

Diagnosis and treatment of acute pulmonary embolism: A single center experience

Akut pulmoner emboli tanı ve tedavisi: Tek merkez deneyimi

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ABSTRACT

Aim: Pulmonary embolism is a potentially life-threatening cardiovascular disease frequently encountered in emergency departments. The computed tomography pulmonary angiography is the imaging modality of choice in the diagnosis of pulmonary embolism. This study aimed to examine the effects of clinical findings and treatment methods on prognosis and mortality by examining patients diagnosed with acute pulmonary embolism in the emergency department.

Methods: In this retrospective cohort study, records of patients with acute pulmonary embolism were accessed from the archive. Patients' age, gender, medical complaints, co-morbidities, the treatment method applied to the patients, and the clinical outcomes of the patients were analyzed. The statistical distribution of the patients' demographic and clinical information was calculated.

Results: The most common complaint of 206 patients with acute pulmonary embolism was dyspnea. 25.7% patients had massive pulmonary embolism. The blood d-dimer, lactate and troponin T levels of patients with massive pulmonary embolism were found to be higher than patients with sub-massive pulmonary embolism. Thrombolytic therapy was administered to 6.8% of acute pulmonary embolism patients and it was found to be a method that had a statistically positive effect on survival. D-dimer, white blood cell, neutrophil, blood urea nitrogen, lactate and troponin T values were found to be higher in mortal patients. It was determined that 13.1% of the patients died.

Conclusion: The sooner the early diagnosis of acute pulmonary embolism, which can be mortal in the emergency department, is made and the treatment is started, the mortality rate will decrease significantly.

Keywords: pulmonary embolism, thrombolytic therapy, emergency department.

ÖZ

Amaç: Pulmoner emboli, acil servislere sıklıkla karşılaşılan, potansiyel olarak yaşamı tehdit eden bir kardiyovasküler hastalıktır. Bilgisayarlı tomografi pulmoner anjiyografi, pulmoner emboli tanısında tercih edilen görüntüleme yöntemidir. Bu çalışmada, acil serviste akut pulmoner emboli tanısı konulan hastaları inceleyerek klinik bulguların ve tedavi yöntemlerinin prognoz ve mortalite üzerine etkilerini incelemeyi amaçladık.

Yöntem: Bu retrospektif kohort çalışmada akut pulmoner emboli hastalarının kayıtlarına arşivden ulaşıldı. Hastaların yaşı, cinsiyeti, tıbbi şikayetleri, ek hastalıkları, hastalara uygulanan tedavi yöntemi ve hastaların klinik sonuçları analiz edildi. Hastaların demografik ve klinik bilgilerinin istatistiksel dağılımı hesaplandı.

Bulgular: Akut pulmoner embolili 206 hastanın en sık şikayeti nefes darlığıydı. Hastaların %25.7'sinde masif pulmoner emboli vardı. Masif pulmoner emboli hastalarında kan d-dimer, laktat ve troponin T düzeyleri submasif pulmoner emboli hastalarına göre daha yüksek bulundu. Akut pulmoner emboli hastalarının %6.8'ine trombolitik tedavi uygulanmış ve sağ kalımı istatistiksel olarak olumlu etkileyen bir yöntem olduğu saptanmıştır. Mortal hastalarda d-dimer, beyaz küre, nötrofil, kan üre nitrojen, laktat ve troponin T değerleri daha yüksek bulundu. Hastaların %13.1'inin hayatını kaybettiği belirlendi.

Sonuç: Acil serviste ölümcül olabilen akut pulmoner emboli ne kadar erken teşhis edilir ve tedavisine başlanırsa mortalite oranı önemli ölçüde azalacaktır.

Anahtar Kelimeler: pulmoner emboli, trombolitik tedavi, acil servis.

Received: 03.11.2021 Accepted: 21.01.2022 Published (Online):27.03.2022

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To cited: Ertekin A, Balcı A, Bozkurt E, Atay E, Aktaş RS. Diagnosis and treatment of acute pulmonary embolism: a single center experience. Acta Med. Alanya 2022;6(1): 87-92 doi:10.30565/medalanya.1017887

INTRODUCTION

Pulmonary embolism (PE) is a potentially life-threatening cardiovascular disease frequently encountered in emergency departments (EDs) [1]. Venous thromboembolism (VTE) is the third most common acute cardiovascular syndrome after myocardial infarction and stroke, manifesting clinically as deep vein thrombosis (DVT) or acute PE with its most dangerous complication [2]. The incidence of PE is 39-115/100 000 people and it. PE causes 300 000 deaths annually in the United States. Although PE is diagnosed in only 35% of suspected PE cases in EDs, the mortality rate is 10% [3].

