockings	31	94
Sequential compression devices	33	100
No prophylaxis	11	22

LE = lower extremity, DVT = deep venous thrombosis, UE = upper extremity, PE = pulmonary embolus, UFH = unfractionated heparin, LMWH = low molecular weight heparin.

VTE Prophylaxis Use

Of patients diagnosed with VTE, 21 (43%) received either prophylactic UFH or LMWH. Ten patients were prescribed UFH and seven patients were prescribed LMWH; four patients received both treatments during their hospitalization. Seventeen (35%) received only mechanical prophylaxis (i.e., sequential compression devices and/or thromboembolic disease compression stockings; Covidien, Mansfield, MA), and 11

TABLE 2. Unadjusted and Adjusted Odds Ratios for Venous Thromboembolism Risk in Johns Hopkins Trauma Registry Patients Less Than or Equal to 21 Years Old

Risk Factor	Unadjusted OR (95% CI)	*p*
Female gender (vs male)	0.76 (0.39–1.45)	0.4
Race (vs white)		
Black	2.13 (1.11–4.11)	0.02
Other/unknown	1.72 (0.38–7.69)	0.5
Operation (vs none)	26.08 (10.34–65.82)	< 0.001
Penetrating trauma (vs nonpenetrating trauma)	3.63 (2.05–6.44)	< 0.001
ISS (vs mild, 0–8)		
Moderate (9–15)	12.02 (2.60–55.67)	0.001
Severe (16–24)	39.46 (8.96–173.78)	< 0.001
Very severe (25–75)	129.50 (30.40–551.64)	< 0.001
GCS (vs mild, 13–15)		
Moderate (9–12)	5.58 (2.12–14.74)	0.001
Severe (3–8)	9.04 (4.64–17.62)	< 0.001
Blood transfusion (vs none)	26.90 (15.21–47.58)	< 0.001
Length of stay (per 1 d increase)	1.02 (1.01–1.02)	< 0.001
Age (vs 0–12)		
13–15	3.06 (1.14–8.21)	0.03
≥ 16	8.32 (3.98–17.40)	< 0.001
Risk Factor	**Adjusted OR (95% CI)**	***p***
Operation (vs none)	8.03 (2.64–24.40)	< 0.001
Penetrating trauma (vs nonpenetrating trauma)	0.66 (0.31–1.40)	0.3
ISS (vs mild, 0–8)		
Moderate (9–15)	4.15 (0.85–20.33)	0.08
Severe (16–24)	10.78 (2.26–51.33)	0.003
Very severe (25–75)	15.67 (3.26–75.39)	0.001
GCS (vs mild, 13–15)		
Moderate (9–12)	2.82 (0.98–8.08)	0.05
Severe (3–8)	2.37 (1.08–5.21)	0.03
Blood transfusion (vs none)	2.79 (1.36–5.74)	0.005
Length of stay (per 1 d increase)	1.01 (1.00–1.02)	0.005
Age (vs 0–12)		
13–15	3.81 (1.37–10.56)	0.01
≥ 16	5.22 (2.15–12.69)	< 0.001

OR = odds ratio, ISS = Injury Severity Score, GCS = Glasgow Coma Scale.

The regression equation is log-odds of venous thromboembolism = −9.93 + 2.08 × (operation) − 0.41 × (penetrating trauma) + 1.42 × (moderate ISS) + 2.38 × (severe ISS) + 2.75 × (very severe ISS) + 1.04 × (moderate GCS) + 0.86 × (severe GCS) + 1.03 × (blood transfusion) + 0.01 × (length of stay) + 1.34 × (age 13–15) + 1.65 × (age ≥ 16). The Hosmer–Lemeshow χ^2 statistic for multivariable model is 1.51 ($p = 0.98$).

(22%) received neither mechanical nor pharmacologic prophylaxis (Table 1). Among those who did receive pharmacologic prophylaxis, all were 11 years old or older; 18 were from the adult registry and only 3 were from the pediatric registry.

