# Venous Thromboembolism in Patients With Blunt Trauma: Are Comprehensive Guidelines the Answer?

Keith Baldwin, MD, MPH, MSPT, Surena Namdari, MD, MSc, John L. Esterhai, MD, and Samir Mehta, MD

## Abstract

**Objectives:** This study was designed to determine the outcome of implemented guidelines for venous thromboembolism (VTE) prophylaxis.

**Methods:** This study was a retrospective review of a series of consecutive blunt orthopaedic trauma patients with thromboembolic complications. The patients were compared to controls over the same 10-year period. Univariate and multivariate statistical methods were used to determine the odds of VTE in the setting of this management guideline and risk factors for thromboembolic complications that may be refractory to this strategy.

**Results:** In the 10 years following institution of clinical management guidelines at our institution, the rate of VTE events was 3.2%, and the rate of pulmonary embolus was 0.3%. Risk factors for VTE that were refractory to our clinical management guidelines were pelvic fractures, major lower extremity injury, greater than 3 days of mechanical ventilation, increasing injury severity, and spinal cord injury.

**Conclusions:** The implementation of a clinical management strategy for decreasing the incidence of VTE in blunt trauma patients and other potentially preventable complications is essential. Our data suggest that patients with certain injuries are particularly at risk for VTE and warrant special attention in clinical management and risk stratification, despite effective clinical management guidelines.

The venous thromboembolic events (VTEs) that occur after orthopedic blunt trauma—including pulmonary embolisms (PEs) and deep vein thrombosis (DVT)—continue to be a serious problem in orthopedic and trauma surgery. PEs may be more common than recognized, with estimates in the United States ranging from 500,000 to 600,000 cases per year, resulting in up to 200,000 fatalities per year.[1] Some authors have reported that many cases go undiagnosed.[1] Patients with acute trauma and patients with little physiologic reserve may have a decreased capacity to survive the insult of a PE. Therefore, it is important to identify patients at risk for DVT and PE early.

Factors associated with increased risk for PE include pelvic fractures,[2] lower extremity fractures,[2,3] spinal cord injury,[2,4] age,[3] immobilization,[5,6] and Injury Severity Score (ISS).[3-6] However, previous series either have been insufficiently powered to draw conclusions or have incorporated multiple centers, with variable data collection and recording, to generate large sample sizes that lack consistency.[5]

The retrospective series reported here used a prospectively collected, single-institution database at a level I trauma center over a 10-year span to examine the risk factors for thromboembolic disease in patients with blunt trauma. In addition, since June 1996, our institution has approached VTEs according to a well-established clinical management guideline (CMG).[7] CMGs are a prophylactic and diagnostic strategy system. This study investigated VTE risk factors that persist despite established CMGs. We hypothesized that, though use of our CMG leads to low VTE rates, certain patient and injury characteristics may be refractory to this CMG.

## Materials and Methods

A power analysis for multiple logistic regression was calculated[8] assuming a difference in probability of a VTE for any given parameter of 20%. This analysis was conducted with a desired 2-sided $\alpha$ of .05 and a power of .80. Calculations demonstrated that a sample size of 188 patients would be necessary for logistic regression. For multiple regression analysis, our total sample size needed to be 376 patients (188 cases, 188 controls) for a balanced design. When appropriate, the level of significance was adjusted for multiple tests using the Bonferroni method.

This study protocol (80826) was reviewed and approved by the institutional review board at our hospital. We retrospectively reviewed our trauma database for patients admitted through the resuscitation bay between January 1, 1997 and December 31, 2007. Inclusion criteria for the VTE group (cases) included

Dr. Baldwin is Instructor B, PGY 5 resident, Dr. Namdari is Instructor B, PGY 4 resident, Dr. Esterhai is Professor, and Dr. Mehta is Assistant Professor and Chief of Orthopaedic Trauma and Fracture Service, Department of Orthopaedic Surgery, Hospital of the University of Pennsylvania, Philadelphia Pennsylvania.

