

## Analysis of Patients Received Intravenous t-PA with a Diagnosis of Acute Pulmonary Thromboembolism in Emergency Department

### *Acil Serviste t-Pa Uygulanmış Akut Pulmoner Tromboemboli Tanılı Hastaların İncelenmesi*

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#### ABSTRACT

**Aim:** In this study we aimed to evaluate the demographic characteristics, comorbid conditions, risk factors, laboratory findings, imaging results, risk scores, post-treatment complications and outcome patterns of patients who received t-PA treatment for pulmonary thromboembolism in emergency department. The second aim of the study was both the evaluation of treatment efficacy and the determination of which parameters could be used to determine the patient group at risk.

**Material and Methods:** Individuals diagnosed PE and treated with thrombolytic agents in a tertiary emergency department of university hospital were included into this retrospective study. Complaints at admission, demographic data, biochemical results, radiological findings, clinical features and outcome were analyzed. Wells scores were calculated from the medical records of the patients. In addition, the medical treatment, complications and termination methods of the patients after thrombolytic therapy were evaluated. PESI values of patients included in the study were calculated and prognosis was evaluated.

**Results:** Fifty-nine patients were included to this study. Of 59 patients, 30 (50.8%) were female and 29 (49.2%) were male. Mean age was 58.1 (Range: 18-84; SD: 18). Clinical grading of patient cohort revealed 31 (52.5%) high-risk PE patients and 28 (47.5%) low-risk PE patients. There were no statistically significant differences between high- and low-risk PE patients in terms of demographic and clinical data ( $p>0.05$ ). PESI score was high in high-risk group (24 vs 9,  $p<0.01$ ). Rate of complications, and outcome between high- and low-risk groups showed no statistically significant differences ( $p>0.05$ ).

**Conclusion:** With the exception of a higher PESI score in high-risk PE group, we determined no expected correlation between pulmonary embolism risk scoring systems and post-treatment complications of pulmonary embolism.

**Key words:** Emergency medicine, intravenous thrombolysis, pulmonary embolism

#### ÖZET

**Amaç:** Bu çalışmada acil serviste pulmoner tromboemboli nedeniyle t-PA tedavisi alan hastaların demografik özellikleri, komorbid durumları, risk faktörleri, laboratuvar bulguları, görüntüleme sonuçları, risk skorları, tedavi sonrası komplikasyonlar ve sonlanımı değerlendirmeyi amaçladık. Çalışmanın ikinci amacı, hem tedavi etkinliğinin değerlendirilmesi hem de risk altındaki hasta grubunu belirlemek için hangi parametrelerin kullanılabileceğini belirlemektir.

**Metod:** Bu retrospektif çalışmaya PE tanısı almış ve üniversite hastanesinin üçüncü bir acil servisinde trombolitik ajanlarla tedavi edilen bireyler dahil edilmiştir. Başvuru sırasındaki şikayetler, demografik veriler, biyokimyasal sonuçlar, radyolojik bulgular, klinik özellikler ve sonuçlar analiz edildi. Hastaların tıbbi kayıtlarından Wells skorları hesaplanmıştır. Ayrıca hastalarda trombolitik tedavi sonrası tercih edilen medikal tedavi, gelişen komplikasyonlar ve hastaların sonlanış biçimleri incelendi. Çalışmaya dahil edilen hastaların PESI değerleri hesaplanarak prognoz değerlendirilmesi yapılmıştır.

**Bulgular:** Çalışmaya 59 hasta dahil edildi. Hastaların 30'u (%50,8) kadın ve 29'u (%49,2) erkekti. Hastaların yaş ortalaması 58,1 (18-84; SS:18) idi. Klinik sınıflandırmaya bakıldığında; 31 (%52,5) hasta yüksek riskli PTE, 28 (%47,5) hasta düşük riskli PTE olarak gruplandı. Yüksek ve düşük riskli PE hastalar arasında demografik ve klinik veriler açısından istatistiksel olarak anlamlı bir fark yoktu ( $p>0.05$ ). Yüksek riskli grupta PESI skoru yüksek saptandı (24 vs 9,  $p<0.01$ ). Yüksek ve düşük riskli gruplar arasındaki sonlanım ve komplikasyon oranı açısından gruplar arasında istatistiksel olarak anlamlı farklılık bulunmadı ( $p>0.05$ ).