Risk Factor Analysis and Risk Assessment Model

We examined factors associated with VTE in the 17,366 patients entered in the Johns Hopkins Trauma Registry. Undergoing an operation and receiving a blood transfusion were identified as risk factors for VTE. In addition, patients assessed to be more severely injured (with an ISS ≥ 9 and/or Glasgow Coma Scale [GCS] ≤ 8) as well as those with longer hospital stay were at increased odds for developing a VTE (unadjusted odds ratios) (**Table 2**). After adjustment by multivariable logistic regression, each of these remained statistically significant independent risk factors for the development of VTE with trauma (adjusted odds ratios) (Table 2). Race and penetrating trauma were not independent risks by multivariable logistic regression analysis.

TABLE 3. Weighted Scoring Systems Based on Clinical Risk Factors to Predict Venous Thromboembolism in Pediatrics After Trauma

Clinical Factor	Adjusted ORs for Venous Thromboembolism		β-Coefficient[a]		Weighted Score (Rounded to Nearest Integer)	
	National Trauma Data Bank (2008–2010)[b]	Johns Hopkins Trauma Registry	Model 1	Model 2	Model 1	Model 2
Age (yr)						
0–12	[c]	[c]	[c]	[c]	0	0
13–15	2.0	3.8	0.65	0.64	2	1
16–21	3.8	5.2	1.31	1.36	4	2
Injury Severity Score						
0–8	[c]	[c]	[c]	[c]	0	0
9–15	4.0	4.2	1.59	1.71	5	5
16–24	5.9	10.8	1.59	1.71	5	5
25–75	7.2	15.7	2.21	2.59	7	7
Glasgow Coma Scale						
13–15	[c]	[c]	[c]	[c]	0	0
9–12	1.3	2.8	[c]	[c]	0	0
3–8	1.3	2.4	0.31	0.9	1	3
Blood transfusion						
No	[c]	[c]	[c]	[c]	0	0
Yes	1.5	2.8	0.51	0.61	2	1
Intubation						
No	[c]	NA	[c]	–	0	–
Yes	2.5	NA	1.25	–	4	–
Major surgery						
No	[c]	[c]	[c]	[c]	0	0
Yes	3.8	8.0	1.55	1.71	5	5

OR = odd ratio, NA = not available.

ORs rounded to nearest tenth of a decimal.

[a]From the regression equation for models with and without intubation.

[b]Reported from the study by Van Arendonk et al (3).

[c]Reference for ORs.

Regression equation for model 1: log-odds of venous thromboembolism (VTE) = −9.39 + 0.646 × (age 13–15) + 1.31 × (age 16–21) + 0.308 × (Glasgow Coma Scale [GCS]) + 1.59 × (Injury Severity Score [ISS] 9–24) + 2.21 × (ISS 25–75) + 0.51 × (blood transfusion) + 1.55 × (surgery) + 1.25 × (intubation); The *p* value for the Hosmer–Lemeshow for this multivariable model is $p = 0.0040$. Regression equation: model 2: log-odds of VTE = −9.42 + 0.636 × (age 13–15) + 1.36 × (age 16–21) + 0.9 × (GCS) + 1.71 × (ISS 9–24) + 2.59 × (ISS 25–75) + 0.61 × (blood transfusion) + 1.71 × (surgery); the *p* value for the Hosmer–Lemeshow for this multivariable model is $p = 0.0007$.

Dashes indicate data was not calculated for model 2.

A risk assessment model was developed based upon independent risk factors identified in this study and in the study by Van Arendonk et al (3) from 402,329 patients 21 years and younger in the NTDB from 2008 to 2010. In both the Johns Hopkins Trauma Registry and the 2008–2010 NTDB, increasing age, higher ISS, lower GCS, blood transfusions, and surgery were found to be independent risk factors for VTE. Non-white and non-black race was found to be a significant risk in the NTDB cohort, but not in the Johns Hopkins Trauma Registry, and was not used for modeling. Complete data on intubation were not available from the Johns Hopkins Trauma Registry, but intubation was identified as an independent risk for VTE in the 2008–2010 NTDB study and was incorporated in a separate model. In addition, increased length of stay was identified as a significant predictor of VTE in both the Johns Hopkins Trauma Registry and the 2008–2010 NTDB; however, since length of stay could not be determined until hospital discharge, it was not in this predictive model.

