

Fatal pulmonary thromboembolism

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Abstract. – OBJECTIVE: Venous thromboembolism is a complex, multifactorial disease, involving interactions between acquired or inherited predispositions to thrombosis and various risk factors, such as trauma and surgery. This study investigated the clinical features and most important risk factors of fatal pulmonary thromboembolism (PTE).

MATERIALS AND METHODS: Forensic records stored at the Council of Forensic Medicine, Ministry of Justice in Istanbul, Turkey, from January 2010 to December 2014 were screened for deaths of confirmed PTE based on autopsy or computed tomography (CT). Massive pulmonary embolism was the main cause of death in all patients.

RESULTS: The 51 cases with PTE comprised 22 (43.2%) males and 29 (56.8%) females. A diagnosis of PTE was established by autopsy in 76.6% (39/51) of the cases. Overall, 23 (45%) suffered multiple trauma and 14 (27.5%) underwent surgery. The mean time from surgery to death was 10.2 ± 6.8 days. Of the trauma cases, 78% (18/23) comprised orthopaedic trauma. Death occurred in 74% of the cases after the second week following trauma. Of the trauma and surgery cases, 95.6 and 71.4% were outpatients at the time of death, respectively. The origin of the PTE was known in 34.8% and 57% of the trauma and surgery cases, respectively. The mean Injury Severity Score (ISS) was 11.3 ± 7.6. An abbreviated injury score (AIS) extremity ≥ 3 was seen in 23% (4/18) of the extremity trauma cases. The time to death of the patients who underwent surgery was shorter than in the patients who experienced trauma (p=0.001).

CONCLUSIONS: A high ISS is not a determinant of fatal PTE. Immobilization is important in the occurrence of PTE, especially in trauma patients. Frequent follow-up after discharge should inquire about complaints related to PTE and the use of protective precautions.

Key Words:

Dead at pulmonary thromboembolism, Dead time of trauma and surgery at pulmonary thromboembolism, Immobilization at PTE.

Introduction

Venous thromboembolism (VTE) includes deep-vein thrombosis (DVT) of the leg or pelvis and its complication, pulmonary embolism. VTE is a complex multifactorial disease that involves interactions between acquired or inherited predispositions to thrombosis and various risk factors. Major risk factors for VTE include hospitalization for surgery or acute illness, active cancer, neurological disease with leg paresis, nursing-home confinement, trauma or fracture, superficial vein thrombosis and, in women, pregnancy and puerperium, oral contraception, and hormone therapy¹. The reported incidence of pulmonary embolism is 0.11 to 2.3% among patients with traumatic injuries².

Sudden death is the initial clinical presentation for approximately one-quarter of the patients who experience pulmonary embolism¹. Older age, male sex, increasing body mass index (BMI), confinement to a hospital or nursing home at the onset of VTE, congestive heart failure, chronic lung disease, serious neurological disease, and active cancer are independent predictors of reduced early survival after VTE¹. Fatal postoperative pulmonary thromboembolism (PTE) rates range from 0.2% to 0.9%³.

In this study, we aimed to investigate the clinical features and most important risk factors of fatal PTE.

Materials and Methods

Forensic records stored at the Council of Forensic Medicine, Ministry of Justice in Istanbul, Turkey, from January 2010 to December 2014 were screened for deaths due to PTE, which is confirmed by autopsy, echocardiography or computerized tomography (CT) findings. Massive pulmonary embolism was the main cause of death in all patients.

The following data were collected: demographic information, medical history (including major diseases, any recent surgery or trauma, and any ongoing illness), clinical diagnosis, signs and symptoms before death, BMI, origin of PTE. The symptoms and clinical courses of the deceased were determined from reports by family members in the patients' files.

Exclusion criteria consisted of the absence of radiographic imaging confirmation at CT diagnosed cases, lack of clinical documentation and a time interval between risk factor and PTE diagnosis greater than 120 days.

Statistical Analysis

All data were managed and analyzed using the Statistical Package for the Social Sciences ver. 13.0 (SPSS Inc., Chicago, IL, USA). Quantitative data are presented as means ± standard deviations, and categorical data are presented as counts and percentages. The non-parametric Mann-Whitney *U*-test was used to examine the time of death. *p* < 0.05 was considered statistically significant.

