Acute Pulmonary Embolism: Presentation, Diagnosis, Management and Factors Impacting Clinical Outcome in a Tertiary Cardiac Centre in Pakistan

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ABSTRACT

Objective: To evaluate the presentation, diagnosis, management and outcome of acute pulmonary embolism for assessing the factors impacting mortality in such patients.

Study Design: Descriptive study.

Place and Duration of Study: Rawalpindi Institute of Cardiology, Rawalpindi, Pakistan, from July 2015 to July 2018.

Methodology: Patients presenting with clinical suspicion of pulmonary embolism were subjected to a diagnostic algorithm consisting of Wells Rule, D-Dimer testing, echocardiography and CT pulmonary angiogram. Patients diagnosed with pulmonary embolism were subdivided into massive and submassive pulmonary embolism groups. Most patients diagnosed with massive pulmonary embolism were treated with streptokinase injection. For those diagnosed as submassive pulmonary embolism, the standard therapy remained anticoagulation with intravenous heparin, both the subsets of patients were further put on oral warfarin. Clinical outcome was defined as combined end-point including death during hospital stay, recurrence of PE and meed for repeat thrombolysis.

Results: A total of 174 patients diagnosed with pulmonary embolism were studied. The mean age was 49.1 ±14.8 years (range 23-88 years) with 109 (62.6%) patients being male. The in-hospital clinical course was uneventful in 144 (83%) patients. Twenty-two patients (12.6%) patients died, of whom 3 died from major bleeding, one from cancer, and 18 from the pulmonary embolism process (14 patients from refractory shock and 4 patients from recurrent PE). A total of 8 (4.6%) had fatal or non-fatal recurrent PE. In patients who had echocardiography both pre- and post-thrombolysis, initial RV dysfunction was reversible in 136 (78%) within 48h following thrombolytic therapy. By univariate analysis, only shock (SBP) and delay in diagnosis for more than 6 hours were associated with adverse event.

Conclusion: Early diagnosis by doing urgent CTPA in patients with suspected acute PE is the cornerstone in reducing mortality in acute PE patients.

Key Words: *Acute pulmonary embolism, CT pulmonary angiography (CTPA), Diagnostic delay, Adverse event.*

INTRODUCTION

Pulmonary embolism (PE) is common, relatively under-diagnosed clinical condition associated with high morbidity and mortality with most deaths occurring in the first few hours after presentation.[1] Despite advances in the diagnostic modalities, delays in pulmonary embolism diagnosis are common and represent an important issue.

The figures associated with mortality in acute pulmonary embolism are staggering.[2] The International Cooperative Embolism Registry of 2,454 patients reported a surprisingly high 90-day all-cause mortality of 17.4%. The cause of death in 45% of patients was pulmonary embolism itself. Recurrent pulmonary embolism, fatal or nonfatal, occurred in 8% of patients within 90 days.[3]

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Diagnostic delay in acute pulmonary embolism is quite common owing to nonspecific signs and symptoms. In a recent Turkish study up to 30% of patients diagnosed with PE had a delay longer than 7 days.[4,5] In a meta-analysis, it ranged from 4.8 to 8.4 days and is associated with increased mortality.[6,7] This stresses upon the need for prompt and early diagnosis of acute pulmonary embolism.

A tertiary cardiac centre with 24/7 primary PCI facility is usually equipped with a robust medical team of doctors and nurses in the emergency department with a highly efficient clinical laboratory, an echocardiography machine on the floor, and the facility of CT pulmonary angiogram, if needed. Early diagnosis and prompt treatment can be initiated easily in such a centre in suspected patients with acute pulmonary embolism.

There are very few studies in Pakistan assessing the impact of early diagnosis of acute pulmonary embolism. The aim of this study was to analyse the data of patients diagnosed with acute pulmonary embolism and their subsequent clinical outcomes to determine the factors affecting clinical outcomes.

METHODOLOGY

It is a descriptive study conducted at Rawalpindi Institute of Cardiology, Rawalpindi. Records of all the patients

who were diagnosed with acute pulmonary embolism with CT pulmonary angiogram presenting in the Emergency Department from July 2015 to July 2018, were included in the study. Patients presenting with clinical suspicion of pulmonary embolism were subjected to a diagnostic algorithm consisting of Wells Rule, D dimer testing, echocardiography and CT pulmonary angiogram.[8] Exclusion criteria were patients with no thrombus seen in the main pulmonary, right and left pulmonary, and the segmental arteries.

