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Original Article

The factors affecting the duration of hospitalization in pulmonary embolism

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Abstract

Aim: The factors affecting the duration of hospitalization in PTE were evaluated In this multicenter , retrospective study.

Materials and Methods: A total of 161 patients who were diagnosed as PTE were enrolled in the study. The diagnoses of all patients were confirmed via computed tomographic pulmonary angiography (CTPA). The median duration of hospitalization was calculated as 9 days. Patients were divided into two groups. Short-stay group was consisted of patients who were hospitalized for less than 9 days while the patients who were hospitalized for more than 9 days composed the long-stay group.

Result: The mean hospital stay was 7.84 days (interquartile range, 5-17 days). Concerning CTPA findings; Pulmonary thromboembolism index (%) was significantly higher in long-stay patients (52.61 ± 24 versus 38.59 ± 23, p = 0.001). In addition, right and left pulmonary artery diameter, right ventricle (RV) diameter and RV/LV ratio significantly affected the length of hospital stay. Elevated levels of BNP (516 mg/dL, 10-4694 versus 269 mg/dL, 10-1400 p = 0.014) and troponin (0.7 mg/dL, 0.1-3.7 versus 0.1 mg/dL, 0.1-3 p = 0.024) were also associated with prolonged hospital stay.

Conclusions: Increased right and left pulmonary artery diameters, pulmonary artery pressure, RV diameter/LV diameter ratio and pulmonary artery diameter/aortic conus diameter ratio were found to be associated with prolonged hospital stay. The higher levels of CRP and d-dimer did not have any effect on the duration of hospitalization.The rates of bleeding did not affect the length of hospitalization, regardless of the type of treatment.

Keywords: Pulmonary embolism; duration of hospitalization; risk stratification; anticoagulation

INTRODUCTION

Pulmonary thromboembolism (PTE) continues to be one of the most important reasons of morbidity and mortality despite the technological advances in diagnosis and treatment. More than 10% of the hospital mortality has been found to be associated with PTE (1, 2). Management of acute PTE is a complicated process since the decision on the treatment modality and necessity of hospitalization is quite difficult to reach. An adequate risk assessment and subsequent appropriate treatment may be life-saving whereas inappropriate thrombolytic therapy may result in life-threatening major bleeding and hence prolongation of hospitalization. On the other hand, since cost-effectiveness has come into prominence in the recent years, it is argued that low-risk patients can be treated even without hospitalization (3).

The Pulmonary Embolism Severity Index is a risk stratification tool that has been determine the mortality and outcome of patients with newly diagnosed pulmonary embolism (4). Pulmonary embolism severity index which is a scoring model that includes clinical parameters, transthoratic echocardiography which serves in the assessment of right ventricular function and biochemical parameters such as brain natriuretic peptide (BNP) and cardiac troponin I are widely used in the evaluation of the severity and prognosis of PTE (5). However, the data about the association between these parameters and hospital stay is missing. This study was conducted to investigate the parameters predicting the duration of hospitalization in acute pulmonary thromboembolism.

MATERIALS and METHODS

A total of 161 patients who were diagnosed as PTE between January 2014 and October 20016, were enrolled in the retrospective study. Computed tomographic pulmonary angiography (CTPA), the gold standard in the diagnosis of pulmonary embolism was accepted as the objective

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test. Eight patients who were clinically diagnosed as PTE by considering the high probability ventilation perfusion scintigraphy findings but were unable to undergo CTPA due to elevated creatinine levels were excluded from the study. A total of 17 patients who were diagnosed as pulmonary artery thrombosis in CTPA and who died in the hospital were also excluded from the study. The remaining 136 patients with definite PTE diagnosis composed the study population.

CTPA was performed before any treatment was given via a 64-detector computed tomography (Brilliance BT device, Philips Medical Systems, Cleveland, Ohio). Vascular access was established in the antecubital vein via an 18-20 G catheter before imaging and 100 mL nonionic contrast agent was administered at a rate of 4 mL/sec with the help of a automatic injector. After contrast material injection, cross sections were taken with a delay of 18.5 seconds from the time when the density of contrast material reached the threshold value in the pulmonary trunk. Hematological and biochemical test results of patients were collected. Clinical probability was calculated via Wells and Geneva pulmonary thromboembolism clinical prediction scores (6).