**Sonuç:** Bizim görüşümüze göre bu çalışmadan çıkan en önemli sonuç; yüksek riskli olan PTE grubunda PESI değerlerinin daha yüksek olması dışında, trombolitik tedavi süreci ve sonrası gelişen komplikasyonlar açısından her iki grup arasında önemli bir fark saptanmamış olmasıdır.

**Anahtar Kelimeler:** Acil Tıp, intravenöz trombolizis, pulmoner emboli

Received:06 June 2018 Accepted: 09 August 2018

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**Introduction:**

Pulmonary embolism is a cardiopulmonary disease leads to high rate of morbidity and mortality (1). In most cases, PE is caused by thromboses in pelvic or lower extremity deep veins (2-3). European Cardiology Association classified PE in 2014 guideline for acute pulmonary embolism diagnosis and treatment into two groups as; high-risk PE presents with shock and hypotension, and low-risk PE without shock or hypotension (4).

Thrombolytic drugs are not only accepted as the choice of treatment in life-threatening high-risk PE, but they may also be efficient in mild-risk PEs with right ventricle dysfunction or myocardial damage (1).

In most cases, high-risk PE is diagnosed with clinical findings and Computed Tomography Angiography (CTA) imaging. Additionally, European guidelines suggest use of thrombolytic therapy in highly suspicious PE cases in the situation of unavailability of CTA or hemodynamic instability, and presence of right ventricle dysfunction in bed-side echocardiography (ECO) (5). Urokinase and streptokinase are two available thrombolytic agents, however administration of 100 mg recombinant tissue plasminogen activator (r-tPA) intravenously is the preferred therapy modality in PE patients (6). The most prominent complication of thrombolytic therapy is hemorrhage; intracranial hemorrhage occurs in 1-3% of patients, and it is the most feared (3). In this study we aimed to evaluate the demographic characteristics, comorbid conditions, risk factors, laboratory findings, imaging results, risk scores, post-treatment complications and outcome patterns of patients who received t-PA treatment for pulmonary thromboembolism in emergency department. The second aim of the study was both the evaluation of treatment efficacy and the determination of which parameters could be used to determine the patient group at risk. It was thought that the data to be reached at the end of the study may help to determine which patient groups benefit from treatment and in which patient group, the complication rate is higher and treatment should be performed more carefully in this group.

**Material and Methods:**

Patients admitted to a third level university emergency department and received thrombolytic therapy due to diagnosis of PE for the last 9 years were analyzed retrospectively. Thrombolytic therapy was applied with 100 mg r-tPA intravenously within two hours. Diagnosis PE was determined with thorax CTA, echocardiography (ECO), Doppler ultrasonography (Doppler USG), and D-dimer. Risk factors for PE were

determined by using patient charts in terms of gender, chronic lung disease, coronary heart disease, previous PE history or deep venous thrombosis (DVT), malignancy, immobilization, and kidney failure. Shock signs, new onset arrhythmia, and systolic blood pressure lower than 90 mmHg or a decrease of 40 mmHg in systolic blood pressure without hypovolemia or sepsis were considered as signs of high-risk PE. Localization of thrombosis within pulmonary arteries was also recorded as main pulmonary, segment, or subsegmental.

Several scoring systems have been proposed to facilitate the diagnosis of PE; among them, Wells' Score is the most commonly used (4). This scoring system keeps track of heart rate over 100 / minute, history of PE or DVT, surgery or immobilization within last month, hemoptysis, cancer, clinical signs of DVT, and weak possibility of diagnosis other than PE (4). Wells' score of all patients were calculated from patient charts. Moreover, medical drugs after thrombolytic therapy, complications, and outcome of patients were recorded in the study form.