PE risk factors may be related to both genetic and acquired risk factors, although the former's risk factors are less common. As acquired risk factors, we may include recent hospitalization history, previous surgical intervention, immobilization, cancer (20% VTE risk), hormone and steroid therapy (risk 2-3 times higher); pregnancy should also be considered [4]. However, it has been shown that 30% of patients with PE do not have any risk factors [3].

Clinical suspicion is important in the diagnosis of PE. In cases with risk factors such as immobility, cancer, previous trauma and major surgery, PE should be suspected in the presence of complaints such as sudden onset of shortness of breath, chest pain, syncope or hemoptysis [5]. Modified Geneva and Wells scoring systems are most commonly used among clinical prediction scoring systems [6]. It is recommended to use the d-dimer test to exclude PE in cases with low and moderate probability predictive scoring. The computed tomography pulmonary angiography (CTPA) is the imaging modality of choice for imaging the pulmonary vessels in cases with suspected PE [7]. Transthoracic echocardiography (TTE) and CTPA are important in rapid diagnosis in hemodynamically unstable cases. Anticoagulant treatment should be started while waiting for diagnostic test results in suspected cases of PE with high and moderate clinical probability. Hypoxemia is frequently seen in severe PE cases and oxygen support is applied in cases with oxygen saturation values of less than 90%. The first treatment option in high-risk PE cases is reperfusion therapy and mostly systemic

thrombolytic therapy [8]. The main indication for thrombolytic therapy is massive PE with persistent hypotension, unrelated to cardiogenic shock and/or another cause (such as sepsis, hypovolemia, new-onset arrhythmia) [9].

Massive PE presents with acute right ventricular failure accompanied by hypotension, shock, or cardiopulmonary arrest. Patients with syncope, severe hypoxemia, cardiac arrest, or undergoing cardiopulmonary resuscitation, should be evaluated for massive PTE. In sub-massive PE, there are signs of right ventricular dysfunction detected on echocardiography (ECO) despite normal systemic blood pressure [9].

Due to the incidence of acute PE and the high mortality rate, rapid identification and accurate risk stratification of patients with acute PE, play an important role in treatment. In this study, it was aimed to examine the effects of clinical findings and treatment methods on prognosis and mortality, by examining patients diagnosed with acute PE in the ED.

METHODS

This retrospective cohort study was approved by the Ethical Committee of Afyonkarahisar Health Science University, Faculty of Medicine (2021/344 on 04/06/2021). Patients (18-99 years old) diagnosed with acute PE in the ED of Afyonkarahisar Health Science University Faculty of Medicine between 01.08.2016 and 01.01.2021, based on clinical, laboratory and radiological findings, were retrospectively accessed from the archive. The patients' age, gender, medical complaints, co-morbidities, the treatment method applied and the clinical outcomes were analyzed. Patients diagnosed with PE according to clinical, laboratory and CTPA results were included in the study. The statistical distribution of the patients' demographic and clinical information was calculated. Patients with suspected pulmonary embolism but not diagnosed with PE were excluded from the study.

Statistical analysis

Statistical analyzes of the study were performed using the SPSS software version 22.0. The distribution of data was analyzed with the

Kolmogorov-Smirnov test. Data groups that did not show homogeneous distribution as a result of the evaluation were evaluated using the Mann-Whitney U test. Values with $p < 0.05$ were considered statistically significant. All values were expressed as mean \pm standard deviation (mean \pm sd).

RESULTS

In our study, it was determined that 14.6% (n=206) of 1414 patients admitted to the ED with the suspicion of PE were diagnosed with acute PE according to clinical, laboratory findings and CTPA reports. 51.9% (n=107) of the PE patients were female and 48.1% (n=99) were male patients, and the mean age was 64.94 ± 15.85 years. PE was detected in 114 patients of advanced age (>65 years). The most common clinical presentations were dyspnea 90.8% (n=187), chest pain 20.4% (n=42), hemoptysis 5.3% (n=11), syncope 4.4% (n=9), flank pain 1.5% (n=3) and cough 0.9% (n=2). When comorbid diseases of patients with pulmonary embolism were examined, it was found that malignancy (27.2%) was the most common comorbidity in patients (Table 1). In this study, it was found that 5.8% (12) patients had a previous history of PE, 3.9% (8) patients had a previous history of DVT, and 0.5% (1) patient had a heterozygous methylenetetrahydrofolate reductase (Mthfr) gene mutation. When the clinical findings were evaluated, tachycardia was detected in 24.8% (n=51), hypotension in 21.8% (45), atrial fibrillation in 6.3% (n=13) and fever in 1.5% (n=3) of the patients. Lung cancer constituted 34% of malignancy patients. There were 44 (21.4%) patients with a surgical history and 32 (15.5%) patients with a history of immobilization.

