Annals of Medical Research

DOI: 10.5455/annalsmedres.2019.11.778 2020;27(3):774-9

Original Article

Examination of pulmonary embolism in patients in a university hospital

Idris Kirhan[1], Fatih Uzer[2], Iclal Hocanli[3], Hamdiye Turan[3]

[1]Harran University, Faculty of Medicine, Department of Internal Medicine, Sanliurfa, Turkey
[2]Kastamonu Public Hospital, Clinic of Thoracic Diseases, Kastamonu, Turkey
[3]Harran University, Faculty of Medicine, Department of Thoracic Diseases, Sanliurfa, Turkey

Abstract

Aim: Pulmonary embolism (PE) is responsible for 5-15% of hospital deaths. The rate of mortality from PE in untreated cases is about 25-30%, while this rate drops down to 2-8% in treated cases. In this study, we aimed to investigate general features of the patients hospitalized in our center due to PE and the factors affecting prognosis.

Material and Methods: Patients hospitalized due to PE in Harran University Medical Faculty Hospital between January 2015 and December 2017. Patients' demographic data, comorbidities, hemogram outcomes at the time of admission, liver function tests, renal function tests, electrolytes and cardiac markers, status of the patients during follow-up (referral to intensive care unit, exitus, ward follow-up) and PE clinical picture (massive, submassive, nonmassive) were recorded. All patients requiring hospitalization due to PE were included in the study, while patients with chronic thromboembolic pulmonary disease, those requiring recurrent hospitalization and patients discharged on own demand were excluded from the study.

Results: The study included 40 (38.8%) male and 63 (61.2%) female patients with a mean age of 66±18.1 years. The mean duration of hospitalization was found as 11 days. Of the patients included in this study, 7.7% (n=8) were diagnosed with massive, 10.6% (n=11) with submassive, and 81.5% (n=84) with non-massive PE. Four patients (3.8%) were accepted as in-hospital exitus, 30 (29.1%) patients were transferred to the intensive care unit and 69 (66.9%) patients were followed-up in the thoracic diseases service. When patients diagnosed with non-massive PE were compared with those diagnosed with submassive and massive PE; the levels of magnesium (p=0.003), and troponin (p=0.000) were statistically significantly higher in the group diagnosed with submassive and massive PE. When the groups with and without the need for intensive care were compared, platelet counts were statistically lower in the group which required intensive care (p=0.038).

Conclusion: More often hospitalization is needed in female patients due to PE. Although routine laboratory tests give a partial information about the prognosis of PE, cardiac markers are the most commonly used in clinical practice.

Keywords: Hospitalization; laboratory; pulmonary embolism; intensive care

INTRODUCTION

Pulmonary embolism (PE) can be defined as a blockage in the pulmonary artery or its branches by a material originated from another part of the body (thrombus, tumor, air or fat) (1-3). PE was described for the first time in 1819 as pulmonary apoplexia, and in 1846 von Virchow described the relationship between venous thrombosis and PE and coined the term of 'embolism'. The mean annual incidence of venous thromboembolism (VTE) is between 23-269/100000 (1-7). VTE is the most important cause of mortality with estimated 548.000 annual hospitalizations only in the USA. Some studies have shown that one fourth of patients face sudden death (2). It is one of the most common causes of hospital mortality. Pulmonary embolism (PE) is responsible for 5-15% of hospital deaths (4). The rate of mortality from PE in untreated cases is about 25-30%, while this rate drops down to 2-8% in treated cases (4-5). Mortality is the highest within the first three months following the development of PE. Mortality is usually linearly associated with cancer, chronic cardiopulmonary comorbidity and advanced age (7-8). In this study, we aimed to investigate general features of the patients hospitalized in our center due to PE and the factors affecting prognosis.