Address correspondence to: Samir Mehta, MD, Department of Orthopaedic Surgery, 2nd Floor, Silverstein Building, Hospital of the University of Pennsylvania, 34th St & Spruce St, Philadelphia, PA 19104 (tel, 215-432-7432; fax, 215-349-5890; e-mail, samir.mehta@uphs.upenn.edu).

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**Table I. Differences in Characteristics Between Controls and Patients With Venous Thromboembolic Events**

| Variable | Group: Control | Group: VTE | *P* Value vs Control Group | PE Subgroup | *P* Value vs Control Group |
|---|---|---|---|---|---|
| Age, y | 46.05 | 48.54 | .196[b] | 32.13 | .002[a,b] |
| Sex, % female | 28.8 | 26.2 | .607[c] | 22.6 | .613[c] |
| Injury Severity Score | 14.82 | 26.82 | <.001[a,b] | 23.77 | .005[a,b] |
| Weight, kg | 81.20 | 83.09 | .370[b] | 88.22 | .066[b] |
| Ventilation, d | 2.17 | 13.22 | <.001[a,b] | 10.03 | .004[a,b] |
| Length of stay, d | 7.77 | 27.81 | <.001[a,b] | 24.68 | <.001[a,b] |
| Mortality, % | 3.5 | 10.3 | <.006[a,c] | 22.58 | <.001[a,c] |

Abbreviations: PE, pulmonary embolism; VTE, venous thromboembolic event.
[a]Statistically significant. [b]Independent-sample *t* test, equal variances not assumed. [c]$\chi^2$ test for independence with Yates correction.

blunt mechanism of injury and diagnosis of DVT or PE during hospital stay. Exclusion criteria included discharge directly from resuscitation bay, missing crucial data points, and lack of confirmation of diagnosis of DVT or PE. In our database, DVT is defined as an acute, occlusive thrombus documented by Doppler, ultrasound, venogram, impedance plethysmography, or autopsy, and PE is defined as a documented positive study on pulmonary arteriography, or post mortem examination, or treatment initiated on the basis of radionucleotide scanning, or spiral computed tomography (CT).[7] Patients during this period were subject to routine DVT prophylaxis as outlined in the CMG (Figure 1).[7] VTEs were identified by the screening protocols outlined or by screening based on clinical suspicion. Frankel and colleagues[7] found the rate of adherence to the CMG to be 74%. The intent-to-treat model was used in terms of adherence to the CMG.

During the study period, 10,268 patients were admitted through the resuscitation bay. Of these patients, 324 had VTEs and 31 had PEs. Of the 324 patients with VTEs, 233 met the inclusion criteria (Figure 2). Of the 233 patients included, 202 had a DVT only, 20 had a PE only, and 11 had both. Only VTEs that occurred during acute hospitalization were listed in the database.

We obtained control patients by searching the database of consecutive blunt trauma patients admitted to our institution during the same period and then eliminated those who were missing crucial data points. We identified 4706 potential controls. As we wanted to compare VTE patients with "average" trauma patients to determine which were at higher risk for these events, we randomly selected and did not match controls. To