DVT was detected in lower extremity venous doppler ultrasonography, performed in 39 (61.9%) of 63 patients examined for DVT. Right ventricular dysfunction was detected in 39.4% (n=26) of 66 patients who underwent ECO in the ED, and left atrial thrombus was observed in 1 patient.

PE rates in low, moderate and high probability groups, respectively; Wells (Canadian) PE was found to be 34%, 64.5%, and 1.5% in the clinical prediction scoring method, and 9.2%, 84.5%, and 6.3% in the Modified Geneva scoring method. As a result of clinical findings, d-dimer and CTPA,

153 (74.3%) patients had sub-massive PE and 53 (25.7%) massive PE (Figure 1).

Table 1. Comorbid diseases of patients with pulmonary embolism

Comorbid Diseases	%	n	Comorbid Diseases	%	n
Malignancy	27.2	56	Chronic renal failure	2.4	5
Chronic pulmonary disease	23.8	49	Immune thrombocytopenic purpura	0.9	2
Hypertension	17.9	37	Cerebral vein thrombosis	0.5	1
Coronary artery disease	12.1	25			
Diabetes	11.7	24			
Neurological diseases	7.8	16			
Congestive heart failure	6.3	13			

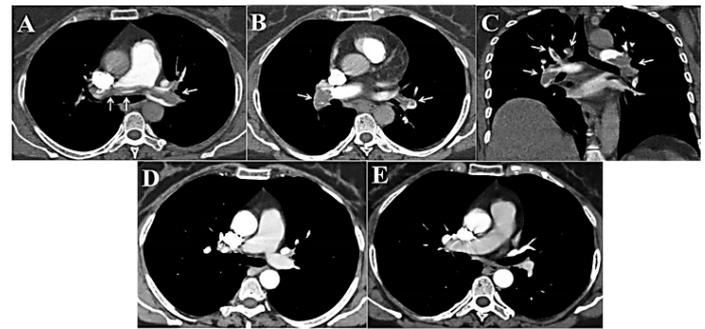


Figure 1. 63-year-old female patient. Axial (A, B) and coronal (C) pulmonary CT Angiography images reveal bilateral massive pulmonary embolism extending from the carina to both main pulmonary arteries (arrows). Follow-up axial CT angiography images (D, E) show completely resorption of bilateral massive pulmonary embolism.

It was determined that 14 (6.8%) patients were treated with thrombolytic therapy and 192 (93.2%) patients were treated with anticoagulant drug therapy. When evaluated according to the treatment groups, it was determined that the application of thrombolytic treatment to massive PE patients had a better effect on healing the patients. Thrombolytic therapy was found to be a method that had a statistically positive effect on survival ($p < 0.001$). No patient who underwent pulmonary embolectomy or percutaneous catheter intervention was found in our study.

The mean hospital stay was 7.94 ± 8.54 days. When the patient outcomes were evaluated, it was determined that 42 (20.4%) patients were admitted to the intensive care unit and 27 (13.1%)

patients died. In the evaluation of survival-mortality in massive and sub-massive PE groups, the discharge frequency of massive PE patients was found to be higher than that of sub-massive PE patients (p= 0.002). Age, d-dimer, white blood cell (WBC), neutrophil, blood urea nitrogen (BUN), lactate and troponin T values were found to be higher in patients who died than those who survived (respectively p= 0.001, 0.037, 0.003, 0.008, 0.001, 0.03, 0.001).

It was determined that patients with sub-massive PE had a statistically longer hospital stay than patients with massive PE (p=0.04). Blood d-dimer, lactate, and troponin T values were found to be higher in patients with massive PE than in patients with sub-massive PE (0.001, 0.032, 0.011, respectively), (Table 2).

DISCUSSION

PE clinical findings and non-invasive diagnostic methods are not 100% diagnostic. In order to exclude and diagnose PE, it is recommended to evaluate patients together with anamnesis, physical examination, laboratory results, lower extremity doppler ultrasonography, radiological imaging, and non-invasive diagnostic methods [10]. In this study, PE was diagnosed in 14.6% of 1414 patients based on clinical suspicion and radiological imaging results.