Results

The final study population consisted of 51 patients with a confirmed PTE, composed of 22 (43.2%) males and 29 (56.8%) females. The median age was 40 (range 16-80) years. Mean BMI was 28.2 ± 40.7 and obesity (defined as a BMI >25) was detected in 14/27 patients (52%);

Diagnosis of PTE was established by CT, echocardiography and autopsy at 17.6% (9/51); 6.0% (3/51); and 76.6% (39/51) of the cases, respectively.

The majority of patients had large, coiled thrombi in the pulmonary trunk and its major branches. In seven patients, dissection of the lobar and segmental pulmonary arteries demonstrated large numbers of smaller thrombi.

Shortness of breath (24/51; 47%), syncope (14/51; 27.5%), and hypovolemic shock (11.4; 21.5%) were the most common symptoms at study population (Table I). Chemical prophylaxis was present in only 8.6% of the cases for PTE.

The origin of PTE was determined in only 24 cases (47.05%) (Table II). However, DVT of a lower extremity was present in only 17 (33.3%) cases. DVT was diagnosed with autopsy and Doppler ultrasonography at 15 and 2 cases, respectively. Also, 5 cases had symptoms of DVT at premortem period.

In all cases, 23 (45%) suffered multiple trauma and 14 (27.5%) had history surgery. For the cases with surgery and trauma, the mean age was 46.14 ± 17.9 (range 16-80) years. Of the surgery cases, 43% (6/14 cases) were found to have DVT at autopsy versus 30.4% (7/23) of the trauma cases.

The mean time of surgery to death was 10.2±6.8 days. Caesarean delivery (43%-6/14) and orthopaedic surgery for nontraumatic situations (congenital hip dislocation and hip prosthesis) 14.3% were the most common indications. Most of the surgery cases (71.4%) were outpatients. The origin of PTE was identified in 57% of the cases. DVT was identified in three caesarean cases.

Most of the trauma cases (78%-19/23) involved orthopaedic traumas: lower extremity trauma in 30.4% (7/23), hip fracture in 35% (8/23), and upper extremity fracture in 17.4% (4/23). Only nine cases (39%) had been operated on because of trauma. The mean time from injury to death was 29±23.2 days. Of the trauma cases, 95.6% were outpatients. The origin of PTE was identified in 34.8% of the trauma cases. The Injury Severity Score (ISS) used to assess patients involved in trauma and the mean ISS was 11.3 ± 7.6 (range 1-29). An abbreviated injury score (AIS) extremity ≥3 was seen in 23% (4/18) of the extremity trauma cases.

The time of death of people who underwent surgery was sooner than in the people who experienced trauma (*p*=0.001).

Table I. Clinical features prior to death.

Findings	No. of PTE (%)
Dyspnea	24 (47)
Syncope	14 (27.5)
Chest pain	4 (07.8)
Hemoptysis	1 (01.9)
Hyperemia, swelling on the leg	5 (09.8)
Hypovolemic shock	11 (21.5)
Presentation with exitus	11 (21.5)

Discussion

Over the age of 40 years and high BMI are risk factors for PTE. Like other studies of fatal PTE^{4,5}, BMI and age were also high in this study.

Pulmonary thromboembolism is a well-known complication of trauma and major surgery⁶. In

Table II. Origin of pulmonary embolism in 24 of 51 cases.

Origin	Underlying condition	Number (%)
Deep veins of lower extremity*	Trauma, surgery, cesarean	17 (33.3)
Heart	Bypass surgery, pregnancy	4 (7.8)
Inferior vena cava	Injury of femoral vein	1 (1.9)
Large vessel of urinary bladder	Prostate surgery	1 (1.9)
Vessel of uterus wall	Cesarean section	1 (1.9)

*Diagnosed with autopsy in 15 cases, with Doppler ultrasonography in 2 cases.

this study, 14/51 (27.5%) subjects were postoperative and 23/51 (45%) had trauma. In previous studies of fatal PTE, the overall frequency of potential risk factors was 73.2% (30/41) and 18.1% (89/491) involved trauma and 18% (88/491) and 24% (48/195) involved surgery^{5,7,8}. According to our results, PTE in Orthopaedic Departments (78% of trauma cases) is a serious problem.