Based on clinical presentation and findings of CT pulmonary angiogram, the patients diagnosed with pulmonary angiogram were subdivided into two groups; massive and submassive pulmonary embolism. Massive pulmonary embolism was defined as acute pulmonary embolism (confirmed on CTPA) with hypotension (defined as systolic blood pressure, SBP, <90 mm Hg for at least 15 minutes, or persistent bradycardia (heart rate <40 bpm with signs or symptoms of shock).[9] Submassive pulmonary embolism was defined as acute pulmonary embolism (confirmed on CTPA) with no hypotension (systolic blood pressure >90 mm Hg) and RV dysfunction with myocardial necrosis defined as elevated troponin levels, RV dilatation and ECG changes.[10]

Most patients diagnosed with massive pulmonary embolism were treated with streptokinase injection with 50,000 units intravenously over half hour followed by continuous infusion of 100,000 units/hour for the next 12-24 hrs depending upon the response.[11] For those diagnosed as submassive pulmonary embolism, the treatment remained anticoagulation, initially with an intravenous bolus of 5000 IU of unfractionated heparin followed by an infusion to maintain the APTT at 1.5-2.5 times the control value until adequate replacement by oral warfarin, aiming for a target INR of 2-3 for 6-12 weeks.[12] Clinical outcome was defined as combined end-point including death during hospital stay, recurrence of PE and need for repeat thrombolysis.

The Statistical Package for Social Science SPSS version 11 was used for data analysis. Continuous variables are expressed as mean ±SD; and categorical variables, as frequency with percentages. Fisher's test was used to compare baseline results for massive and submassive pulmonary embolism as well as for clinical outcome. A p-value <0.05 was considered significant.

RESULTS

A total of 174 patients diagnosed with pulmonary embolism were studied. The mean age was 49.1 ±14.8 years with 109 (62.6%) patients being male. The clinical characteristics of these patients on admission are reported in the Table I.

One hundred and thirty-one patients (75.3%) presented with clinical features; their investigations suggestive of massive pulmonary embolism. Among these, 113 (86.2%) patients were in shock with systolic blood pressure less than 90 mm Hg and/or heart rate >110 beats/minute. Dyspnea was the most frequent presenting symptom, occurring in 166 (95.4%) patients. Eighty-five (48.9%) patients had an evidence of deep vein thrombosis while 45 (25.9%) patients had history of immobilisation; mostly prolonged travel. Interestingly, 17 (9.8%) patients had a history of recent pregnancy.

Among the 174 patients with PE, ECG findings depicting RV overload was present in 132 (75.8%) patients. RV strain pattern on echocardiography was present in 153 patients (87.9%), while 140 patients (80.5%) had positive D dimers.

The mean duration of hospital stay was 9 ±3 days. Of the 174 patients, 69 (39.6%) were treated with streptokinase (as a 12-24h infusion). In 146 (84%) patients, streptokinase infusion was started within 5 days of diagnosis of PE; while in 28 (16%) patients, it was administered between 5-15 days of diagnosis of PE. Infusion heparin (80 IU/kg IV stat followed by 15 IU/kg/hr with target APTT 1.5-2.5) was given to 54 (31%) of the patients. Among the 127 patients receiving streptokinase, 121 (95%) had massive PE. Among the 43 patients diagnosed with submassive pulmonary embolism, 37 (86%) received heparin.

Table I: Baseline characteristics of patients.

Patient characteristics at diagnosis	n = 174
Gender	
Male	109 (62.6%)
Female	65 (37.3%)
Age	49.1 ±14.8 years
Dyspnea	166 (95.4%)
Tachycardia	143 (82.2%)
Chest pain	32 (18.4%)
SBP <90 mm Hg	113 (64.9%)
Heart rate	112 ±8
ECG with RV overload	132 (75.8%)
Echocardiography with dilated RA and RV	153 (87.9%)
Massive PE	131 (75.3%)
Submassive PE	43 (24.7%)
D dimer	140 (80.5%)
Deep vein thrombosis	85 (48.9%)
Peripartum period	17 (9.8%)
Recent surgery	8 (4.6%)
Cancer	8 (4.6%)

Table II: Impact of different factors on adverse events in patients with acute pulmonary embolism.