Received: 28.11.2019 **Accepted:** 04.02.2020 **Available online:** 10.03.2020
Corresponding Author: Idris Kirhan, Harran University, Faculty of Medicine, Department of Internal Medicine, Sanliurfa, Turkey
E-mail: idriskirhan@gmail.com

MATERIAL and METHODS

Patients hospitalized due to PE in Harran University Medical Faculty Hospital between January 2015 and December 2017. Patients' demographic data, comorbidities, hemogram outcomes at the time of admission (hemoglobin, neutrophils, platelets, lymphocyte, MPV, eosinophils, basophils), liver function tests (ALT, AST, albumin), renal function tests (urea, creatinine), electrolytes (magnesium, calcium, phosphorus) and cardiac markers (troponin), status of the patients during follow-up (referral to intensive care unit, exitus, ward follow-up) and PE clinical picture (massive, submassive, nonmassive) were recorded. Clinical classification of the patients (massive, submassive, nonmassive) was made according to the European Society of Cardiology (ESC) guidelines (6). According to this guidelines patients with normal systemic blood pressure and right ventricular function were accepted as to have nonmassive PE, those with normal systemic blood pressure, but right ventricular dysfunction on echocardiography as having submassive PE, and patients with hypotension resistant to treatment as to have massive PE. Routine hemogram and biochemical levels were compared between the patients discharged with recovery, patients requiring referral to the intensive care unit, and patients with a mortal prognosis. All patients requiring hospitalization due to PE were included in the study, while patients with chronic thromboembolic pulmonary disease, those requiring recurrent hospitalization and patients discharged on own demand were excluded from the study.

Statistical Analysis

Data obtained in the study were analyzed using IBM Statistical Package for Social Sciences (SPSS) v. 22 software (SPSS Inc, Chicago, IL, USA). Normality of the variables was assessed with Kolmogorov Smirnov test. Non-normally distributed variables were evaluated with non-parametric tests. Non-normally distributed continuous variables were analyzed with the Mann-Whitney U test. The correlation between non-parametric data was evaluated with Spearman's correlation analysis. Quantitative data are expressed as mean, standard deviation, interquartile range, minimum, and maximum values. Categorical variables are expressed as frequency (n) and percentage (%). $p<0.05$ values were considered statistically significant.

RESULTS

The study included 40 (38.8%) male and 63 (61.2%) female patients with a mean age of 66±18.1 years. The mean age was found as 60.8±18.6 years in female and 61.3±17.6 years in male patients. The mean duration of hospitalization was found as 11 days. Of the patients included in this study, 7.7% (n=8) were diagnosed with massive, 10.6% (n=11) with submassive, and 81.5% (n=84) with non-massive PE. Four patients (3.8%) were accepted as inhospital exitus, 30 (29.1%) patients were transferred to the intensive care unit and 69 (66.9%) patients were followed-up in the thoracic diseases service. Shortness of breath was found as the most common cause of presentation (86 patients). Basic clinical and laboratory values of the patients are given in Table 1.

Table 1. General characteristics of patients

	Median	Standard deviation	Range
Age (years)	61	18.10	20-92
Hospitalization (days)	11	7.20	1-31
Hemoglobin (g/dl)	13.20	2.10	7-17
Platelet (10^3/µL)	285.20	102.00	112.50-599.60
MPV (µm³)	7.29	1.36	7-17
RDW (%)	12.99	2.17	10.42-24.13
Basophils (10^3/µL)	0.08	0.08	0.00-0.76
Eosinophils (10^3/µL)	0.12	0.15	0-0.84
Neutrophils (10^3/µL)	8.30	4.60	1.60-23.70
Lymphocytes (10^3/µL)	1.90	1.00	3.20-5.30
Urea (mg/dl)	39	21.20	6-119
Creatinine (mg/dl)	0.78	0.40	0.25-3.44
ALT (IU/L)	**17**	**102**	6-926
AST (IU/L)	21	238	6-2361
Albumin (g/dl)	3.15	0.66	1.80-4.63
D.dimer (ng/L)	2	3.90	0.22-22.20
Troponin (ng/mL)	0.02	1.04	0-7.26
Calcium (mg/dl)	8.90	0.79	6.10-13
Magnesium (mg/dl)	2.02	0.26	1.49-3.14
Phosphorus (mg/dl)	3.50	0.78	1.50-6.50

When patients diagnosed with non-massive PE were compared with those diagnosed with submassive and massive PE; the levels of magnesium (p=0.003), and troponin (p=0.000) were statistically significantly higher in the group diagnosed with submassive and massive PE (Table 2). When the groups with and without the need for intensive care were compared, platelet counts were statistically lower in the group which required intensive care (p=0.038) (Table 3). The comparison of patients according to gender is given in Table 4.