Although a lot of scoring systems based on clinical parameters have been found useful in predicting the prognosis of acute PE, Pulmonary Embolism Severity Index (PESI) is the most commonly accepted grading system in the literature (4). It focuses on the parameters of age, male gender, history of cancer, chronic heart failure, chronic lung disease, heart rate over 110 / min., systolic pressure below 100 mmHg, respiratory rate over 30 / min., fever over 36°C, altered mental status, and arterial oxyhemoglobin saturation lower than 90% (4-5). For each patient PESI score was calculated and recorded to predict clinical outcome.

**Statistical Analysis:**

Data acquired from this study were evaluated with SPSS (Statistics for Windows, Version 16.0, IBM, USA). Shapiro-Wilk test was conducted as normality test. Discrepancy of age between patient and control groups was compared with student t test, and categorical variables are compared with qi-square test. A value of  $p < 0,05$  was accepted as statistical significant.

**Results:**

Fifty-nine patients were included to this study. Of 59 patients, 30 (50.8%) were female and 29 (49.2%) were male. Mean age was 58.1 (Range: 18-84; SD: 18). Clinical grading of patient cohort revealed 31 (52.5%) high-risk PE patients and 28 (47.5%) low-risk PE patients.

Although 28(47.5%) of the patients included in the study had a low risk score in terms of risk scoring systems, it was decided to apply t-PA treatment

because of the main pulmonary artery embolism in the CT angiography or ventricular dysfunction in the echocardiography, septal wall motion abnormality or hemodynamic instability.

Comorbidities of the patients, main complaints at emergency department admissions, risk factors for PE, and electrocardiographic findings at emergency department were examined. Demographic and clinical data of the patients were listed in Table 1. There were no statistically significant differences between high- and low-risk PE patients in terms of demographic and clinical data ( $p>0.05$ ).

**Table 1.** Baseline characteristics of the patients

Characteristic	High-risk PE (n:31)	Low-risk PE (n:28)	p
<b>Age</b>	59.3±18	56.8±18.2	0.6
<b>Gender</b>			
Male	14 (45.2)	15 (53.6)	0.7
Female	17 (54.8)	13 (46.4)	
<b>Comorbidity</b>			
DM	7 (22.6)	5 (17.9)	0.9
HT	9 (29)	7 (25)	0.95
Coronary artery disease	2 (6.5)	4 (14.3)	0.4
Chronic lung disease	3 (9.7)	4 (14.3)	0.69
Cerebrovascular disease	3 (9.7)	1 (3.6)	0.61
Chronic renal disease	3 (9.7)	0	0.24
Cancer	1 (3.2)	4 (14.3)	0.18
Other	3 (9.7)	6 (21.4)	0.28
<b>Main complaint</b>			
Dyspnoea	20 (64.5)	24 (85.7)	0.12
Chest pain	13 (41.9)	11 (39.3)	1
Palpitation	3 (9.7)	5 (17.9)	0.45
Syncope	15 (48.4)	7 (25)	0.11
Hemoptysis	5 (16.1)	1 (3.6)	0.19
Cough	1 (3.2)	0	1
Other	3 (9.7)	2 (7.1)	1
<b>Risk factors</b>			
DVT	7 (22.6)	3 (10.7)	0.39
Surgery	8 (25.8)	6 (21.4)	0.93
Cancer	1 (3.2)	3 (10.7)	0.34
Use of OCS	1 (3.2)	0	1
Immobilization	10 (32.3)	9 (32.1)	1
Current smoker	8 (25.8)	10 (35.7)	0.59
Pregnancy	0	1 (3.6)	0.47
Prior PE	0	2 (7.1)	0.22
<b>Electrocardiography</b>			
NSR	1 (3.2)	2 (7.1)	0.59
Sinus tachycardia	18 (58.1)	12 (42.9)	0.36
T-wave inversion	9 (29)	3 (10.7)	0.15
S1Q3T3	11 (35.5)	10 (35.7)	1
Atrial dysrhythmia	4 (12.9)	5 (17.9)	0.72
Low voltage	1 (3.2)	0	1

DM: Diabetes Mellitus, HT: Hypertension, DVT: Deep Venous Thrombosis, OCS: Oral Contraceptive, PE: Pulmonary Embolism, NSR: Normal Sinus Rhythm,

\* Values are mean ± SD. Values in parentheses are percentages. There is no significant difference between two groups.

