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Early pulmonary embolism after injury: A different clinical entity?

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ABSTRACT

Background: We sought to characterize pulmonary embolism (PE) occurring early after injury. We hypothesized that early PE may represent a different clinical entity than those occurring later in the post-injury period.
Methods: All trauma patients diagnosed with PE from 2005 to 2010 were examined. PEs diagnosed within 72 h of admission were compared against those occurring later.
Results: 19 out of 54 PEs were diagnosed early. Early PE patients had a higher rate of lower extremity fractures, a lower mean injury severity score, and a lower average length of stay. Early PE patients had a shorter average time to start of chemical prophylaxis, were less likely to have had a femoral line, and less likely to have operative intervention under general anaesthesia.
Conclusions: Early PE after trauma may occur with different underlying pathophysiology than previously thought. Further study is indicated as this has implications concerning the prevention of PE in trauma patients.

Introduction

Pulmonary embolism (PE) among trauma patients is relatively uncommon, but carries a significant risk of morbidity and mortality.[1–3] Classical teaching would suggest that most PEs occur as a result of deep venous thromboses (DVT) in the lower extremities or pelvis that form and eventually embolize to the pulmonary circulation. Importantly, this suggests that there is an interval during which the formation of DVT and eventual PE may be prevented through the use of appropriate prophylaxis. However, this must be balanced by the association of anticoagulant prophylactic therapy with increased bleeding complications.[4–7] Bleeding concerns often lead to a significant delay in the start of chemical venous thromboembolism (VTE) prophylaxis, often >72 h among patients with traumatic brain injury, solid organ injury, etc. Adding to the complexity is the fact that recent literature has demonstrated that many PEs present very early in the post-traumatic period.[8–11] Further, there is suggestion that some PEs may occur as a result of unknown biochemical processes and may not even originate in the peripheral veins.[8,12] These concepts have profound implications for clinicians trying to determine optimal and safe strategies for VTE prophylaxis among trauma patients.

The purpose of this study was to examine the timing of pulmonary embolism among trauma patients, specifically looking at those patients diagnosed with PE within 72 h of admission. We had hoped to identify patient characteristics and risk factors specific for the development of early pulmonary embolism. If specific patients at risk for early PE could be identified, more informed decisions regarding prophylaxis could be made. We had additionally hypothesized that some patients with early pulmonary embolism may have a different underlying pathophysiology as a cause for their PE (see Fig. 1).

Methods

This study was conducted at the Hospital of the University of Pennsylvania, state-accredited level 1 urban trauma centre. After obtaining institutional review board approval, we performed a retrospective review of the trauma registry for all patients admitted to the trauma service over a 5 year period from January 2005 until January 2010 with a diagnosis of pulmonary embolism. The diagnosis of PE was made via helical computed tomography, ventilation perfusion scanning, or autopsy findings. There were no specific exclusion criteria.

Patient age, body mass index (BMI), injury severity score (ISS), hospital length of stay (LOS), type of chemical prophylaxis used (subcutaneous un-fractionated heparin (UH) vs. low-molecular-weight heparin (LWMH)), days until start of chemical prophylaxis, presence of a femoral venous line, operative interventions requiring

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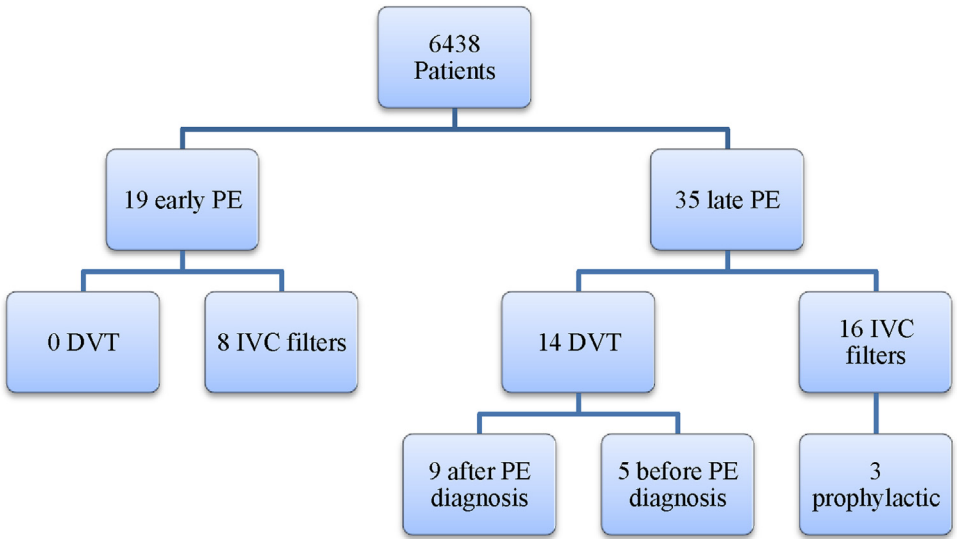