Table 2. Comparison of the patients according to clinical features

	Nonmassive (n:84)	Submassive+massive (n:19)	p
Age (years)	61	60.70	0.943
Hospitalization (days)	12	14.20	0.243
Hemoglobin (g/dl)	12.80	13.50	0.226
Platelet (10^3/µL)	287.70	174.50	0.613
MPV (µm^3)	7.33	7.64	0.379
RDW (%)	13.55	13.28	0.680
Basophils (10^3/µL)	0.09	0.09	0.891
Eosinophils (10^3/µL)	0.15	0.16	0.716
Neutrophils (10^3/µL)	8.80	10.50	0.146
Lymphocytes (10^3/µL)	2.00	2.00	0.995
Urea (mg/dl)	41	47	0.260
Creatinine (mg/dl)	0.86	0.98	0.262
ALT (IU/L)	20	23	0.68
AST (IU/L)	16	19	0.044
Albumin (g/dl)	3.10	3.63	0.129
D.dimer (ng/L)	3.47	3,60	0.927
Troponin (ng/mL)	0.01	0.21	0.000
Calcium (mg/dl)	8.85	8.84	0.906
Magnesium (mg/dl)	1.97	2.25	0.003
Phosphorus (mg/dl)	3.50	3.70	0.205
Ejection fraction (%)	55	54	0.724

Table 3. Comparison of the patients according to clinics of hospitalization

	Service (n:69)	Intensive Care (n:30)	p
Age (years)	59.40	63.80	0.268
Hospitalization (days)	11.90	14.60	0.095
Hemoglobin (g/dl)	12.90	13.20	0.571
Platelet (10^3/µL)	298.30	253.00	0.038
MPV (µm^3)	7.42	7.23	0.516
RDW (%)	13.69	12.91	0.156
Basophils (10^3/µL)	0.08	0.08	0.755
Eosinophils (10^3/µL)	0.16	0.15	0.798
Neutrophils (10^3/µL)	8.60	9.50	0.352
Lymphocytes (10^3/µL)	2.10	2.10	0.939
Urea (mg/dl)	40.20	44	0.409
Creatinine (mg/dl)	0.84	0.98	0.131
ALT (IU/L)	17.50	29	0.332
AST (IU/L)	21	29	0.312
Albumin (g/dl)	3.10	3.10	0.882
D.dimer (ng/L)	3.29	4.05	0.520
Troponin (ng/mL)	0.01	0.04	0.002
Calcium (mg/dl)	8.91	8.76	0.391
Magnesium (mg/dl)	2.00	2.01	0.931
Phosphorus (mg/dl)	3.50	3.60	0.435
Ejection fraction (%)	55	54	0.603

Table 4. Comparison of the patients according to gender			
	Male (n:40)	Female (n:63)	P
Age (years)	61.30	60.83	0.514
Hospitalization (days)	13.33	11.90	0.060
Hemoglobin (g/dl)	13.58	12.61	0.620
Platelet (10^3/µL)	269.93	307.01	0.311
MPV (µm^3)	7.06	7.59	0.254
RDW (%)	13.25	13.62	0.196
Basophils (10^3/µL)	0.09	0.09	0.826
Eosinophils (10^3/µL)	0.17	0.13	0.021
Neutrophils (10^3/µL)	9.80	8.69	0.579
Lymphocytes (10^3/µL)	2.10	2.05	0.309
Urea (mg/dl)	41.68	42.50	0.311
Creatinine (mg/dl)	0.86	0.89	0.421
ALT (IU/L)	45.95	34.66	0.570
AST (IU/L)	44.60	21.31	0.656
Albumin (g/dl)	3.01	3.23	0.936
D.dimer (ng/L)	2.24	4.40	0.026
Troponin (ng/mL)	0.16	0.33	0.910
Calcium (mg/dl)	8.73	8.93	0.047
Magnesium (mg/dl)	2.01	2.01	0.216
Phosphorus (mg/dl)	3.48	3.61	0.144
Ejection fraction (%)	54.19	55.43	0.028

DISCUSSION

In this study, basic characteristics of the patients who presented to a tertiary university hospital were examined. While female patients were more often hospitalized due to PE, a considerable portion of patients hospitalized due to PE were found to require intensive care follow-up. In addition, although in the evaluation of prognosis we found that AST and magnesium levels were statistically significantly higher in moderate-to-high risk group, we observed that there were no laboratory parameters showing PE prognosis as well as cardiac markers in clinical practice. In our study, we concluded that patients with a low platelet counts were in more need for intensive care. In the literature various studies have been conducted about that diagnosis and prognosis of embolism can be estimated through routine hemogram and biochemical outcomes.