Arterial blood gas analysis, complete blood count, biochemical parameters, troponin, and d-dimer levels are shown in Table 2. Recent PE guideline suggests a cut-off value of d-dimer level for patients over 50 years-old with “age x 10 microgram/L” formula (4). Therefore, three patients, one from low-risk PE group and two

from high-risk PE group, were recorded as d-dimer negative. Echocardiography results were unavailable in three patients, which were possibly due to performing the ECO bedside and not recorded the results. According to the other clinical findings, these patients placed into the high-risk group. In one patient from high-risk group who presented with strong clinical signs, supporting findings with ECO, Doppler USG, and high Wells' and PESI scores, r-tPA was applied without performing thorax CTA.

**Table 2.** Laboratory findings of the patients

	High-risk PE (n:31) (mean±SD)	Low-risk PE (n:28) (mean±SD)	p
pH	7.34±0.2	7.44±0.1	0.14
SO <sub>2</sub> (%)	88.7±8.2	91.7±5.1	0.19
PO <sub>2</sub> (%)	65.2±20.3	62.8±12	0.59
PCO <sub>2</sub> (%)	30.2±9.2	29.8±8.4	0.85
HCO <sub>3</sub> (mEq/L)	16±4.2	18.1±4	0.12
Hb (g/dL)	13.3±2.4	13.3±1.9	0.98
Plt (x 10 <sup>9</sup> /μL)	215±78.8	233±76.1	0.37
Cre (mg/dL)	1.2±0.5	1±0.3	0.09
CK (U/L)	202.6±291.3	110±147.4	0.23
CK-MB (U/L)	42.8±38.2	38.5±57.4	0.29
Troponin (ng/mL)	0.2±0.3	0.12±0.2	0.48
INR	1.4±0.3	1.2±0.3	0.05
D-dimer (ng/mL)	13883.8±11972.6	9050.5±7072.8	0.18

Hb: Hemoglobin, Plt: Platelets, Cre: Creatinine, CK: Creatinine Kinase, CK-MB: Creatinine Kinase Myocardial Band, INR: International Normalised Ratio

\* Values are mean ± SD. There is no significant difference between two groups.

Patients were divided into different groups as the location of thrombus detected on thorax CTA. Pulmonary CTA and ECO results were listed in Table 3. There were no statistically significant differences among groups ( $p>0.05$ ).

Complications following r-tPA treatment were; hematuria in 2 patients, hemoptysis in 1 patient, subcutaneous hematoma in three patients, and rectus sheet hematoma in one patient. Of these seven patients, cardiac arrest occurred in three patients during intensive care unit (ICU) follow up period. Following thrombolytic therapy, the treatment was continued with low-molecular-weight heparin (LMWH) only in two patients from low-risk group. Medical treatment regime after thrombolytic therapy, complications, and outcomes were summarized in Table 4. Rate of complications, and outcome between high- and low-risk groups showed no statistically significant differences ( $p>0.05$ ).

**Table 3.** Pulmonary CT angiography, Echocardiography results of the patients\*

	High-risk PE (n=30) (n - %)	Low-risk PE (n=28) (n - %)	P
<b>Pulmonary CT angiography</b>			
Common pulmonary artery embolism	24 (80)	26 (92.9)	0.26
Segmental pulmonary artery embolism	15 (50)	9 (32.1)	0.27
Subsegmental pulmonary artery embolism	5 (16.7)	10 (35.7)	0.17
<b>Echocardiography</b>			
RV dysfunction	4 (14.3)	8 (28.6)	0.33
LV dysfunction	5 (17.9)	4 (14.3)	1
RV dilatation	21 (75)	19 (67.9)	0.77
Decreased EF	17 (57)	15 (54)	0.33
Increased PASP	9 (33)	3 (11)	0.57
Aortic insufficiency	2 (7.1)	4 (14.3)	0.67
Mitral insufficiency	3 (10.7)	5 (17.9)	0.7
Tricuspid insufficiency	11 (39.3)	16 (57.1)	0.28

RV: Right Ventricle, LV: Left Ventricle, EF: Ejection Fraction, PASP: Pulmonary Arterial Systolic Pressure

\* Numbers in parentheses are percentages. There are no significant differences between two groups.