Echocardiography findings of patients diagnosed with definitive PTE on CT angiography were collected. Pulmonary artery pressure, right ventricular diameter, left ventricular diameter datas via measured with echocardiography were collected, left pulmonary artery diameter, pulmonary conus diameter, RV diameter/LV diameter and Pulmonary conus diameter/aortic conus diameter datas via measured with CTPA were collected. The median duration of hospitalization was calculated as 9 days. Patients were divided into two groups and compared with each other. Short-stay group was consisted of patients who were hospitalized for less than 9 days while the patients who were hospitalized for more than 9 days composed the long-stay group. Creatinine, D-dimer, Brain natriuretic peptid and C-reactive protein as biochemical parameters were recorded. The relationship between hospitalization time and biochemical, echocardiographic and radiologic findings was evaluated.

Statistical analyzes

Quantitative variables were expressed asmean value+standard deviation (SD), and qualitative variables were expressed as percentage (%). Comparison of parametric values between the 2 groups was performed using the 2-tailed Student t test. Categorical variables were compared by means of the likelihood ratio w2 test or Fisher exact test. Two-tailedP values<.05were considered significant. The subjects were divided into two groups considering the median value of hospital stay. All statistical studies were carried out with the SPSS program (version 20.0; SPSS).

RESULTS

A total of 161 patients were enrolled initially however 17 patients who died in the hospital and 8 patients who were unable to undergo CTPA because of elevated creatinin levels were excluded from the study. The statistical evaluation was performed in the remaining 136 patients. The baseline characteristics of the patients are shown in Table 1. The mean age of the patients was 66 ± 17. The frequency of pulmonary thromboembolism (PTE) was higher in females compared to males (76, 55.88% versus 60, 44.1%). The mean hospital stay was 7.84 days (interquartile range, 5-27 days). Concomitant deep vein thrombosis was diagnosed in 61 patients (44.85%) (Table 1). Echocardiography revealed right ventricular enlargement in 48 (35.2%) of the patients. Troponin was elevated in 42 patients (30.8%).

Table 1. Baseline Characteristics of the Patients (All patients)

	n (%)
Age, year	66±17
Interquartile range,year	44-77
Median length of hospitalization, day	9
Interquartile range	5-27
Mean length of hospitalization, day	7.84
Male	60 (44.1)
Female	76 (55.88)
Hypertension	63 (46.3)
Active cancer	14 (10.29)
Obesity or BMI30 kg/m2	38 (27.94)
Deep Venous thromboembolism	61 (44.85)
Diabetes mellitus	27 (19.85)
Ischemic coronary artery disease	17(12.5)
Chronic obstructive pulmonary disease	13 (9.55)
Smoker	16 (11.76)
Clinically diagnosed congestive heart failure	15 (11.02)
Oral contraceptive or hormone replacement therapy	5 (3.67)
Trauma	4(2.94)
Left ventricular ejection fraction 40%	3 (2.20)
Transferred from another hospital	27 (19.85)
Recent surgery	16 (11.76)
Wells score	2.19±0.14
Geneva score	3.37±0.68
Hemoglobin(g/dl)	17±4
Platelet	319±57
Wbc	3.102±0.81
Creatinin	0.94± 0.3

Anticoagulation was achieved with low-molecular-weight heparin in 114 (83%) patients and with unfractionated heparin in 22 (17%) patients. Systemic thrombolytic therapy was used in 5 patients (3.8%) (Table 2). Sixteen (12.4%) patients experienced bleeding complications. Bleeding rates did not differ between the groups.

Pulmonary thromboembolism severity index (%) was significantly higher in long-stay patients (52.61 ± 24 versus 38.59 ± 23, p = 0.001). When the CTPA findings are evaluated; increased right and left pulmonary artery diameter, right ventricle diameter and RV diameter/LV diameter ratio were associated with prolonged hospital stay. Detailed CTPA findings are shown in Table 3. Furthermore, increased pulmonary artery pressure in echocardiographic evaluation was also a predictor of prolonged hospital stay (p<0.001) (Table 3).