The 2008–2010 NTDB was used as a derivation cohort to develop VTE risk assessment model. In model 1, weighted scores were assigned based on the normalized β-coefficients for six individual risk factors (age, ISS, GCS, intubation, blood transfusion, and major surgery) obtained from logistic regression analysis of these factors (**Table 3**). Model 2 was developed using this set of factors without intubation. Three possible scores were assigned for ISS and for age and two possible scores for GCS, with higher scores given for older age, increasing ISS, and decreasing GCS. Patients receiving a blood transfusion or undergoing intubation or major surgery received a single weighted score. Using this scoring system, a total score (0–23 in model 1 and 0–19 in model 2) was derived for individual patients by summing the individual weighted scores.

To determine if the risk assessment scoring system identified patients at risk for VTE, we applied the two models to an independent cohort of 282,535 patients 21 years and younger in the NTDB over a 1 year period from 2011 to 2012. The demographics of this group is shown in **Table 4**; similar to the Johns Hopkins Trauma Registry, patients with VTE in the 2011–2012 NTDB were older than those without VTE. Males represented the majority of patients in both the Johns Hopkins Trauma Registry and 2011–2012 NTDB; however, black race was most common in the Johns Hopkins Trauma Registry compared with white race in the 2011–2012 NTDB. The overall prevalence of VTE in this 2011–2012 NTDB cohort was 0.41%, compared with 0.28% from the Johns Hopkins Trauma Registry. Patients with VTE had significantly higher scores than those without VTE using both models (17.3 vs 7.2 for model 1; $p < 0.0001$; 13.7 vs 5.8 for model 2; $p < 0.0001$). For both models, increasing score was associated with higher frequency of VTE (**Fig. 1**). In model 1, the maximum frequency of VTE was 9% in patients with a score of 22 out of 23. In model 2, the maximum frequency of VTE was 6% with the highest score of 19 of 19. Based on the ROC analysis, the best performing score which maximized the sum of sensitivity and specificity was 13 for model 1, with a sensitivity of 87% and a specificity of 81%. The area under the ROC curve for this model was 91% (0.911; 95% CI, 0.905–0.917) (**Fig. 2**). For model 2, the best performing score was 11, with a sensitivity of 86% and a specificity of 80%. The area under the ROC curve for model 2 was 90% (0.901; 95% CI, 0.894–0.907) (Fig. 2). Although the AUC was high for the derivation cohort, the *p* values for the Hosmer–Lemeshow test rejected the null hypothesis for goodness of fit ($p = 0.0040$ for model 1, $p = 0.0007$ for model 2). However, when the risk assessment models were cross-validated on the 2008–2010 NTDB, the area under the ROC curve remained high (Fig. 2). For model 1, the AUC was 91% (0.908; 95% CI, 0.900–0.916), and for model 2, it was 90% (0.897; 95% CI, 0.889–0.905). As the Johns Hopkins Registry did not have intubation data, we validated model 2 on this cohort. The area under the ROC curve was 93% (0.935; 95% CI, 0.906–0.963).

DISCUSSION

We identified older age, very severe ISS score, low GCS, surgery, and blood transfusion as independent risk factors for VTE from the Johns Hopkins Trauma Registry. These factors,

TABLE 4. Demographics of Johns Hopkins Trauma Registry and National Trauma Data Bank (2011–2012) Patients Less Than or Equal to 21 Years Old

	Johns Hopkins Trauma Registry		National Trauma Data Bank (2011–2012)	
Patient Demographics	VTE ($n = 49$)	No VTE ($n = 17,366$)	VTE ($n = 1,168$)	No VTE ($n = 281,248$)
Age (median years, SD)	18 (5.7)	11 (7)	19 (5)	14 (7)
Gender (%)				
Males	76	70	76	68
Race (%)				
Black	71	55	22	18
White	24	41	56	57
Other/unknown	4	4	21	25

VTE = venous thromboembolism.