The incidence of pulmonary embolism increases with ageing. In the literature, mean age of patients has been reported in a wide range between 47 and 76 years (4, 8-11). Compared to the literature, in our study patients tended to be slightly older (mean age: 61 years). This result may explain why patients were hospitalized for a longer time and why the need for intensive care was higher compared to the other studies. Many studies could not found a relationship between PE and gender. However, there is evidence that PE is more commonly seen in women of reproductive age and older men (4). Miniati et al. reported that male gender is one of the ten factors increasing the risk of developing PE in male gender (12). Unlike from the literature, in our study women who required hospitalization due to PE were dominant.

In PE, mainly one of three clinical pictures is determined as massive, submassive and nonmassive PE. Massive PE is seen between 5-10% and its mortality has been reported as 40% (7). In our study, massive PE was found in 7.7% (n=5), submassive in 10.6% (n=10) and nonmassive in 81.5% (n=84) of the patients. Of our patients with a mortal prognosis, three were diagnosed with massive PE, and the other two patients with submassive PE. As expected, the rate of mortality was higher among the patients with massive and submassive PE.

It was found in some studies that low blood hemoglobin levels increase mortality in patients diagnosed with pulmonary embolism (13,14). Low hemoglobin and hematocrit levels are associated with low blood viscosity. As a result, it is stated that these patients are prone to thrombosis, because the anti-thrombotic mechanism in their vascular endothelium does not work correctly. In the literature, anemia is used as a prognostic factor for

survival in patients with pulmonary embolism (13). In our study, no correlation was found between hemoglobin levels and pulmonary embolism clinic.

When other parameters that can be studied in full blood count are considered; some studies have argued that high MPV and RDW levels can show the prognosis in acute PE, but in our study we found that both parameters were insufficient in showing the prognosis in PE (15, 16).

Cardiac markers (troponin and BNP) are the most commonly used parameters in order to determine the prognosis of pulmonary embolism. Although not specific as cardiac markers, leukocytes, LDH, AST and bilirubin levels may be elevated in patients diagnosed with PE. In a study by Aslan et al., ALT and AST levels were statistically significantly higher in patients with massive PE compared to the patients with nonmassive PE (17). In addition, in the literature a submassive PE case mimicking acute liver failure has been reported (18). In our study, when patients were clinically divided into groups; AST levels were statistically significantly higher in massive and submassive groups compared to the massive group, consistently with the literature. In a study by Aslan et al., hypoalbuminemia was statistically significantly higher in the group with severe hypoxemia (17). Likewise our study, in that study also no significant difference was found between clinical classes of the patients (massive-nonmassive) and albumin levels.

There are numerous studies showing that renal failure is a risk factor for PE (19-21). However, studies investigating the prognosis of PE through kidney function values are limited. In a cohort study by Chang et al. investigating acute renal failure in patients diagnosed with PE, acute renal failure was statistically significantly higher in patients with massive PE (19). In our study, no statistically significant difference was found between the groups in terms of urea and creatinine levels. High or low levels of magnesium have been associated with mortality in critical patients. In our study, magnesium levels were statistically significantly lower in patients with massive and submassive PE than those with nonmassive PE.

This study has some limitations. These limitations include a small number of patients, small number of patients with massive PE and small number of patients with a mortal prognosis. In addition, files resulted with I-26 ICD diagnostic code according to the ICD 10 coding system were retrospectively evaluated, and patients diagnosed with pulmonary embolism with computed pulmonary angiography remained limited with imaging and not with clinical evaluation.

CONCLUSION

In conclusion; it was found that female patients were more commonly hospitalized due to PE. Although routine laboratory tests give a partial information about the prognosis of PE, cardiac markers are the most commonly used in clinical practice In conclusion; it was found that female patients were more commonly hospitalized due to PE. Although routine laboratory tests give a partial information about the prognosis of PE, cardiac markers are the most commonly used in clinical practice.

