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Risk factors for venous thromboembolism after pediatric trauma☆,☆☆,★

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ABSTRACT

Background/purpose: The purposes of this study were to identify independent predictors of venous thromboembolism (VTE), to evaluate the relative impact of adult VTE risk factors, and to identify a pediatric population at high-risk for VTE after trauma.

Methods: 1934 consecutive pediatric admissions (≤17 years) from 01/2000 to 12/2012 at a level 1 trauma center were reviewed. Logistic regression was used to identify predictors of VTE.

Results: Twenty-two patients (1.2%) developed a VTE, including 5% of those requiring orthopedic surgery, 14% of those with major vascular injury (MVI), and 36% of those with both. Most (84%) were diagnosed at the primary site of injury. 86% of those who developed a VTE were receiving thromboprophylaxis at the time of diagnosis. Independent predictors were age (odds ratio (OR): 1.59, 95% confidence interval (CI): 1.11–2.25), orthopedic surgery (OR: 8.10, CI: 3.10–21.39), transfusion (OR: 3.37, CI: 1.26–8.99), and MVI (OR: 15.43, CI: 5.70–41.76). When known risk factors for VTE in adults were adjusted, significant factors were age ≥13 years (OR: 9.16, CI: 1.08–77.89), indwelling central venous catheter (OR: 4.41, CI: 1.31–14.82), orthopedic surgery (OR: 6.80, CI: 2.47–18.74), and MVI (OR: 14.41, CI: 4.60–45.13).

Conclusion: MVI and orthopedic surgery are synergistic predictors of pediatric VTE. Most children who developed a VTE were receiving thromboprophylaxis at the time of diagnosis.

Trauma remains the leading cause of morbidity and mortality in children and adolescents [1,2]. Although traumatic injury induces a state of hypercoagulability in both adult [3] and pediatric [4] patients, venous thromboembolism (VTE) rates are significantly lower in children [5–13] yet carry significant morbidity [14]. Although risk factors in the adult population are established [15–20], the factors leading to VTE in children are not clear. Therefore, the purposes of this study are to identify the independent predictors of VTE after pediatric trauma, to assess the relative impact of known risk factors for VTE in adult trauma on the pediatric population, and to identify a population at high-risk for VTE in children.

1. Methods

After approval from the University of Miami Miller School of Medicine Institutional Review Board, consecutive pediatric admissions (≤17 years old) from January 2000 to December 2012 at the Ryder Trauma Center in Miami, Florida were retrospectively reviewed. Those pregnant, incarcerated or not admitted to either the trauma or pediatric surgery services were excluded from analysis.

Demographics, mechanisms of injury (MOI), injuries sustained, interventions performed, initial vital signs and laboratory values, length of stay (LOS), and survival were reviewed. Hypotension and tachycardia were defined as any value outside of normal age-specific range for the child. Major vascular injury (MVI) was defined as any injury to a named vessel. Patient injuries and other diagnoses, including obesity, were identified with use of International Classification of Diseases, Ninth Revision (ICD-9) coding.

Adult risk factors for VTE included advanced age, obesity, head injury, MVI, indwelling central venous catheter (CVC), operation, orthopedic injury, spinal cord injury (SCI), pelvic fracture, and transfusion. An ISS >15 was used to define a patient who was "severely injured".

VTE is defined as either a deep vein thrombosis (DVT) or pulmonary embolism (PE). The diagnosis of DVT and PE was obtained from ICD-9 coding and confirmed upon review of physician notes and radiology reports. No routine surveillance for DVT was performed. Thromboprophylaxis was given at the physician's discretion, and the agent used was as per institutional standards and pharmacy formulary during the study period. As children >13 years of age are managed by the trauma surgery service at our institution, these patients typically receive thromboprophylaxis following injury, such as do the adult patients. Methods of

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thromboprophylaxis were reviewed and included low-dose unfractionated heparin (UFH; 5000 U subcutaneously three times daily) or low molecular weight heparin (LMWH; either dalteparin 5000 U subcutaneously once daily, or enoxaparin 30 mg subcutaneously once daily) as guided by the hospital formulary. In addition, sequential compression devices were used if not prohibited by plaster immobilizers or external fixators.

Statistical analyses were performed using SPSS version 22 (IBM Corporation; Armonk, NY). Parametric data are reported as mean ± standard deviation and nonparametric data are reported as median (interquartile range). Data were compared using a t-test or Mann–Whitney U test, as appropriate. Categorical variables were compared using a chi-square or Fisher's exact test, as appropriate. The results of the univariate analyses were used to include variables of significant association in a stepwise logistic regression model to identify the independent predictors of VTE. In addition, known risk factors for VTE in adults were included in a regression analysis to identify the adjusted risk factors in children. Statistical significance was determined at alpha level 0.05.

2. Results

The study population was composed of 1934 pediatric patients (Table 1). VTE developed in 1.2% (22/1934) of the overall population. LOS was 3[1–8] days, and mortality was 3.5%. VTE occurred in 5% of those requiring orthopedic surgery, 14% of those with MVI, and 36% of those with both. Most (84%) VTE were diagnosed at the primary site of injury compared to 16% at an uninjured site. Three patients (0.2%) developed a PE, yet none were concomitantly diagnosed with DVT (negative lower extremity venous duplex ultrasounds). Of those diagnosed with VTE, the majority was actively receiving thromboprophylaxis at time of diagnosis (86%). Methods of thromboprophylaxis included UFH (42%) and LMWH (58%).