Elevated levels of BNP (516 mg / dL, 10-4694 versus 269 mg / dL, 10-1400 p = 0.014) and troponin (0.7 mg / dL 0.1-3.7 versus 0.1 mg / dL 0.1-3 p = 0.024) were remarkable in long-stay patients when compared with short-stay patients. On the other hand, there was no association between duration of hospitalization and elevated levels of CRP and d-dimer (Table 3).

Table 2. Medication used in the patients with pulmonary embolism and rates of bleeding events

Hospital Treatments of Patients With Pulmonary Embolism and bleeding event (n=136)	Grup 1. (n=74) >9 day	Grup 2. (n=62) <9 day	P value
Low-molecular-weight heparin (n,%83)	58	56	0.652
Unfractionated heparin (n,%17)	16	6	0.148
Warfarin (n,%78)	57	48	0.530
Thrombolytic therapy (n,%3,8)	3	2	0.780
Major and minor bleeding events (n,%12.4)	9	7	0.720

Table 3. Comparision of epidemiological, clinical, biochemical and radiological findings between thr groups

Characteristics of Patients With Pulmonary Embolism (n=136)	Long-stay group (n=83) >9 day	Short-stay group (n=53) <9 day	P value
Age, year	66±17	72±14	0.036
Wells score	5.32±2.27	5.11±4.6	0.72
Geneva score	6.46±1.75	6.26±4.69	0.73
Pulmonary artery pressure (mmHg)	53.59±18	42.17±14	<0.001
Pulmonary thromboembolism seveirty index(%)	52.61±24	38.59±23	0.001
Right ventricular diameter (mm)	44.13±8	39.43±8	0.003
Left ventricular diameter (mm)	26.70±4.46	24.45±4.5	0.007
Left pulmonary artery diameter (mm)	25.63±4.22	23.02±4.32	0.001
RV diameter/LV diameter	1.21±0.25	1.08±0.177	0.006
Pulmonary conus diameter	32.76±5.39	29.91±4.62	0.002
Pulmoner conus diameter/aortic conus diameter	0.92±0.17	0.84±019	0.023
Troponin	0.7(0.1-3.7)	0.1(0.1-3)	0.024
Brain Natriuretic Peptide	516(10-4694)	269(10-1400)	0.014
D-dimer	3452(978-9000)	3025(258-8524)	0.263
C-reactive protein	4.7(1-37)	5(1-43)	0.842

DISCUSSION

The results of our study revealed that higher degree of pulmonary artery obstruction and increased pulmonary artery pressure, right and left pulmonary artery diameter and age were associated with longer duration of hospitalization. The hospital stay was also prolonging with increasing ratio of RV diameter/LV diameter and pulmonary artery diameter/artic conus diameter. Elevated levels of troponin and BNP were biochemical predictors of longer hospital stay. These findings suggest that when these radiologic, echocardiographic and biochemical parameters are used together, a rational evaluation about hospital stay and hospitalization costs can be feasible.

PTE is usually caused by obstruction of the pulmonary artery or branches by the clothes originated from deep venous thrombosis (DVT). When advanced diagnostic methods are used, deep venous thrombus can be detected in 79% of PTE patients (7). PTE is the third most common acute cardiovascular disease after myocardial infarction and stroke (8). It is also a common complication of hospitalization and a leading cause of preventable hospital deaths. Although hospitalization is less common in PTE compared to stroke and acute coronary syndrome, in-hospital mortality is higher (9).

Actually, health spending studies are performed to present health services more efficiently. The economic burden that the community will be exposed to because of the disease is called cost of illness (10). Hospitalization costs are known to be the most important part of the health expenditures (10,11). Therefore, the parameters regarding the duration of hospitalization in PTE can be useful in terms of both prognosis of the patient and efficient use of health expenditures. Especially in the last two decades, the rate of hospitalization in PTE has increased disproportionally to the severe PTE diagnosis and therefore the cost of PTE in total health expenditures has increased (12). In a study investigating the cost of PTE in Spain, it was observed that 14021 patients were diagnosed with PTE in a 3 years period and found to have a cost of 16-20.2 million euros (13). In another study, it was found that the PTE increased the health spendings by about 2 times in patients who underwent major orthopedic surgery (14). As a result, PTE continues to be an expensive disease to diagnose and treat and also continues to have a high mortality rate despite advanced diagnosis and treatment modalities. For this reason, the findings of our study can be used for predicting duration of hospitalization and hence eventual health spending.