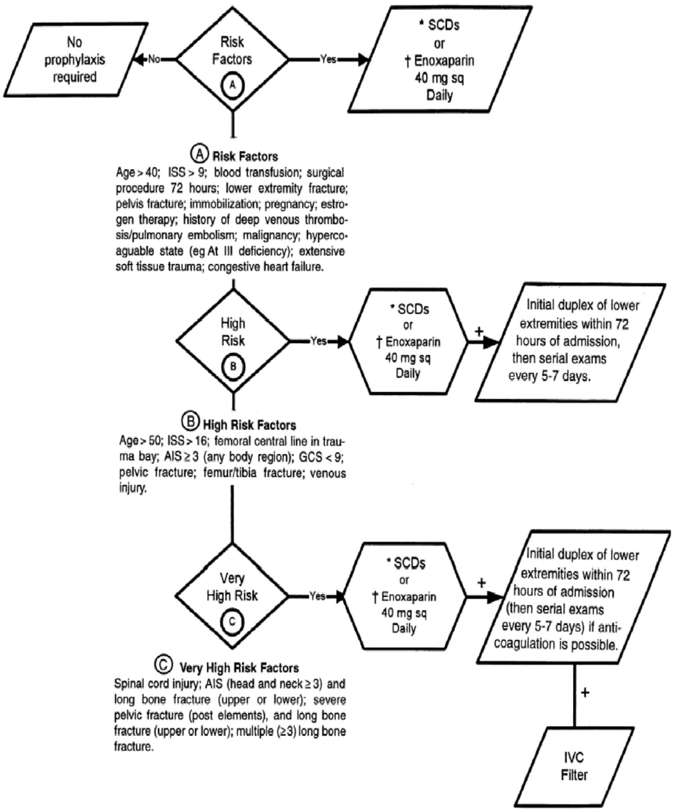


**Figure 1.** Hospital of the University of Pennsylvania deep venous thrombosis prophylaxis clinical practice guidelines as described by Frankel and colleagues.[7] *Sequential compression devices are used when one or both lower extremities are accessible. †Excluded or contraindicated in patients with epidural catheters. AIS, Apache Injury Score; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; IVC, inferior vena cava; SCD, sequential compression device.[8] Reprinted from *Journal of the American College of Surgeons,* 189(6), Strategies to improve compliance with evidence-based clinical management guidelines, p. 6, © 1999, with permission from Elsevier.

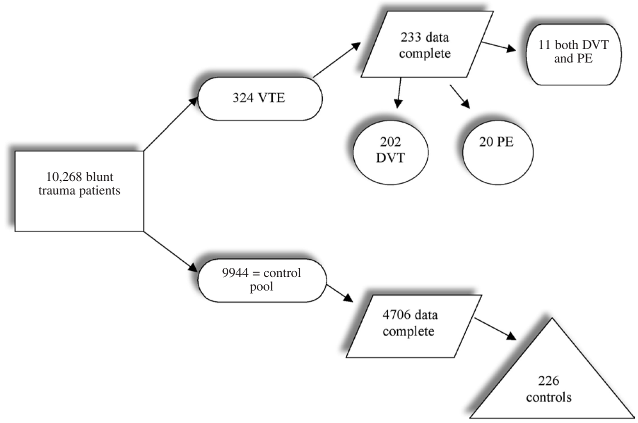


**Figure 2.** Patient selection diagram. Controls were selected by chronologically selecting every 20th patient to achieve a random sample.

**Table II.** Percentage Chance of Finding Given Injury Pattern in Each Cohort of Patients

| Variable | Group, % Control | VTE | *P* Value[a] vs Control Group | PE Subgroup, % | *P* Value[a] vs Control Group |
|---|---|---|---|---|---|
| Pelvic ring injury | 9.7 | 25.8 | <.0001[b,d] | 19.4 | .124[c] |
| Major lower extremity skeletal injury | 25.2 | 30.5 | .233 | 32.3 | .523 |
| Minor lower extremity skeletal injury | 8.8 | 9.9 | .851 | 3.2 | .487[c] |
| Major upper extremity skeletal injury | 8.8 | 13.7 | .110 | 6.5 | 1.000[c] |
| Minor upper extremity skeletal injury | 13.7 | 16.7 | .417 | 16.1 | .782[c] |
| Spine fracture | 13.7 | 29.6 | <.0001[b,d] | 41.9 | .0002[b,d] |
| Spinal cord injury | 2.2 | 8.6 | .0018[b,c,d] | 16.1 | .0026[b,c,d] |
| Major head injury | 25.2 | 46.8 | <.0001[b,d] | 32.3 | .525 |
| Major thoracic injury | 17.7 | 33.5 | .0002[b,d] | 29.0 | .215 |
| Minor thoracic injury | 10.6 | 13.7 | .3775 | 12.9 | .758[c] |
| Abdominal injury | 14.6 | 17.6 | .449 | 22.6 | .374 |

Abbreviations: PE, pulmonary embolism; VTE, venous thromboembolic event.
[a]Calculated with 2-tailed $\chi^2$ test for independence with Yates correction, except where otherwise noted. [b]Statistically significant based on *z* approximation. [c]Calculated with 2-tailed Fisher exact test. [d]Statistically significant after Bonferroni correction (threshold *P* = .00417).

