Original Article

Outcome of pulmonary embolism and clinico-radiological predictors of mortality: Experience from a university hospital in Saudi Arabia

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Abstract:

OBJECTIVES: The objective of this study is to determine the outcome of pulmonary embolism (PE) and the clinico-radiological predictors of mortality in a university hospital setting.

METHODS: A Prospective observational study conducted at King Khalid University Hospital, Riyadh Saudi Arabia between January 2009 and 2012. A total of 105 consecutive patients (49.9 ± 18.7 years) with PE diagnosed by computed tomography pulmonary angiography were followed until death or hospital discharge.

RESULTS: Overall in hospital mortality rate was 8.6%, which is lower than other international reports. Two-thirds of patients developed PE during the hospitalization. The most common risk factors were surgery (35.2%), obesity (34.3%) and immobility (30.5%). The localization of the embolus was central in 32.4%, lobar in 19% and distal in 48.6%. A total of 26 patients (25%) had evidence of right ventricular strain and 14 (13.3%) were hypotensive. Multivariate analysis revealed that heart failure (Beta = −0.53, $P < 0.001$), palpitation (Beta = −0.24, $P = 0.014$) and high respiratory rate (Beta = −0.211, $P < 0.036$) were significant predictors of mortality.

There was no significant difference in the localization of the embolus or obstruction score between survivors and non-survivors.

CONCLUSION: The outcome of PE is improving; however, it remains an important risk factor for mortality in hospitalized patients. Congestive heart failure, tachypnea and tachycardia at presentation were associated with higher mortality. These factors need to be considered for risk stratification and management decisions of PE patients. Radiological quantification of clot burden was not a predictor of death.

Key words:

Outcome, pulmonary embolism predictors, obstruction score

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Pulmonary embolism (PE) is a devastating clinical problem with the mortality rate as high as 73% including mortality due to recurrent PE.[1-3] It is well-recognized now that early diagnosis is vital for reducing the mortality rate. Various prediction rules and validation models have been proposed to assist clinicians in the early diagnosis of PE.[4] Furthermore, it is important to stratify PE patients according to their expected prognosis as this may have consequences on management decisions.[5] The present study was undertaken to determine the outcome and clinico-radiological characteristics of patients with PE managed at a university hospital in Riyadh, Saudi Arabia.

Methods

This prospective observational study was conducted from January 2009 to 2012. The diagnosis of PE was made by computed tomography pulmonary angiography (CTPA), which was reviewed by two independent radiologists. Visualization of filling defects and cut-off within the contrast pacified pulmonary arteries down to its segmental branches on at least two subsequent scans was regarded as diagnostic of PE.[6] Patients with PE were followed-up until hospital discharge or death. The following data were recorded: Demographic features (age, sex), venous thromboembolism (VTE) risk factors (obesity, immobility, recent surgery, etc.), co-morbid diseases (chronic lung disease, cancer, congestive heart failure, central nervous system disorders, history of previous deep vein thrombosis [DVT]), presenting symptoms and signs (shortness of breath, chest pain, hemoptysis, heart rate, respiratory rate [RR], etc.), radiological findings (localization of emboli in central, lobar or distal arteries and obstruction index),[7] echocardiographic findings, treatment given and clinical outcome until hospital discharge. The primary outcome was in-hospital mortality rate, clinical deterioration and length of hospital stay. Clinical deterioration was defined as the development of hypotension

(blood pressure <90/60), endotracheal intubation, vasopressors, cardiopulmonary resuscitation and rescue thrombolytics.

The study was approved by the Institutional Review Board of the College of Medicine, King Saud University. Patient's informed consent was obtained from all patients before enrollment.

Statistical methods

Continuous variables and characteristics of the study population were described as mean ± standard deviation and percentage. Comparisons between two categorical variables were made using the Chi-square test or Fisher's exact test as appropriate. A *P* value less than 0.05 indicated statistical significance. Odds ratios (OR) and their corresponding 95% confidence intervals (CI) were computed to estimate the risk of death associated with the various risk factors that had significant *P* value. Nearly 95% CI that did not include the value of 1.0 indicated that the risk factor was significantly related to the occurrence of death. Multiple regressions were used to identify the best predictors of mortality. SPSS version 15 software (SPSS Inc, Chicago, Illinois) and Stats Direct version 1.9.8 software (Cam Code, Herts, United Kingdom) were used for the statistical analysis.

Results

We identified 105 Saudi patients with radiologically confirmed diagnosis of PE. Their mean age was 49.9 ± 18.7 years and 61 (58%) were males. Two-thirds of them (67 patients) developed PE during hospitalization, while the remaining presented to the emergency room with PE. The majority of hospitalized patients (39 patients, 58%) were from medical wards followed by general surgery (11 patients, 16%), trauma (8 patients, 12%) 4 patients from Obstetrics and gynecology, 2 patients each from Urology and Orthopedic wards and 1 patient developed PE in intensive care unit (ICU). Among hospitalized patients, 7 patients (10.4%) were not receiving DVT prophylaxis before the diagnosis of PE. Two of them died.