PE is more common in women over the age of 50 [11]. In this study, 51.9% (n=107) of the PE patients were female and 48.1% (n=99) were male patients, and the mean age was 64.94±15.85 years. In this study, the incidence in women was

Table 2. Age, hospitalization period and blood test results of patients diagnosed with massive and sub-massive pulmonary embolism

	Massive PE (n= 53)		Sub-massive PE (n=153)		Total (n=206)		p value
	Mean±SD	Median (Max-Min)	Mean±SD	Median (Max-Min)	Mean±SD	Median (Max-Min)	
Age (year)	65.06±15.65	66.00 (92.00-25.00)	64.90±15.98	67.00 (91.00-24.00)	64.94±15.85	67.00 (92.00-24.00)	.950
Hospitalization period (day)	7.08±9.34	5.00 (47.00-0.00)	8.25±8.24	6.00 (54.00-0.00)	7.94±8.54	6.00 (54.00-0.00)	.040
d-dimer (ng/mL)	9.27±9.63	6.18 (38.60-0.00)	3.96±4.55	2.90 (34.00-0.30)	5.54±6.88	3.55 (38.60-0.00)	<.001
WBC (10 ³ /UL)	14.37±17.55	11.96 (134.00-2.27)	11.49±4.89	10.90 (24.34-0.48)	12.24±9.93	11.27 (134.00-0.48)	.378
Neutrophil (10 ³ /UL)	7.83±6.56	6.22 (30.17-0.86)	13.39±54.28	7.03 (660.00-0.06)	11.92±46.72	6.65 (660.00-0.06)	.988
Lymphocyte (10 ³ /UL)	1.88±1.66	1.32 (9.16-0.23)	1.47±0.87	1.28 (4.71-0.19)	1.58±1.14	1.30 (9.16-0.19)	.294
NLR	7.82±6.55	6.22 (30.17-0.86)	13.31±53.92	7.02 (660-0.06)	11.88±46.49	6.65 (660-0.06)	.351
Thrombocyte (10 ³ /UL)	221.42±78.64	212.00 (492.00-74.00)	237.68±115.19	225.00 (592.00-0.01)	233.43±106.91	218.00 (592.00-0.01)	.466
Hemoglobin (g/dL)	15.02±14.97	13.00 (121.10-8.90)	13.58±10.56	12.90 (139.00-6.40)	13.95±11.85	12.90 (139.00-6.40)	.472
CRP (mg/dL)	8.62±9.74	5.00 (40.30-0.63)	7.21±7.55	4.90 (38.50-0.18)	7.58±8.18	5.00 (40.30-0.18)	.424
Creatinine (mg/dL)	1.07±0.84	0.88 (6.40-0.34)	1.90±12.26	0.80 (151.00-0.25)	1.68±10.55	0.82 (151.00-0.25)	.069
BUN (mg/dL)	46.38±25.79	40.80 (168.20-4.60)	46.88±27.08	40.30 (166.20-13.30)	46.75±26.69	40.60 (168.20-4.60)	.738
pH	7.17±1.28	7.45 (7.59-0.77)	7.35±0.80	7.45 (7.70-0.43)	7.30±0.95	7.45 (7.70-0.43)	.445
Lactate (mg/dL)	25.66±24.08	16.00 (123.00-3.00)	16.42±7.57	15.00 (65.00-6.00)	18.83±14.43	16.00 (123.00-3.00)	.032
hs-Troponin T (ng/mL)	0.17±0.76	0.04 (5.14-0.00)	0.05±0.09	0.02 (0.90-0.00)	0.08±0.39	0.03 (5.14-0.00)	.011

PE: Pulmonary embolism, WBC: white blood cell, CRP: C-Reaktif Protein, NLR: neutrophil/lymphocyte ratio, BUN: blood urea nitrogen, SD: standard deviation.

similar to the literature [11] but the incidence was higher in the advanced age group (>65 years), with a rate of 55.34%. Similar to the study conducted by Sevim et al., in our study PE patients applied to the ED with the most common complaints of dyspnea (90.8%) and chest pain (20.4%) [10]. Similar to the studies [5,10] 24.8% of our PE patients had tachycardia.

The presence of predisposing factors increases clinical suspicion. The most common predisposing factors are long-term immobilization, previous history of VTE, surgery and malignant diseases [10]. In our cases, which were included in our study, the most common predisposing factors were found to be malignancy (27.2%), surgery (21.4%) and immobilization (15.5%) in line with the literature. In our study, DVT was detected in most of the patients (61.9%) who underwent lower extremity venous doppler ultrasonography. Malignancies increase the risk of VTE by 6 times, and 20% of VTE cases constitute patients with malignancy [12]. In our study, 26.6% of the patients with DVT had a history of malignancy.