**Table III.** Multiple Logistic Regression Analysis of Risk Factors for Venous Thromboembolic Events

| Variable | OR | 95% CI | *P* Value[a] |
|---|---|---|---|
| Ventilation, >3 d | 8.151 | 4.634-14.337 | <.001 |
| Injury Severity Score (continuous) | 1.038 | 1.016- 1.059 | .001 |
| Spinal cord injury | 4.299 | 1.366-13.524 | .013 |
| Major lower extremity bony trauma | 1.826 | 1.090- 3.058 | .022 |
| Pelvic ring injury | 3.623 | 1.929- 6.803 | <.001 |

Abbreviations: CI, confidence interval; OR, odds ratio.
[a]All *P* values were statistically significant.

obtain 226 unique random patients, we selected every 20th patient (by admission date) as a control (Figure 2).

Data that other investigators have found to be important (ISS, age, injury types, days on mechanical ventilation) were included in the database. In addition, we wanted to investigate body mass index as a potential risk factor, but, because height was not consistently included, we considered weight only.

Individual injuries were not considered, but classes of injuries were. Given the method for scoring injury severity, this decision regarding injury classification conferred a more accurate representation of the data and provided smaller variability. Pelvic ring injuries were any bony injuries about the pelvis, sacrum, or acetabulum. Major lower extremity skeletal injuries were any fractures of the femur or tibia, including pilon fractures, open ankle fractures, hip or knee dislocations, ankle fracture-dislocations, and traumatic amputations. Major upper extremity skeletal injuries were shoulder or elbow fractures or dislocations, forearm shaft fractures, traumatic amputations, and open wrist fractures. Minor upper or lower extremity skeletal injuries were closed hand or foot fractures, minor distal radius or ankle fractures, and clavicle fractures. Spine fractures or dislocations were all bony injuries to the spinal column, except the sacrum. Major head injuries were subdural or epidural hematomas, subarachnoid or intraventricular bleeds, pneumocephalus, and depressed skull fractures. Minor head injuries were concussions and brief losses of consciousness. Major thoracic injuries were any aortic or cardiac injuries, major pneumothorax or hemothorax, fractures of 3 or more ribs, and scapula fractures. Minor thoracic injuries were minor pulmonary contusions and fractures of 1 or 2 ribs.

Descriptive statistics, odds ratios (ORs), and logistic regression were calculated with SPSS processor version 15.0 (SPSS Inc, Chicago, Illinois).

## Results

We analyzed 233 patients with VTEs and 226 control patients with orthopedic blunt trauma without VTEs. Of the VTE patients, 31 had PEs. The overall incidence rate for VTEs (DVT or PE) was 3.2% (324/10,268), and the overall incidence rate for PE in the blunt trauma population was 0.3% (31/10,268). Of the VTE patients, 233 had sufficient data for analysis. There was no significant difference in age between VTE patients and control patients. PE patients, specifically, were significantly (*P* = .002) younger than controls, however. There were no significant sex differences between groups. Compared with control patients, VTE patients (*P*<.001) and PE patients (*P*<.005) tended to have more severe injuries. There was no statistical difference between groups in terms of weight, though there was a trend (*P* = .066) toward PE patients having a higher body weight. Patients with VTEs (*P*<.001) and, more specifically,