Characteristic at baseline	n	Adverse event (n = 22)	p-value
Age >65 years	35	7 (20.0%)	0.158
Massive PE	131	17 (28.8%)	0.799
SBP <90mm Hg	113	21 (15.8%)	0.007
D dimer	140	16 (11.4%)	0.386
RV dilatation	153	18 (11.7%)	0.311
Thrombolysis	127	14 (11.0%)	0.309
Delay in diagnosis >6 hrs	52	18 (34.6%)	0.001

The in-hospital clinical course was uneventful in 144 (83%) patients. The mortality was 12% (n=22). Out of these 22 patients, 18 died from the disease process (14 from shock and 4 from disease recurrence), 3 suffered major bleeding and 1 had terminal cancer. A total of 8 (4.5%) had fatal or non-fatal recurrent PE. In patients who had echocardiography both pre- and post-thrombolysis, initial RV dysfunction was reversible in 136 (78%) within 48h following thrombolytic therapy; and among the 43 patients with sub-massive PE, it was reversible in 30 (69.7%) patients after treatment with infusion heparin. By univariate analysis, only shock (SBP <90mm Hg) and delay in diagnosis for more than 6 hours were associated with adverse event. Interestingly none of the other variables, including age >65 years, presence of DVT, massive PE, RV dilatation on echocardiography and thrombolysis were associated with the adverse event as shown in Table II.

DISCUSSION

This study is the first in the country discussing in detail the management and subsequent outcome of acute pulmonary embolism; a clinical condition with high mortality and the impact of various factors affecting it. The mean age of the patients diagnosed with acute pulmonary embolism was 49.1 $\pm$14.8 years. This is much younger than that in other studies,[13] which is mostly due to the lack of awareness and various cultural and socioeconomic factors. In this cohort, the commonest clinical presentation was of dyspnea (96.6%) and tachycardia (82.2%), which is consistent with other studies.[14]

The overall in-hospital mortality was 12.6%, which was comparable to Carson *et al*. and by the ICOPER investigators (9.5% and 11.4%).[3,15] A local study done by Zubairi *et al*. showed a mortality of 13% in acute pulmonary embolism;[16] but in that, only 30 patients were studied. A study done by Rajput *et al*., showed mortality of 15% in Indian population,[17] which is slightly higher than in this study. The main reason of the lower mortality in our study was early diagnosis of PE as the mortality was 4 out of 122 patients (3.3%) in whom the CTPA was done within 6 hours of presentation compared to 18 deaths out of 52 patients (34.6%) in whom the CTPA was done more than six hours of presentation.

In addition, the two sub-groups of patients – massive and submassive – PE were compared. The division was based on combination of hemodynamic profile on presentation and thrombus burden on CTPA. Interestingly, the mortality in the two subgroups was not significantly higher in the massive PE subgroup. This was in contrast to the study done by the ICOPER investigators.[3] Again, the main reason was that in most patients diagnosed with massive PE, diagnosis with CTPA was within six hours of the patient presentation in the hospital; and hence, early management.

In addition to diagnostic delay >6 hours, the presence of shock (defined as SBP <90 mm Hg) was another factor with significantly higher mortality. This was despite the fact that most of these patients were kept in intensive care and mostly treated with intravenous thrombolysis in the form of streptokinase. One-third of the patients, in whom CTPA was done six hours after the patients' arrival, had an adverse outcome. Similarly, 15.8% of patients who presented with shock had an adverse event. These findings were similar to other international studies,[18] thus stressing upon the fact that shock with SBP <90 mmHg and diagnostic delay were the main factors in acute PE related to high mortality.

In this study, the authors were able to discuss the impact of various factors affecting mortality in acute PE. This is the first study done in Pakistani population; that too in a centre where diagnostic modalities like arterial blood gases, D dimers, echocardiography and CT pulmonary angiogram were readily and easily available. Two factors that we found impacting the clinical outcomes were diagnostic delay and presence of shock. These results were achieved in a single centre and may not be reproducible in all centres. Larger long-term studies are required to determine the clinical value of these results.

CONCLUSION

Early diagnosis by doing urgent CTPA in patients with suspected acute PE is the cornerstone in reducing mortality in a clinical disease, which has a high mortality; and thus necessitating the presence of CT scan on the emergency floor.

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