Competing interests: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports.
Ethical approval: The study were approved by the Harran University of Local Ethics Committee (protocol number: 08.06.18).
Idris Kirhan ORCID: 0000-0001-6606-6078
Fatih Uzer ORCID: 0000-0001-9318-0458
Iclal Hocanli ORCID: 0000-0002-8577-3111
Hamdiye Tran ORCID: 0000-0002-5959-542X

REFERENCES

1. Arseven O. Pulmoner Tromboembolizm. Özlü T (editör). Solunum Sistemi ve Hastalıkları Temel Başvuru Kitabı. Cilt I. İstanbul, İstanbul Tıp Kitapevi 2010;1185-219.
2. Martinez C, Cohen AT, Bamber L, et al. Epidemiology of first and recurrent venous thromboembolism: a population-based cohort study in patients without active cancer. Thromb Haemost 2014;112:255-63.
3. Puurunen MK, Gona PN, Larson MG, et al. Epidemiology of venous thromboembolism in the Framingham Heart Study. Thromb Res 2016;145:27-33.
4. Arseven O, Sevinç C, Alataş F, et al. Türk Toraks Derneği Pulmoner Trombo-embolizm Tanı ve Tedavi Uzlaşı Raporu. Türk Toraks Dergisi 2015;10:1-49.
5. Demir M, Erdemli B, Kurtoğlu M, et al. Ulusal Venöz Tromboembolizm Profilaksi ve Tedavi Klavuzu 2010; 1-127.
6. Konstantinides SV, Torbicki A, Agnelli G, et al. ESC guidelines on the diagnosis and management of acute pulmonary embolism.Eur Heart J 2014;35:3033-69.
7. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet 1999;353:1386-9.
8. Kostadima E, Zakynthinos E. Pulmonary embolism: pathophysiology, diagnosis, treatment. Hellenic J Cardiol 2007;48:94-107.
9. Bateson D, Butcher BE, Donovan C, et al. Risk of venous thromboembolism in women taking the combined oral contraceptive: A systematic review and meta-analysis.Royal Australian College of General Practitioners 2016;59-67.
10. Johnson SA, Eleazer GP, Rondina MT. Pathogenesis, Diagnosis, and Treatment of Venous Thromboembolism in Older Adults. J Am Geriatr Soc 2016;64;1869-78.
11. Caprini JA. Update on Risk Factors for Venous Thromboembolism. Am J Med 2005;1-10.
12. Miniati M, Prediletto R, Formichi B, et al. Accuracy of clinical assessment in the diagnosis of pulmonary embolism. Am J Respir Crit Care Med 1999;159:864-71.

13. Jiménez D, Escobar C, Martí D. Association of anaemia and mortality in patients with acute pulmonary embolism. Thromb Haemost 2009;102:153-8.
14. Donze J, Labarere J, Mean M, et al. Prognostic importance of anaemia in patients with acute pulmonary embolism. Thromb Haemost 2011;106:289-95.
15. Şen HS, Abakay Ö, Taylan M, et al. The importance of mean platelet volume in early mortality of pulmonary embolism. Clinical and Experimental Investigations 2013;4:298-301.
16. Pazarlı AC, Bekar L. Clinical Utility of Red Blood Cell Distribution Width Parameter in Patients with Hemodynamically Stable Acute Pulmonary Embolism. Eurasian J Pulmonol 2014;16:27-30.
17. Aslan S, Meral M, Akgun M, et al. Liver dysfunction in patients with acute pulmonary embolism. Hepatol Res 2007;37:205-13.
18. Vizcaychipi M, Burt C, Burnstein R. Pulmonary embolism: An Unusual Cause Of Acute Liver Failure. Internet J Emergency and Intensive Care Med 2006;10.
19. Chang C, Fu C, Fan P, et al. Acute kidney injury in patients with pulmonary embolism: a population-based cohort study. Medicine 2017;96:5822.
20. Kuo TH, Li HY, Lin SH. Acute kidney injury and risk of deep vein thrombosis and pulmonary embolism in Taiwan: A nationwide retrospective cohort study. Thromb Res 2017;151:29-35.
21. Al-Dorzi HM, Al-Heijan A, Tamim HM, et al. Renal failure as a risk factor for venous thromboembolism in critically Ill patients: a cohort study. Thrombosis Res 2013;132:671-5.