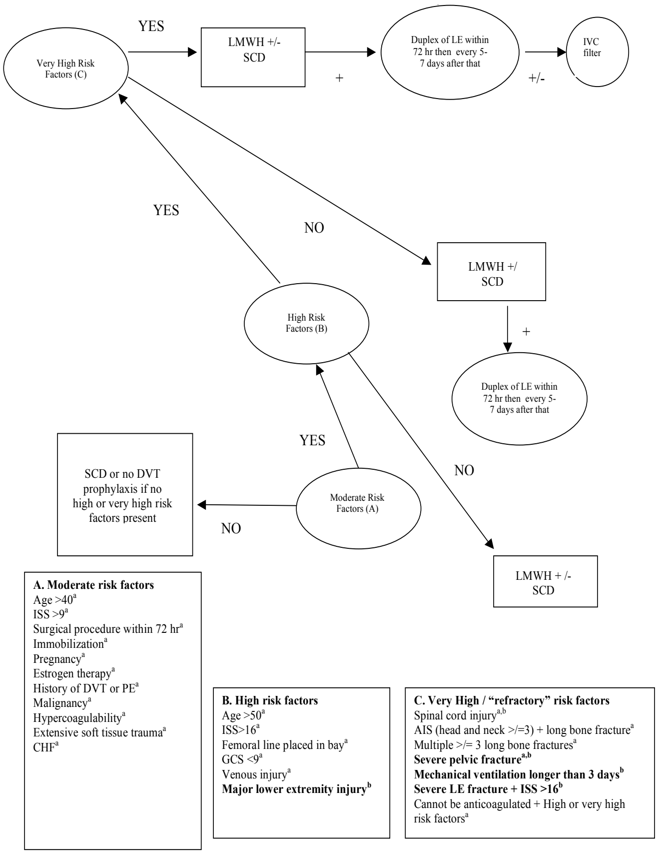


**Figure 3.** Adjusted venous thromboembolic event prophylaxis: proposed model for trauma patients. [a]Based on Eastern Association for the Surgery of Trauma (EAST) 1998 guidelines and 2001 update. [b]Refractory risk factor based on present study. Low-molecular-weight heparin (LMWH) is used unless contraindicated. AIS, Abbreviated Injury Score; CHF, congestive heart failure; DVT, deep vein thrombosis; GCS, Glasgow Coma Score; IVC, inferior vena cava; ISS, Injury Severity Score; LE, lower extremity; PE, pulmonary embolism; SCD, sequential compression device.

patients with PEs ($P$ = .004), were placed on ventilation longer than patients without these complications. Length of stay was also affected by VTEs. All VTE patients and the subgroup of PE patients stayed in the hospital significantly ($P$s<.001) longer than control patients. Mortality was significantly higher in the VTE group ($P$ = .006) and in the PE subgroup ($P$<.001) than in the control group. Table I summarizes these data.

Table II summarizes the incidence of different injuries within the subgroups analyzed. Compared with controls, PE patients had significantly higher rates of spine fractures (13.7% vs 41.9%; $P$<.0002) and spinal cord injuries (2.2% vs 16.1%; $P$ = .0026). Compared with controls, patients with DVT and all VTE patients had higher rates of pelvic ring injuries, spine fractures, spinal cord injury, major head injuries, and major thoracic trauma.

ISS was significantly higher in the VTE cohort than in the controls, so we calculated raw ORs as well as ORs adjusted for ISS. After ISS adjustment, patients with pelvic ring injuries had a 2.5 times higher chance of developing a VTE ($P$ = .002), and patients with major lower extremity injuries had a 1.6 times higher chance ($P$ = .04). Major lower extremity injuries were not significant after correction for multiple tests. When specifically evaluating risk for PE, only patients with bony injuries about the spine (OR, 3.4; $P$ = .005) and patients with spinal cord injuries (OR, 5.4; $P$ = .019) were at significantly increased risk for PE after adjusting for ISS when compared with controls.

ISS higher than 15 and ventilation longer than 3 days were the only noninjury patient characteristics that were significant risk factors for VTEs (4.9 times and 11.4 times, respectively; $P$s<.001) and PEs (3.2 times and 7.2 times, respectively; $P$s<.005) after correction for multiple tests. Age, sex, body weight, and medical comorbidity (cardiac, vascular disease, diabetes, hypertension, cancer) were not significant risk factors after adjusting for multiple tests.

Factors available in our data set that had been identified in other series as increasing the risk for VTEs or PEs, along with factors identified during the course of this study, were selected for inclusion in our multiple logistic regression model. Only ventilation longer than 3 days (adjusted OR, 8.2; $P$<.001), ISS (adjusted OR, 1.04 for each level of ISS; $P$ = .001), spinal cord injuries (adjusted OR, 4.3; $P$ = .013), major lower extremity trauma (adjusted OR, 1.8; $P$ = .022), and pelvic ring injuries (OR, 3.6; $P$<.001) were found to be significant risk factors for VTEs (Table III). Post hoc diagnostics demonstrated that the model fit the data well. The regression model correctly predicted VTEs in 72.5% of cases.