VTE is multifactorial and associated with acquired and hereditary conditions. Individuals with inherited causes of thrombophilia are at increased risk of thrombosis, but most of these individuals do not develop thrombosis [13]. In our study, heterozygous Mthfr gene mutation was detected in only one patient and the diagnosis of pulmonary embolism occurred on the basis of hereditary thrombophilia, similar to the literature.

ECO is valuable in deciding the cases that need thrombolytic therapy and embolectomy, since it provides information about right ventricular functions and provides a rapid risk analysis [14]. In a study, ECO performed in 43 (55.1%) of the patients revealed increased pulmonary artery pressure (PAP) in 95.3% of the patients [11]. In our study, it was determined that right ventricular dysfunction was detected in 39.4% (n=26) patients and PAP elevation was observed in 56.1% (n=37) patients of 66 patients who underwent ECO in the ED.

Massive PE causes tachycardia, hypotension, cerebral perfusion disorder and syncope, which is caused by the left ventricular dysfunction due to acute right ventricular failure. Hypotension

develops due to occlusion of the main pulmonary artery by thromboembolism [15]. In a study of 560 syncope patients, PE was diagnosed in 17.3% and PE in the main pulmonary artery was detected in 41.7%. In our study, PE was detected in syncope patients with a lower rate of 4.4%, and similar to the literature, it was determined that 33.3% had embolism in the main pulmonary artery [5].

In the literature, neutrophil/lymphocyte ratio (NLR) and high troponin were evaluated as mortality indicators in PE patients [1,16]. In a study designed by Jia et al., NLR, platelet/lymphocyte ratio, d-dimer, troponin I and NT-ProBNP values were found to be significantly higher in patients with right ventricular dysfunction in acute PE patients in the ED [1]. In a study conducted by Çil et al., although the mean troponin and the mean NLR value were higher in bilateral PE patients than in unilateral PE patients, no statistically significant difference was found [16]. In our study, d-dimer, lactate and troponin T values were found to be higher in patients with massive PE than in patients with sub-massive PE, but no statistically significant difference was found in NLR between these two groups. In addition, patients with a mortal course were found to have higher d-dimer, WBC, neutrophil, BUN, lactate and troponin T values, than those who survived.

PE treatment is carried out according to the risk of mortality. Undoubtedly, reperfusion treatments should be applied in a patient presenting with shock and hypotension. Thrombolytic therapy can be applied to patients who present with shock and hypotension in emergency departments or who are diagnosed with perioperative PE. Thrombolytic therapy is preferred because it has a quick effect, can be applied in a short time and has a short half-life [17]. In our study, although 93.2% of patients were treated with anticoagulant drugs, 11% (n=21) patients died. As we mentioned in our results, this study supports that thrombolytic therapy has a statistically positive effect on survival. Due to the frequency and high mortality rate of acute PE, rapid identification of patients and accurate risk stratification play an important role in its management. About 11% of patients with acute PE die suddenly [1]. In our study, 4.4% of the acute PE patients detected died on the same day.

The present study has some limitations. Due to the retrospective nature of the study and the change in the hospital file system before 2016, patient information was not available. In addition, our research was constrained as a result of its single center nature.

CONCLUSION

The most common ED admission clinic in acute PE patients was found to be dyspnea. D-dimer, lactate and troponin T values were higher in patients with massive PE (25.7%) than in patients with sub-massive PE (74.3%). We believe that this can strengthen our hand in the diagnosis of embolism by evaluating troponin and lactate increases together with d-dimer in patients with whom we suspect PE. In addition, d-dimer, WBC, neutrophil, BUN, lactate and troponin T values were found to be higher in patients who died, than in patients who survived. Thrombolytic therapy was found to be a method that had a statistically positive effect on survival. Our results showed us that the sooner the early diagnosis of acute PE, which can be fatal in the ED, is made and the treatment is started, the more the mortality rates decrease significantly.

Conflict of Interest: The author declares no conflict of interest related to this article.

Funding sources: The author declares that this study has received no financial support

Ethics Committee Approval: This retrospective cohort study was approved by the Ethical Committee of Afyonkarahisar Health Sciences University, Faculty of Medicine (2021/344 on 04/06/2021).

Peer-review: Externally peer reviewed.

ORCID and Author Contributions: **AE (0000-0002-9947-9917):** Supervisor, Concept, Design, Data collection, Material, Literature search, Writing, Editing. **AB (0000-0002-6723-2418):** Data collection, Processing, Analysis, Critical review. **EB (/0000-0002-1853-7098):** Literature search, Analysis, Writing. **EA (0000-0002-2378-1183):** Literature search, Analysis, Writing, Critical review. **RSA (0000-0003-1072-382X):** Literature search, Analysis, Writing.

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