Fig. 1. DVT and IVC filter rates among PE patients.

general anaesthesia, venous duplex scan results, and the use of blood transfusion during the first 72 h were recorded for all patients. In addition, injury characteristics such as the presence of head injury, spinal cord injury (SCI), lower extremity fracture, chest injury, or pelvic fracture were recorded.

Patients who were diagnosed with a PE within 72 h of admission were classified as having "early" PE and were compared with those who were diagnosed with PE later in their hospital course. Univariate statistical analysis of categorical variables was performed using Fisher's exact test. Qualitative variables were analyzed using the Wilcoxon test. Multivariable logistic regression analysis was then used to identify factors independently associated with early PE using a forward step-wise approach. A *P* value less than 0.05 was considered statistically significant for all analyses.

Venous thrombo-embolism prophylaxis during the time period analyzed followed specific clinical practice guidelines.[13] Intermittent Pneumatic Compression (IPC) stockings were utilized in all patients unless contraindicated by lower extremity injuries. Pharmacologic prophylaxis was considered standard therapy for all trauma patients. However, the timing of initiation of pharmacologic prophylaxis was at the discretion of the trauma team and depended highly on bleeding risk and injury patterns. Trauma patients received pharmacologic prophylaxis in the form of enoxaparin at a standard dose (30 mg subcutaneously, twice daily). Patients with diminished renal function (creatinine clearance < 30 cc/min) were given unfractioned heparin (UFH) at a dose of 5000 units subcutaneously every 8 h. UFH was also considered for patients at the extremes of weight (<50 kg or > 150 kg) and at the discretion of the trauma team. Duplex ultrasonography was used to screen for DVT among trauma patients with a length of stay greater than 3 days. Patients would receive weekly duplex exams until 3 successive negative results were recorded. Prophylactic vena cava filter insertion was utilized in patients with 3 or more long bone fractures, pelvic fracture with one or more associated long bone fractures, or spinal cord injury (any level).

Results

There were a total of 6483 patients included in the registry search. Among these patients, 54 (0.83%) were diagnosed with a pulmonary embolism. 19 patients (35%) were diagnosed with PE within 72 h following injury. 2 of these patients were diagnosed with PE on imaging as part of their initial trauma evaluation. Univariate analysis of these two groups demonstrated several significant differences between the two groups. Early PE patients were less likely to have had a femoral line, less likely to have suffered a traumatic brain injury (TBI), and more likely to have lower extremity orthopaedic injuries. In addition, early PE patients had a lower average LOS, ISS, and less of a delay in the start of chemical prophylaxis. There were no differences seen in age, BMI, requirement of a blood transfusion, or type of chemical prophylaxis used. There were also no differences seen in the presence of spinal cord injury, pelvic fracture, or chest injury. These results are summarized in Table 1.

There were five in-hospital deaths recorded, all of them within the late PE group. Among these deaths, 3 were directly attributed to PE.

Only 5 out of the 54 patients were diagnosed with a DVT by lower extremity duplex scanning prior to the development of their PE. All of these patients were in the later PE group. The majority of patients underwent duplex scanning after their PE was diagnosed (84.2% of early PE patients, 68.6% of later PE patients). These studies revealed 9 patients with occult DVT, all within the later PE group. 2 patients in the early PE group and 4 patients in the later PE group had negative lower extremity duplex exams within 48 h prior to the development of their PE.

8 of the patients in the early PE group and 16 of the patients in the later PE group received an IVC filter. The majority of these were placed as part of a treatment plan following the diagnosis of PE, but 3 patients developed PE after the placement of a prophylactic IVC filter. All three patients were in the late PE group and occurred at 4, 6, and 15 days following filter placement. All three patients had an ISS of greater than 30 (45, 34, 38), had a delay in the start of chemical prophylaxis of greater than 5 days (6, 9, 11), and received chemical prophylaxis in the form of un-fractionated heparin.

Multivariable logistic regression analysis revealed only the presence of lower extremity orthopaedic injuries to be independently associated with the development of early PE ($p = 0.004$, OR 16.36).

Discussion

It has been well established that trauma patients carry a significantly increased risk for the development of venous thrombo-embolic disease.[1,14–16] Classical teaching has been that