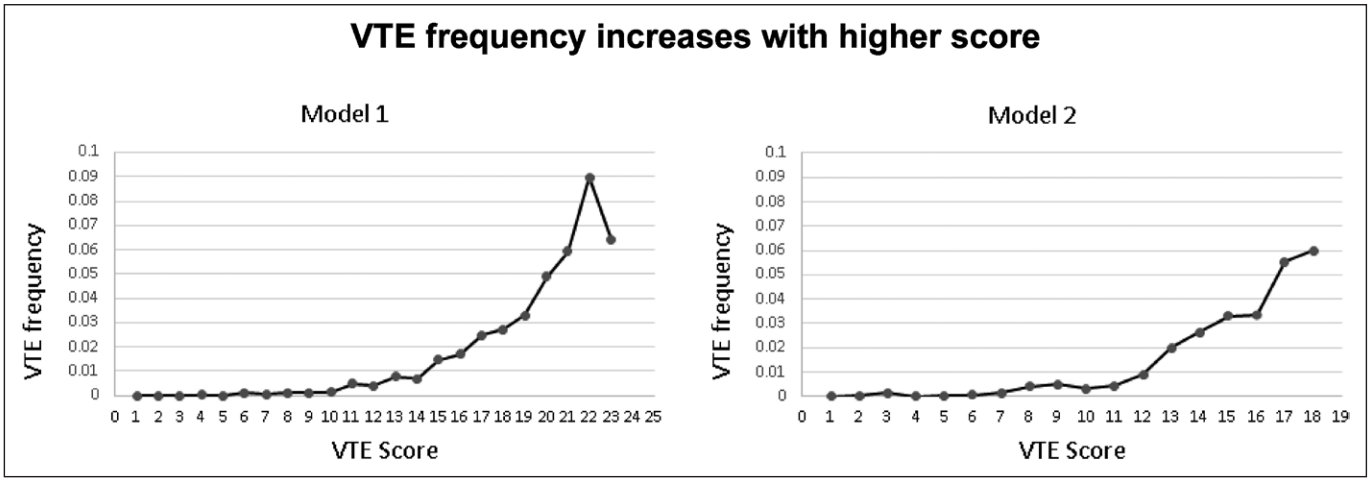

Figure 1. The frequency of venous thromboembolism (VTE) in pediatric patients with risk scores derived from the two risk assessment models. Model 1 incorporates six factors (age, Glasgow Coma Scale, Injury Severity Score, intubation, blood transfusion, and major surgery). Model 2 uses five factors from model 1 and does not incorporate intubation. Scores from the two models were applied to 402,329 pediatric patients less than or equal to 21 yr from the National Trauma Data Bank from 2008 to 2010.

in addition to intubation, were identified previously from the 2008–2010 NTDB (3); we incorporated these factors into a novel weighted risk assessment model. Using a score of 17 or above for model 1 and 13 or above for model 2, the prevalence of VTE was over 2%; this is a cutoff that has been suggested as threshold for implementation of VTE prophylaxis (16). These models performed well when it was validated in two independent cohorts: 1) the NTDB 2011–2012 with an AUC of 90–91% and 2) the Johns Hopkins Trauma Registry with an AUC of 93%. Although the AUC and cross-validation showed a good fit of these scores to the modeling and cross-validation datasets, the Hosmer–Lemeshow test, a test of goodness of fit, rejected the null hypotheses of the model fitting the data well. This may be mostly due to the fact that the large number of data points (> 36,000) were sensitive to small deviations of the data from the model, and hence this test was overpowered. Net reclassification indices may provide additional measures of the models' performance that can be considered in future studies.

The prevalence of VTE in trauma patients 21 years old and younger in this study was 0.28%. The prevalence of VTE in the derivation cohort was 0.41%; these frequencies are in the range of what has been reported in other studies (3, 5, 8–10, 13, 20–25). Many of the identified risk factors from our study have also been identified in other studies (5, 8–10, 20, 22, 25–27). In particular, older age, higher ISS, lower GCS, surgery, and blood transfusion have been reported as VTE risk factors in children and adults (2, 3, 5, 8–10, 20, 28). Hanson et al have implemented clinical guidelines that used some of the risk factors identified in this study to classify high-risk patients; these included older age (> 13 yr) and GCS less than 9. However, their guideline incorporated other risks that were not included in this model (12). These other risks (such as immobility and spinal cord injury) may also be important, but these data were not captured in the NTDB. Implementation of this guideline has decreased VTE prevalence in children with trauma at their institution, suggesting the benefit of risk stratification.