Clinical signs and symptoms may vary depending on the size, number and localization of the embolus, age and cardiopulmonary reserve of the patient, development of infarction, rate of resolution and recurrence. As expected, age and cardiopulmonary reserve of the patients were associated with the length of hospital stay in our study. Clinical presentations of PTE are classified as massive, submassive and non-massive (6). Acute right ventricular failure accompanied by hypotension, shock or cardiopulmonary arrest is present in massive PTE. Submassive PTE is characterized by normal systemic blood pressure and right ventricular dysfunction in echocardiography. In non-massive PTE, both systemic blood pressure and right ventricular function are normal (6). Patients with right heart overload are at higher risk for mortality (15). Consisted with the previous knowledge, the patients with right heart overload experienced prolonged hospital stay in our study.

Patients with suspected PTE are clinically classified to have low, moderate, and high probability by using scoring models including signs, symptoms and risk factors. Wells (Canadian) scoring model is the most frequently used one (6). The second is the Geneva score. In the analysis of 4 controlled trials involving the patients who were suspected to have PTE and underwent pulmonary angiography after emergency department admission, it was observed that the prevalence of PTE was 10% in low-probability patients, 30-40% in moderate probability patients and 67-81% in high probability patients (16). Interestingly, there was no association between clinical scoring models and duration of hospitalization in our study. The main reason for this can be the exclusion of patients with in hospital mortality.

CTPA is non-invasive method and currently more easily accessible. It provides rapid evaluation, direct visualization of the embolism and high diagnostic accuracy compared to scintigraphy. It enables evaluation of other causes of chest pain. CT venography can also be performed concomitantly (17) . A RV / LV diameter ratio > 0.9 in CTPA has been shown to be an independent predictor of the short-term complications (18). Another CT finding used to assess the severity and prognosis of PTE is the pulmonary artery obstruction index. Studies have shown that hemodynamic status deteriorates significantly when 30% and 50% of the pulmonary vascular bed occludes (19). In addition to their superiority in diagnosis, our findings demonstrated that CTPA parameters such as RV diameter/LV diameter ratio, pulmonary artery obstruction index and pulmonary artery diameter can serve in predicting prolonged hospital stay.

Transthoracic echocardiography may reveal right ventricular dysfunction and tricuspid regurgitation in patients with PTE. It is very useful in determination of severity of the diseases and selection of patients who are candidates for thrombolytic therapy (20). In patients with submassive PTE, the presence of right ventricular dilatation is a sign of short term mortality and thrombolytic therapy instead of anticoagulation is recommended in some of these patients (21). We found that in addition to CTPA, right ventricular overload findings in echocardiography can also be used to predict duration of hospital stay.

D-dimer is a plasmin-derived fibrin degradation product that is released after the endogenous fibrinolytic system breaks down the newly formed thrombus. Although the sensitivity of the D-dimer test is high, the specificity is low (22). In PTE, increased BNP, NT-proBNP and troponin levels secondary to acute right heart failure have been found to be associated with early mortality and poor prognosis (5).

In our study, elevated BNP and troponin levels were also associated with prolonged hospital stay. However, serum D-dimer and CRP levels did not different between short-stay and long-stay patients.

CONCLUSION

In PTE, the first step is rapid anticoagulation with intravenous unfractionated heparin or subcutaneous low molecular weight heparin (15). Thrombolytic drugs have shown to provide more rapid thrombus resolution within the first 24 hours when compared to heparin, whereas the improvement in pulmonary perfusion is similar at the end of 5-7 days (23). Although it is argued that the use of new direct oral anticoagulants may reduce the length of hospital stay (24), the treatment modality did not have any effect on the duration of hospitalization in our study.

Study limitations

The first is that the patients with chronic renal failure could not be included in the study. However, only clinical diagnosis without CTPA would affect the objectiveness of the study negatively. Secondly, cost-effectiveness analysis was not performed. Limited number of patients can also be considered as a limitation. However, our study is the first to demonstrate a correlation between duration of hospital stay and echocardiographic, radiologic and biochemical parameters.

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