Wells score was registered as low, mild, and high-risk, and PESI score was recorded in five groups (Table 5). The comparison of PESI scores between high-risk and low-risk PE groups revealed statistically significant difference ( $p < 0.05$ ).

**Table 4.** In-hospital outcomes

	High-risk PE (n:31, %100)	Low-risk PE (n:28, %100)	P
<b>Continued therapy</b>			
No	4 (12.9)	2 (7.1)	0.32
Heparin infusion LMWH	27 (87.1)	24 (85.7)	
<b>Outcome</b>			
Exitus in ED	3 (9.7)	2 (7.1)	
Exitus in ICU	8 (25.8)	4 (14.3)	0.52
Discharged	20 (64.5)	22 (78.6)	

LMWH: Low Molecular Weight Heparin, ED: Emergency Department, ICU: Intensive Care Unit

\* Values in parentheses are percentages. There are no significant differences between two groups.

### Discussion:

Acute pulmonary embolism has a 30-day mortality rate of 41% and it is responsible for 15% of hospital deaths. Because of this clinical feature, it is a potentially life-threatening medical situation (7). High-risk PE, defined as with the presence of shock or resistant low blood pressure, has a mortality rate more than 30% (8).

First clinical study, which reports use of thrombolytic agents in the treatment of acute PE, backs to forty years ago (3). Meta-analysis reports in the literature discuss the benefits and risks of thrombolytic therapy in acute pulmonary embolism (1). In this study, we aimed to analyze the clinical outcomes of patients treated with thrombolytic therapy. Similar to the study of Sharifi *et al.* our results showed no significant differences between patient groups in demographic and clinical data categories (9). In addition to this, laboratory results and radiological features also showed no significant differences. While clinical studies on patients with pulmonary embolism treated

with thrombolytic therapy reported 0.5% intracranial hemorrhage and 10.4% major bleeding, respectively (7), bleeding rate in our study was 11.9% similar to previous studies and there was no intracranial hemorrhage. On the other hand, in a study of Curtis *et al.*, 45% major bleeding rate was reported in patients who underwent thrombolytic therapy (7). Since no autopsies were performed in patients that died in emergency department or eventually in ICU after r-tPA treatment, we think that; intracranial hemorrhage and major bleeding rates in those patients may be not specified.

**Table 5.** Wells' score and PESI classification

	High-risk PE (n=31; %100)	Low-risk PE (n=28; %100)	P
<b>Wells' score</b>			
<2 low risk	1 (1,7)	1 (1,7)	
2-6 intermediate risk	23 (39)	21 (35,6)	0.97
>6 high risk	7 (11,8)	6 (10,2)	
<b>PESI class</b>			
Class I <65	1 (1,7)	5 (8,5)	
Class II 66-85	0	6 (10,2)	
Class III 86-105	1 (1,7)	5 (8,5)	<0.01
Class IV 106-125	5 (8,5)	3 (5,1)	
Class V >125	24 (40,6)	9 (15,2)	

Values in parentheses are percentages.

Wells scores of patients revealed that 3.4% of patients are from low-risk group. Consistent with clinical status and examination results of patients treated with thrombolytic drugs, the rate of patients with mild- and high-risk Wells score were higher. We also think that; PESI scoring system may be used to describe risk categories with the inclusion of clinical comorbidities (5). We compared outcome status of the patients and PESI scores, to have a better understanding on prognosis of patients, which revealed statistically significant difference between groups of patients who are discharged and patients who died ( $p < 0.001$ ).

### Conclusion:

In our opinion, the most important finding of this present study is that there are no significant differences between high and low risk PE groups in terms of thrombolytic treatment process and complications with the exception of PESI scores which have been found to be higher in high-risk PE group. There is need for prospective studies with larger patient cohorts to evaluate the use of thrombolytic agents in emergency department and their effects.

### Funding

None Declared

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