The main risk factors for PE in our study population were recent surgery (35.2%), obesity (34.3%), immobility (31.4%), history of previous DVT/PE (21%) and active malignancy (20%) [Table 1]. Neurological diseases was the most common concomitant condition present in 29.5% of the patients, followed by chronic lung disease in 26% and congestive heart failure in 25%. Shortness of breath was the most common presenting symptom in 73.3% of patients followed by chest pain (49.5%), cough (22.9%) and palpitation (21%). Two-thirds of the patients (65%) had tachycardia at presentation and 23% were tachypnic, but only 14 patients (13%) were hypotensive. PE was clinically suspected in 91% of patients and incidentally discovered in 9% of patients whose CTPA was ordered for other reasons. The localization of the embolus was central in 32.4%, lobar in 19% and distal in 48.6%. Forty seven patients (44.8%) had echocardiography (ECHO) and in 26 patients (25%) it showed right ventricular (RV) dysfunction as evidenced by increase tricuspid jet velocity regurgitation and RV dilatation or hypokinesia.

Nine patients (8.6%) died during the hospital stay, three patients within 48 h, five after 4 days and one after 6 days.

Table 1: Descriptive statistics for 105 patients with PE

Variable	Total number, *n*=105 (%)
Risk factors	
Recent surgery	37 (35.2)
Obesity	36 (34.3)
Immobility	32 (30.5)
Previous DVT/PE	22 (21.0)
Active malignancy	21 (20)
Trauma	8 (7.6)
Systemic lupus erythematous	6 (5.7)
Inflammatory bowel disease	6 (5.7)
Post-partum	6 (5.7)
Oral contraceptive	4 (3.8)
Nephrotic-syndrome	4 (3.8)
Antiphospho-lipid syndrome	2 (1.9)
Pregnancy	2 (1.9)
Myeloproliferative disease	2 (1.9)
Central line	2 (1.9)
Others	8 (7.6)
Concomitant conditions	
Neurological diseases	31 (29.5)
Congestive heart failure	26 (25.7)
Chronic lung disease	27 (25.7)
Musculo-skeletal disorders	12 (11.4)
Chronic kidney disease	9 (8.5)
Chronic liver disease	7 (6.6)

PE=Pulmonary embolism, DVT=Deep vein thrombosis

Thirteen patients were admitted to ICU due to clinical deterioration, one patient had cardiopulmonary resuscitation and 10 patients received thrombolytics. The average length of hospitalization was 20.0 ± 17.4 days.

Comparing PE patients who died to those who survived, older patients were insignificantly more prone for death (58.2 ± 12.4 vs. 49.1 ± 19, *P* = 0.12) similarly, non-survivors were more likely to be obese, however the difference did not reach statistical significance (*P* = 0.06). There was no gender predilection with regard to mortality; 55.6% of patients who died were males compared with 58.2% of those who survived (*P* = 0.88).

On the other hand, the risk of death was significantly higher in patients with chronic lung disease (OR = 4.2, 95% CI = 1.03-17.02, *P* = 0.046) and congestive heart failure (OR = 7.6, 95% CI = 1.44-49.8, *P* = 0.006) [Table 2]. However, there was no difference in chronic kidney disease (*P* = 0.17), chronic liver disease (*P* = 0.58) or neurological diseases (0.72).

Patients who presented with palpitations (OR = 10, 95% CI = 1.85-66.06, *P* = 0.0025) and tachypnea (RR >20) were also more likely to die from PE than others (OR = 5.07, 95% CI = 0.97-27.6, *P* = 0.027). Hypotension and tachycardia were more prevalent in patients who died from PE, however, these did not reach statistical significance (*P* = 0.09 and 0.14, respectively) [Table 2].

Similarly, there was no difference between survivors and non-survivors with regard to the localization of the clot or obstruction index as assessed by CTPA [Table 3], On the otherhand, RV dysfunction was statistically higher in patients who died from PE (OR = 0.22, 95% CI = 0.055-0.90, *P* = 0.04) [Table 3].

Table 2: Predictor variables for death

Risk factor		Number (%)		Odds ratio	95% CI
		Survivors (*n*=96)	Non-survivors (*n*=9)		
Obesity					
Yes	*n*=36	30 (31.2)	6 (66.7)	4.4	0.86-28.57
No	*n*=69				
P value	0.06				
Previous DVT/PE					
Yes	*n*=22	19 (19.8)	3 (33.3)	2.03	0.298-10.49
No	*n*=83				
P value	0.39				
Immobility					
Yes	*n*=33	29 (30.2)	4 (44.4)	1.71	0.31-8.56
No	*n*=67				
P value	0.47				
Active malignancy					
Yes	*n*=21	19 (19.8)	2 (22.2)	1.15	0.22-6.03
No	*n*=84				
P value	0.86				
Congestive heart failure					
Yes	*n*=26	20 (20.8)	6 (66.6)	7.6	1.44-49.80
No	*n*=79				
P value	0.006*				
Chronic lung disease					
Yes	*n*=27	22 (22.9)	5 (55.5)	4.20	1.03-17.02
No	*n*=28				
P value	0.046*				
Heart rate >100					
Yes	*n*=68	60 (62.5)	8 (88.8)	4.8	0.57-39.9
No	*n*=37				
P value	0.14				
High respiratory rate RR >20					
Yes	*n*=24	19 (19.8)	5 (55.5)	5.07	0.97-27.6
No	*n*=81				
P value	0.027*				
Hypotension (BP <90/60)					
Yes	*n*=14	11 (11.4)	3 (33.3)	3.86	0.54-21.12
No	*n*=91				
P value	0.098				
Oxygen saturation <90%					
Yes	*n*=42	38 (39.6)	4 (44.4)	1.22	0.31-4.83
No	*n*=63				
P value	0.77				
Palpitation					
Yes	*n*=22	16 (16.7)	6 (66.6)	10.0	1.85-66.09
No	*n*=83				
P value	0.0025*				