In this study, the ISS, which reflects the severity of injury in trauma, was lower than other studies (27.8 in Ho et al⁴, 30±14 in Paffrath et al⁹, and 34±15 in Netto et al¹⁰). The ISS is not a predictor of PTE in trauma cases¹¹.

The time at which death caused by PTE occurs following trauma and surgery has been evaluated only rarely. Gong et al⁷ first reported that death by PTE occurred 3-24 days after injury and 56.7% of the cases occurred in the first week after trauma. In our study, 74% of the deaths occurred after the second week following trauma and the mean time between trauma and death was 29±23.2 days. In another study it was 18 days⁴. For surgery, the mean reported time from surgery to death was 6.8 days⁸, while in our series it was 10.2±6.8 days.

In this study, like the study of Tadlock et al⁵, the mean time to death was shorter in surgery cases than in trauma cases (18.4± 16.2 days in trauma and 12.4 ± 13.4 days in surgery). This

suggests that a thrombus exists in the area of surgery or before the surgery in cases involving immobilization. When the surgery cases were analysed, thrombus was identified in the surgery area in three cases (urinary bladder, uterus, and heart), DVT was identified in two cases of orthopaedic surgery (congenital hip dislocation and hip prosthesis surgery) and varicose vein surgery, while DVT was not detected in a urethral tract surgery case at autopsy

As it is known, pregnancy is a hypercoagulable state. In addition, the presence of inherited thrombophilia and antiphospholipid syndrome increase the risk of PTE during pregnancy and the postpartum period¹². Genetic and other factors may facilitate the occurrence of PTE, especially in patients undergoing a caesarean. One of our pregnant cases had DVT in vessels of the uterus wall after caesarean delivery.

In trauma cases, thromboembolic events occur after hospitalization for 5-7 days, so immobility is the main causative factor of PTE¹⁰. Although PTE can occur a very short time after trauma (before 4 days)², anatomical dissection and radiological imaging studies have shown a high incidence of DVT^{5,13}. In the study that reported the occurrence of early PTE, PTE was related to long bone fractures in the lower extremities and severe extremity trauma, so stasis is not a predominant causative risk factor in all injury cases². It is possible that early PTE results from an unrecognized interplay among various genetic, molecular, and injury-specific mechanisms¹⁴.

A high ISS is not a determinant of fatal PTE¹¹, but severe extremity trauma is related to the early development of PTE². In our series, the ISS and AIS extremity scores were low in most orthopedic cases. In our trauma cases, the time of death was delayed compared with surgery cases, so immobility may be a more important determinant of PTE in this study. A case with an upper

Table III. Potential risk factors.

Risk factor	No. of cases (%)
Trauma	23 (45)
Surgery	14 (27.5)
Age >40 years	25 (49)
Pregnancy	2 (3.9)
Others*	17 (35.4)

*Behçet's disease, asthma, hypertension, history of antipsychotic drug uses, history of deep vein thrombosis, travel.

extremity fracture had DVT, which suggested that the trauma cases were not mobilized early following discharge irrespective of the area of trauma.

When the medical records were examined, few cases received pharmacological prophylaxis for PTE; this could be due to a lack of documentation of prophylaxis treatment or the failure to offer prophylaxis in most cases. Prophylaxis is very common in orthopedic cases¹⁵. However, another study⁹ reported that, despite prophylaxis, PTE developed in many cases. In surgery and trauma cases, some methods can be effective in the prevention of PTE, including pharmacological prophylaxis, mechanical techniques, and a combination of techniques continued for at least 2 weeks after trauma and surgery.

In this study, the small numbers of cases and lack of a control group are main limitations. Another limitation is the lack of exhaustive studies of the leg veins in the post-mortem examinations resulting in the low incidence of the origin of the PTE.

Conclusions

A high ISS is not a determinant of fatal PTE. Immobilization is important in the occurrence of PTE, especially in trauma patients. After discharge, patients require frequent follow-up to ask about complaints related to PTE and the use of protective precautions. It may be possible to determine the origin of PTE when the deep veins and areas of surgery are dissected extensively at autopsy.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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