## Discussion

VTEs in patients with blunt trauma are a complicated problem. In the past, clinical pathways were developed to identify patients at increased risk for VTEs. We conducted the present study to assess the efficacy of a clinical management strategy for decreasing VTEs and to identify risk factors that, despite CMG use, conferred increased risk for VTEs in patients with blunt orthopedic trauma.

Previous investigators have studied injury patterns associated with PEs. Higher risk for PEs has been associated with several factors, including thoracic injuries, lower leg/femur fractures, pelvic ring injuries,[2] age over 55 years, and higher ISS.[3] Azu and colleagues[4] found a 0.49% rate of PEs at trauma centers. Risk factors associated with VTE include age over 40 years, ISS higher than 15, need for surgical procedures, spinal cord injuries, lower extremity fractures (Apache Injury Score, ≥3), head injuries (Apache Injury Score, ≥3), ventilation longer than 3 days, rigid immobilization, non–weight-bearing, and thoracic injuries.[4-6]

In 1996, a DVT/PE prophylaxis CMG was initiated at our institution.[7] Patients listed in the trauma database after that year (including all the cases and controls) were subject to that algorithm. The Eastern Association for the Surgery of Trauma (EAST) has published a variety of CMGs based on original research and meta-analyses of the literature.[9] The guideline for managing VTE was published in 1998 and updated in 2001.[9] This meta-analysis concluded that spine injuries were the only consistently "high" risk factors for VTEs. ISS and blood transfusion seemed to confer higher risk in single-institution studies but were of marginal significance on meta-analysis.[9] Traditional risk factors, such as long bone fractures, pelvic fractures, and head injuries were not of major significance in that study.[9] Nevertheless, many studies have found ISS,[3,4,6,10,11] pelvic fractures,[2,12-14] and lower extremity trauma[2-5,11-16] to be major risk factors for VTEs. However, VTE prophylaxis has varied widely in these studies.[10,11,13,14,16,17] We are not aware of any other study in which patients were examined over a 10-year period and a comprehensive CMG for VTE prophylaxis was operational.

Our study found that trauma patients who develop VTEs tend to be more severely injured. The patients at higher risk in our study represent a group of patients who failed systematic prophylaxis by CMG. The risk factors that were found to be significant on multivariate analysis were ventilation longer than 3 days, spinal cord injury, pelvic ring injury, major lower extremity trauma, and higher ISS. We propose a new algorithm based on this study and the existing EAST guidelines (Figure 3).

Strengths of this study include use of single-institution data collected and maintained across the study period. As a CMG for VTE prophylaxis was used throughout the period from which patients were selected, we can say that the risk factors identified were refractory to a clinical management strategy. In addition, classification of injuries by body region, and as either major or minor, vastly simplifies application of the findings of this study. Weaknesses are that the study was retrospective and that certain data points, including height, readmissions, long-term follow-up, and VTEs that occurred after discharge, were not obtainable. Therefore, we were not able to investigate some of the risk factors that were considered high or very high risk factors in other studies.

In our series, patients with spinal cord injuries, pelvic fractures, major lower extremity fractures, higher injury severity, and longer ventilation tended to be at higher risk for refractory VTEs. The data from this series indicate that the relationship between lower extremity injuries and VTEs is not simple. There was no significant relationship between VTEs and lower extremity injuries when these injuries were examined in isolation. However, multiple logistic regression found lower extremity injuries to be a significant risk factor. This suggests that, when a major lower extremity injury is present in a more severely injured patient, higher risk is conferred. Only injuries involving the spine were risk factors for PEs—a finding consistent with those of the EAST group.

Although we studied a reasonably large population of patients at a single institution over a long period, it seemed that, on the basis of logistic regression analysis, not all the data variability could be explained by our independent variables. Perhaps unrecognized heritable factors or some of the limits of our retrospective study contributed to the unseen portion of data variability—those patients who would have developed VTEs or PEs despite our use of a revised algorithm. We have made recommendations to change the guidelines to incorporate some of the "refractory" risk factors in the high and very high risk categories.

## Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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