Clinical Science

The origin of fatal pulmonary emboli: a postmortem analysis of 500 deaths from pulmonary embolism in trauma, surgical, and medical patients

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Abstract
    BACKGROUND: The traditional theory that pulmonary emboli (PE) originate from the lower extremity has been challenged.
    METHODS: All autopsies performed in Los Angeles County between 2002 and 2010 where PE was the cause of death were reviewed.
    RESULTS: Of the 491 PE deaths identified, 36% were surgical and 64% medical. Venous dissection for clots was performed in 380 patients; the PE source was the lower extremity (70.8%), pelvic veins (4.2 %), and upper extremity (1.1%). No source was identified in 22.6% of patients. Body mass index (adjusted odds ratio [AOR] 1.044, 95% confidence interval [CI] 1.011 to 1.078, $P = .009$) and age (AOR 1.018, 95% CI 1.001 to 1.036, $P = .042$) were independent predictors for identifying a PE source. Chronic obstructive pulmonary disease (AOR .173, 95% CI .046 to .646, $P = .009$) was predictive of not identifying a PE source.
    CONCLUSIONS: Most medical and surgical patients with fatal PE had a lower extremity source found, but a significant number had no source identified. Age and body mass index were positively associated with PE source identification. However, a diagnosis of chronic obstructive pulmonary disease was associated with no PE source identification.
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Traditionally, pulmonary embolism (PE) and deep venous thrombosis (DVT) are thought to be different manifestations of the same disease proccess.[1,2] In 1856, Virchow first described what is our current understanding of the pathophysiology of PE.[3] A series of conditions occur in the deep veins of the lower extremity and a clot develops. Ultimately, a portion of this DVT breaks off, embolizing to the pulmonary arteries.[1] Virchow also described the conditions required for a DVT to develop.[3] The modern interpretation of these criteria are known as Virchow's triad and include venous stasis, vessel endothelial damage, and the presence of a hypercoagulable state.[1]

Recently, many authors have challenged the traditional DVT to PE sequence suggesting that some PEs may not have an embolic source at all, but arise in the pulmonary vasculature de novo.[4–7] Furthermore, several analyses of trauma patients have found that only 15% to 20% of post-injury PEs are associated with an identified DVT,[4,5,8,9] suggesting that in some trauma patients PE and DVT may be a separate disease process.[4,5] The goal of this study was to identify the PE source in trauma, surgical, and medical patients who died from PE and to determine the factors associated with developing a fatal PE without an identified thromboembolic source.

Methods

After approval by the Los Angeles County Coroner's Research and Publication Committee and the University of Southern California Institutional Review Board, all the autopsies performed by Los Angeles County Forensic Medical Division from January 2002 to December 2010, where PE was the cause of death, were identified and retrospectively reviewed. Cases that underwent a dissection to identify a source for the PE were included in this analysis. The primary outcome was identification of a PE source, defined as identification of concomitant venous clot at autopsy. When looking for a DVT at autopsy, medical examiners begin their examination at the level of the popliteal veins and dissect either proximally or distally until a venous clot is identified.

Other data abstracted from the autopsy reports included patient demographics (age, sex, race), available past medical and surgical history as obtained by the medical examiner, the circumstances and location of death, toxicology reports, and body mass index (BMI). Patients were divided into 2 cohorts, medical and surgical patients. Surgical patients were defined as those who died within 3 months (90 days) of a hospitalization for trauma or an elective or emergency surgical procedure. Medical patients were defined as those with no history of recent surgery or trauma (>90 days) and included patients who died during or within 90 days of a hospitalization for medical reasons or who had no recent hospitalization before death.

Comorbid conditions were abstracted from the autopsy reports and used to calculate the Charlson comorbidity index for each patient. The Charlson comorbidity index (nonage adjusted) is a validated tool developed to predict the 10-year mortality in patients who have a range of comorbid conditions. Each comorbidity in the model is assigned a score from 0 to 6.[10] Comorbid conditions considered when calculating the score include myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease (COPD), connective tissue disease, diabetes mellitus, chronic kidney disease, hemiplegia, leukemia, malignant lymphoma, solid tumor, liver disease, and the autoimmune deficiency syndrome.[10]

Data were entered into a spreadsheet (Microsoft Excel 2010; Microsoft Corporation, Redmond, WA) and all analyses were performed using SPSS for Windows, version 21.0 (SPSS, Chicago, IL). Comparisons between the groups created were made using the 2-group t test or one-way analysis of variance for continuous variables and chi-square test or Fisher's exact test for categorical variables. The primary outcome of interest was identified as source of the PE (yes/no). Univariate logistic regression models were tested for each potential risk factor. The final regression model included factors with a P value of less than or equal to .05 along with age and patient grouping (medicine, nonoperative trauma, any surgery) as covariates.

Results

During the 9-year study period, 557 cases were identified where PE was the documented cause of death. Of these, 57 were excluded because either no autopsy or no dissection of the pulmonary arteries was performed. Of the remaining 500 cases, 5 were amniotic embolisms, 3 air, 1 fat, and 491 were venous thromboemboli (VTEs) (Fig. 1). For the remaining 491 PEs due to venous clot, the mean age ± standard deviation was 49.7 ± 15.3, with 56.2% being women and the mean BMI was 33.2 ± 9.4. Of these 491, 88 had a surgical procedure performed; 54.5% had abdominal surgery, 15.9% orthopedic extremity (upper or lower) surgery, 6.8% plastic surgery, 4.5% spinal surgery, and 17% had some other type of surgical procedure performed before death.

Table 1 shows the baseline demographics and clinical characteristics of those who died from a PE because of VTE. Sixty-four percent of patients were medical and 36% surgical; 8.8% had a known cancer diagnosis at the time of death or cancer was found at autopsy, 18.1% were victims of trauma, 13.6% had a history of a psychiatric diagnosis, and 11.6% had positive toxicology for either alcohol or drugs at the time of autopsy. Only 7.3% of patients had a known history of VTE before death. Prodromal symptoms of PE before death were identified by the medical examiner in 44.8% of patients and more likely to be identified in medical patients compared with surgical patients (52.5% vs 31.1%, P = .001). Surgical patients were older (54.1 ± 17.6 vs 47.2 ± 13.3, P < .001), tended to