Factors Associated with Pulmonary Embolism Within 72 Hours of Admission after Trauma: A Multicenter Study

Jamie J Coleman, MD, Ben L Zarzaur, MD, MPH, FACS, Chad W Katona, MD, Zachary J Plummer, BS, Laura S Johnson, MD, FACS, Alison Fecher, MD, FACS, Jamie M O'Rear, BS, David V Feliciano, MD, FACS, Grace S Rozycki, MD, MBA, FACS

BACKGROUND: Recent studies using thromboelastography indicate that patients are at risk for hypercoagulability early after injury. Pulmonary embolism (PE) is also well known to cause significant morbidity and mortality after injury and can occur within 72 hours of admission (early PE). Despite this risk, prophylactic anticoagulation is often delayed in patients with certain injuries due to concerns about bleeding.

STUDY DESIGN: This was a retrospective study of injured patients with a PE from 2007 to 2013 at 3 level I trauma centers. Data collected included patient demographics, injury patterns, length of stay, timing of prophylaxis for deep vein thrombosis (DVT), and diagnosis of PE. Patients with early PE ($\leq$3 days) were compared with those with late PE ($>$3 days) using bivariate and multivariable analysis.

RESULTS: A total of 54,964 patients were admitted to the 3 centers during the study period, and 144 (0.26%) were diagnosed with a PE. Eleven were excluded from the study due to a lack of critical data, leaving 133 patients (43% early PE). Factors associated with early PE included long bone fractures in the lower extremity and an Abbreviated Injury Score (AIS) Extremity $\geq$3. Higher Injury Severity Score, severe chest and head trauma (AIS $\geq$ 3), and not receiving DVT prophylaxis within 48 hours of hospital admission were not associated with early PE.

CONCLUSIONS: Early PE is a significant clinical entity occurring in nearly half the patients who suffered a PE. Early PE is associated with long bone fractures and severe extremity trauma, but not severe thoracic injury. Timing of prophylactic anticoagulation had no impact on early PE. If further studies confirm this incidence of unsuspected early PE, all admitted trauma patients should be assessed for a hypercoagulable state after injury. (J Am Coll Surg 2015;220:731−736. © 2015 by the American College of Surgeons)

Although pulmonary embolism (PE) occurs infrequently after injury, it is associated with serious complications and high mortality rates.[1-4] Prophylactic anticoagulation can lower the incidence of deep vein thrombosis (DVT) and PE, but may increase the risk of bleeding in injured patients. In high volume trauma centers, routine screening for DVT is appropriate even in asymptomatic patients, but limited resources often restrict this screening to "high risk" patients.[5,6] To further complicate the issues of DVT/PE in injured patients, there is emerging evidence that a transient hypercoagulable state due to the increased generation of thrombin and fibrin occurs soon after injury.[7,8] These data lend credence to recent literature demonstrating that a PE may occur within the first 3 days after injury.[9-13]

In recognition of early hypercoagulability and formation of PEs relatively soon after hospital admission, preventability of these early PEs is questioned, even when using prophylaxis regimens. In the face of increasing focus on patient safety, pay-for-performance, and hospital profiling, determination of whether or not a complication is preventable carries significant weight. Considering all of these factors, it would be important to determine which patient factors are associated with development of an early PE. Once known, these factors could lead to earlier recognition and, possibly, prevention of DVT and associated PE. In addition, if early PE can be clearly identified as a separate, nonpreventable clinical entity from late PE, this could strongly affect hospital reporting of adverse events and, potentially, reimbursement.

The purpose of this study was to determine characteristics of injured patients who developed a PE within 3 days of hospital admission, and whether these patients had significant differences when compared with those who developed a PE after 3 days of hospitalization. We hypothesized that patients who developed pulmonary emboli in the first 3 days of hospitalization were more likely to have an Injury Severity Score (ISS) $\geq$ 15, long bone fractures, traumatic brain injuries, and/or experienced a delay in the initiation of prophylaxis against DVT.

METHODS

Site investigators from 3 American College of Surgeons-verified level I trauma centers were recruited to participate in this multi-institutional study. Two of the trauma centers were affiliated with Indiana University (Indiana University Health Methodist Hospital and Eskenazi Health Hospital), Indianapolis, IN, and 1 was located in the District of Columbia (MedStar Washington Hospital Center). Collectively, these trauma centers admit more than 7,000 injured patients annually. After each location obtained approval from the local institutional review board, trauma registry data for all patients admitted to these hospitals from 2007 to 2013 were reviewed for inclusion into the study. Patients were included in the study if they were 17 years of age or older and diagnosed with a PE, as determined by ICD-9 code 415.1. Patients who suffered heat exhaustion, hypothermia, or bites/stings were excluded from the study.
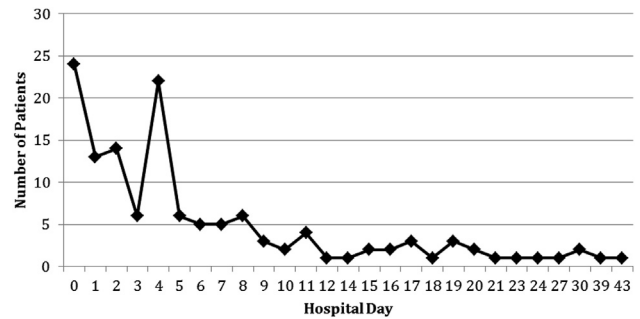

Figure 1. Time to pulmonary embolism in hospital days.

The following data were collected from the trauma registry and from chart review at each institution: patient demographics, Injury Severity Score (ISS), Abbreviated Injury Scale scores (AIS), use and timing of DVT prophylaxis, timing and method of diagnosis of PE, use of general anesthesia, timing and amount of blood transfused, presence of femoral arterial and venous lines, length of hospital stay, discharge disposition, and patient outcomes. All patients were followed throughout hospitalization. For this study, we defined an "early PE" as one that was diagnosed within the first 3 days of the patient's hospital admission. "Late PE" was defined as a PE that occurred on or later than hospital day 4.

The main outcomes measures for the study were the incidence of early PE and associated risk factors. Continuous variables are reported as medians and interquartile ranges (IQR). Categorical variables are reported as proportions. Univariate analysis was used to determine which variables were associated with early PE. Variables with p < 0.20 on univariate analysis were eligible for inclusion in a multivariable model. Using a backward selection approach, variables with a p < 0.05 were eligible for inclusion in the final multivariable model. SPSS 22 was used for all data analysis.

RESULTS

During the 2007 to 2013 study period, a total of 54,964 patients were admitted to the three participating level I trauma centers. The majority (89.5%) of patients sustained a blunt mechanism of injury, were male (69.9%), had a median age of 50 years (IQR 37.5 to 62.5 years), and a median ISS of 19 (IQR 10 to 29). There were 133 patients (0.24%) diagnosed with a PE, with a median time from admission to diagnosis of 4 hospital days (IQR 1 to 8 days). The diagnosis of PE was made using CT of the chest in almost all (98%) patients. Of the 133 patients diagnosed with a PE, 54 (40.6%) were diagnosed with a DVT during hospitalization and almost half of these (48%) were diagnosed with a DVT after the diagnosis