Of those who developed a DVT, the majority (10/19) sustained MVI. Of those, two did not receive thromboprophylaxis, six received some form of thromboprophylaxis, and 2 were therapeutically anticoagulated. Most of the MVI were ligated, rather than repaired, owing to the complexity of the injury or hemodynamic instability at time of surgery.

Table 2 compares patients with VTE to those without. In general, VTE patients were older, had higher injury severity scores (ISS) and worse hemodynamics. They more often had MVI, required orthopedic surgery, and had longer LOS.

Variables of significant association (age, race, base excess, age-specific hypotension, tachycardia, ISS, operation, MVI, orthopedic surgery, CVC, transfusion) were included in a stepwise logistic regression model. Independent predictors of VTE were identified as age (odds ratio (OR): 1.59, 95% confidence interval (CI): 1.11–2.25), orthopedic surgery (OR: 8.10, CI: 3.10–21.39), transfusion (OR: 3.37, CI: 1.26–8.99), and MVI (OR: 15.43, CI: 5.70–41.76); area under receiver operator curve (AUROC): 0.939.

Known associated risk factors for adult VTE were included in a separate regression analysis. The significant adjusted risk factors were identified as age ≥13 years (OR: 9.16, CI: 1.08–77.89), indwelling CVC (OR: 4.41, CI: 1.31–14.82), orthopedic surgery (OR: 6.80, CI: 2.47–18.74), and MVI (OR: 14.41, CI: 4.60–45.13); AUROC: 0.962 (Fig. 1).

If DVTs at the primary site of injury were excluded, two patients had a CVC and DVT. Of these, one had a hemodialysis catheter placed after DVT was diagnosed, and the other patient had a right femoral CVC placed at admission and subsequently developed a DVT at the right common femoral vein.

When comparing risk factors of PE versus DVT, no associations were made probably due to small sample size. Still, those who developed a PE alone (no concomitant DVT) were all blunt trauma victims with hemodynamic instability at admission, required CVC, blood transfusions and operative intervention. Ultimately, their clinical course was prolonged (average LOS 29 d). None of the PE patients sustained MVI. All were actively receiving UFH at time of diagnosis, and, upon recognition, an inferior vena cava filter was placed.

3. Discussion

The major findings of the study are that MVI and orthopedic surgery are synergistic predictors of DVT; the vast majority of all DVT occurred at the primary site of injury; and the independent predictors of VTE after pediatric trauma population are age, orthopedic surgery, MVI, and transfusion. When adjusting for the known risk factors for VTE in adults, MVI and orthopedic surgery were the greatest risk factors in children. Most children (86%) who developed a VTE were receiving thromboprophylaxis at the time of diagnosis.

The incidence of VTE in the pediatric trauma population ranges from 0.02% to 0.33% [1–8] while the rate of VTE in the adult trauma population is 6% to 7% [21,22]. Thus, the risk of VTE varies with age. Van Arendonk et al. found that the risk of VTE was lower among younger

Table 1
Population demographics (n = 1934).

Age, years	11 ± 6
Male	70%
Black	50%
Hispanic	27%
White	23%
Blunt mechanism of injury	76%
Base excess, mEq/L	−3 ± 5
Hematocrit, %	37 ± 6
Hypotension	6%
Tachycardia	32%
Glasgow Coma Score	15 (14–15)
Intracranial hemorrhage	4%
Injury Severity Score	13 ± 12
Transfusion	11%
Operative intervention	22%
Major vascular injury	5%
Orthopedic surgery	13%
Deep vein thrombosis	1.0%
Pulmonary embolism	0.2%
Length of stay, days	3 (1–8)
Mortality	3.5%

Table 2
Comparison of non-VTE vs VTE patients (n = 1934).

	Non-VTE (n = 1912)	VTE (n = 22)	p-value
Age, years	11 ± 6	16 ± 1	<**0.001**
Male	70%	77%	0.495
			0.001
Black	50%	50%	
Hispanic	28%	18%	
White	23%	27%	
Other	0%	5%	
Blunt	76%	64%	0.209
Obesity	1%	5%	0.148
Base excess, mEq/L	−3 ± 5	−6 ± 5	**0.008**
Hematocrit, %	37 ± 5	35 ± 6	0.146
Age-specific hypotension	6%	29%	**0.001**
Age-specific tachycardia	31%	80%	**0.002**
Abnormal coagulation	2%	5%	0.392
Glasgow Coma Score	15 (14–15)	15 (13–15)	0.563
Intracranial hemorrhage	4%	0%	0.622
Injury Severity Score	13 ± 12	23 ± 15	<**0.001**
Central Venous Catheter	4%	36%	<**0.001**
Pelvic fracture	9%	14%	0.454
Spinal cord injury	3%	5%	0.490
Transfusion	10%	47%	<**0.001**
Operative intervention	22%	73%	<**0.001**
Major vascular injury	5%	64%	<**0.001**
Orthopedic surgery	13%	64%	<**0.001**
Length of stay, days	3 (1–7)	26 (14–42)	<**0.001**
Mortality	3.5%	9.1%	0.181