Connelly et al (20) have recently published a clinical prediction tool that was developed similarly by identification of risk factors from the NTDB; a weighted risk assessment model was developed based on these factors. Their analysis focused on younger patients (0–17 yr), but used all the factors that we used in our model 1 (age, GCS, ISS, intubation, blood transfusion, and surgery). Their best performing models incorporated an additional five to eight factors for assessment. The AUCs for their ROC curves ranged from 0.873 to 0.946, similar to that of our models. Their study, together with ours, confirms the clinical utility of the six core factors in a VTE risk assessment and provides compelling evidence to proceed with prospective trials incorporating these and other factors in assessment of risk for the development of VTE in pediatric patients after trauma.

A limitation is that the timing of blood transfusion and surgery in relation to the timing of VTE diagnosis were not available in the NTDB; thus, we could not assess if these were risks present prior to development of VTE. We chose to keep it in this predictive model since there are patients who will undergo surgeries or blood transfusions within the first day of admission, a window when the decision to implement VTE prophylaxis is made. CVCs have been associated with VTE in several studies (5, 8, 9, 20, 26); however, we found that the majority of trauma patients with VTE did not have CVC-associated VTEs. However, we did not have complete data for CVCs on all patients in our registry, so we were not able to assess it as a risk factor. It is also worth noting that although pelvic and femur fractures in adults are recognized as a risk factor for VTE, in our study we found that orthopedic injuries or blunt trauma were not independent risks for VTE in pediatric patients. Similarly, other studies in children with trauma did not demonstrate that pelvic and femoral fractures were significant risk factors for VTE (8, 29).

This study has additional limitations. Because the frequency of VTE is low in this population, we identified only 49 patients

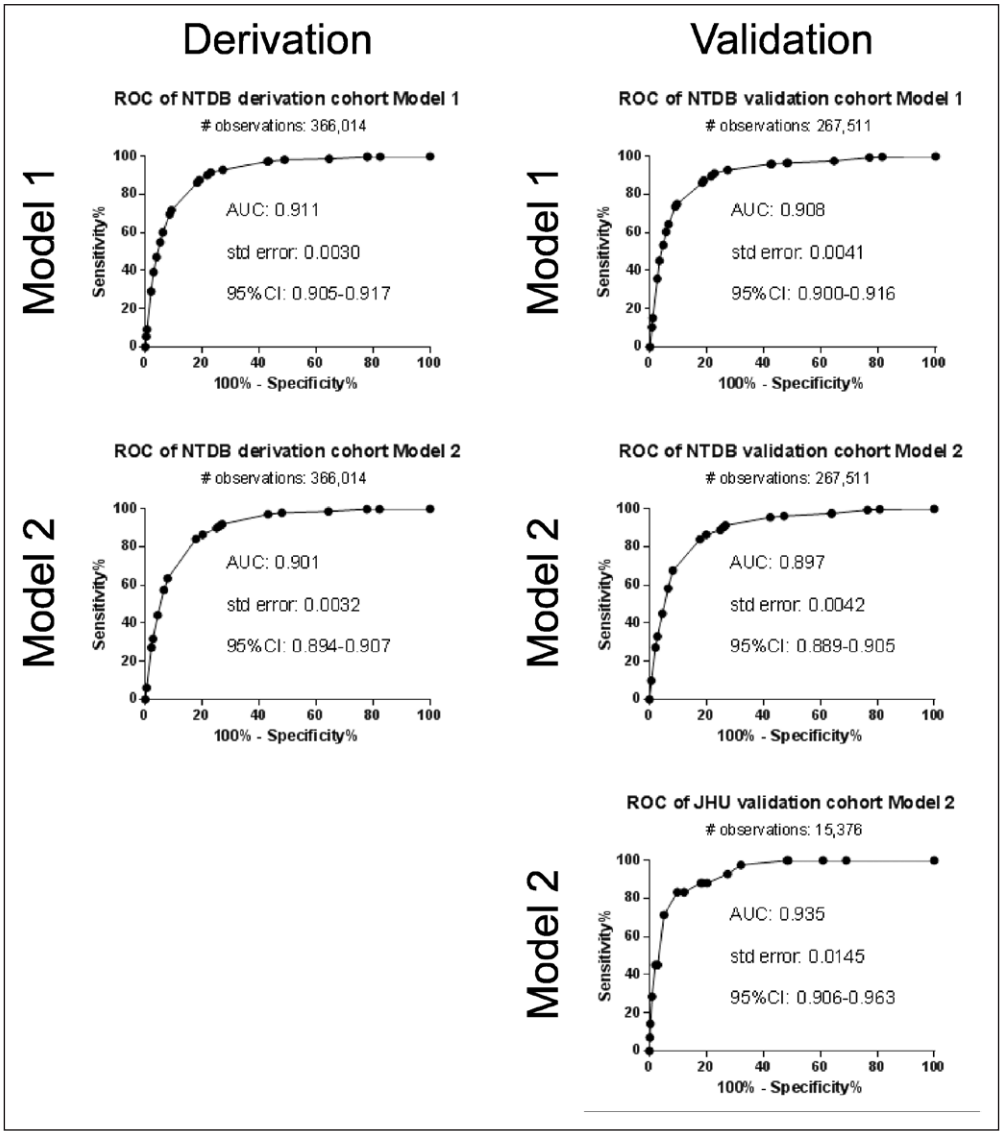

Figure 2. Receiver operating curves (ROCs) for risk assessment score. The two risk assessment models were developed by assigning weighted scores to independent risk factors for venous thromboembolism. The factors were identified from a derivation cohort of 402,329 patients in the National Trauma Data Bank (NTDB) from 2008 to 2010. The score was cross-validated by assessing the area under the curve (AUC) of ROCs for the two models on an independent cohort of 282,535 patients from the NTDB from 2011 to 2012 and 17,366 pediatric trauma patients from Johns Hopkins University.

with VTE in our trauma registry. We found variable prescribing practices of pharmacologic and mechanical prophylaxis in patients with VTE in our registry. Standardized VTE prophylaxis protocols are used by the adult trauma service (14, 30, 31); however, no formal guidelines were followed by the pediatric trauma service, contributing to the variable practice. In addition, the use of VTE prophylaxis was not routinely recorded in the Johns Hopkins trauma registries nor in the NTDB; thus, the development of VTE may be confounded by the use of VTE prophylaxis in this population. In our study, the majority of patients who developed VTE did not receive heparin prophylaxis, but data are not available for the entire cohort; thus we could not analyze it a risk factor and we cannot make any conclusions about the effectiveness of measures to prevent VTE after trauma in the Johns Hopkins Trauma Registry. The issue of surveillance bias must also be considered. It is well known that DVT events in trauma patients are often identified during screening duplex ultrasound in asymptomatic patients (2, 32–34). The adult trauma service has adopted institutional guidelines that suggest screening for VTE, whereas the pediatric trauma service does not, potentially leading to more events being identified on the adult service. The implementation of surveillance screening likely increased the rate of VTE diagnosis over the duration of this study. Another change in practice with unclear impact on VTE rate during the study period is the shift from use of UFH to LMWH for prophylaxis. Additional limitations were that patients who experienced VTE complications shortly after discharge might not have been documented in the registries either because the admission was not identified as being trauma related or the patient was readmitted to a different institution. Complete data on other putative risks such as CVCs, medications, infection, inflammatory conditions, or other medical conditions were also not available for all patients in the registries. However, despite these limitations, the study has a number of strengths. The risk factors identified for the scoring system are standardized. The dataset is large and robust, and common risk factors identified in both the Johns Hopkins Registry and the NTDB increased the strength of the associations.

CONCLUSIONS

The risk of VTE after pediatric trauma is generally low but older age, intubation, high ISS, low GCS, surgery, and blood transfusion increase risk. We have developed a weighted risk assessment scoring system called Risk of Clots in Kids in Trauma. The scores were validated in two large independent cohorts and demonstrated an increased prevalence of VTE with higher scores; it was sensitive and specific for the diagnosis of VTE. The model may

be useful to identify patients at high risk of VTE who may benefit from VTE prophylaxis. However, additional prospective trials are needed to determine the efficacy and safety of risk model–guided VTE prophylaxis in this patient population.

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