*Statistically significant at 5% level of significance Statistically significant at 5% level of significance. DVT=Deep vein thrombosis, CI=Confidence interval, PE=Pulmonary embolism, BP=Blood pressure, RR=Respiratory rate

Table 3: Comparison of CT scan and echocardiography findings in survivors and non-survivors

Variables	Survivors (*n*=96)	Non-survivors (*n*=9)	*P* value
PE localization			
Central no. (%)	29 (30.2)	5 (55.6)	0.15
Distal no. (%)	48 (50)	3 (33.3)	0.49
Lobar no. (%)	19 (19.8)	1 (11.1)	1.00
Obstruction index mean (±SD)	12.14 (±11.4)	13.44 (±14.5)	0.98
Right ventricular dysfunction no. (%)	21 (21.8)	5 (55.5)	0.04*

PE=Pulmonary embolism, SD=Standard deviation, CT=Computed tomography, *Statistically significant at 5% level of significance

When multiple regression analysis was used to test mortality predictors, the results indicated that congestive heart failure (Beta = −0.53, $P < 0.001$), palpitation (Beta = −0.24, $P = 0.014$) and high RR >20 (Beta = −0.211, $P < 0.036$) explained 47% of the variance ($R^2 = 0.469$, $P < 0.001$). Therefore, they were found to be significant mortality predictors.

Regarding the management of PE, low molecular weight heparin (LMWH) was the drug used for treatment in 86.7% of patients, whereas unfractionated heparin (UFH) was used in 31.4%. Patients who died were more likely receiving UFH than those who survived (OR = 0.11, 95% CI = 0.02-0.71, $P = 0.009$). Inferior vena cava filters were inserted in 6 patients preceding thrombolytic therapy.

Discussion

The present study provides an insight into the clinical and radiological characteristics and outcome of PE in Saudi cohort and their adverse prognostic factors. The overall mortality rate in the present study is 8.6%, which is lower than reported in previous studies.[5,8-10]

The MAPPET registry reported an overall mortality rate of 1001 patients with PE to be 29% (14% in the presence of hypotension, 25% in cases of cardiogenic shock and 65% post cardiac arrest)[11] whereas, the JaSPER study, from, Japan reported the in-hospital mortality rate to be 14%.[8]

One possible explanation of this disparity could be the observed younger age of patients in the present study compared with others. In the RIETE registry about 50% of patients were older than 70 years[12] Similarly, Ceylan *et al*. reported the mean age of their patients with PE to be 63 years.[13] This racial difference in age of presentation and mortality from PE has been described before, where Blacks were found to present at a younger age than Whites (57.7 vs. 64.8 years. $P < 0.001$).[1,8,9] This is also in accordance with earlier reports from Saudi Arabia that found the mean age of patients with DVT to be 44 years.[14]

The young age at presentation in our patients can be linked to the increase in thrombophilic mutations among Saudi patients as suggested by thrombophilic factors genotyping, but this remains to be further explored.[15,16] A recent report found a high rate of protein S/protein C deficiency in Saudi subjects who presented to the emergency room with PE.[17] Recent surgery, obesity immobility and history of previous VTE were identified to be the most common risk factors in our study population. This is in accordance with previous reports that showed the importance of these factors in identifying high risk groups for VTE and therefore were incorporated in the clinical prediction rules of PE.[18,19]

Chronic lung disease, congestive heart failure and the initial presentation of palpitation and tachypnea were significantly associated with higher mortality in our patients. Similar findings were also observed by Heit *et al*. who found chronic lung disease, congestive heart failure, neurologic disease to be among the independent predictors of short and long-term survival of patients with VTE.[18] This could be explained by the fact that patients with compromised cardiopulmonary status might be unable to withstand the hemodynamic effects of recurrent thromboembolism.

RV dysfunction was detected in 25% of our patients. This was significantly higher in patients who eventually died. However, ECHO is not recommended for routine diagnosis of PE due to its low sensitivity (60-70%). Several studies have found an increase of PE-related mortality in patients who had evidence of RV dysfunction on ECHO. In contrast, normal echocardiographic findings were associated with better outcome, and accordingly this was considered one of the important tools for assessing the prognosis of PE.[20,21]

The correlation between patient' outcome and embolic burden on computed tomography scan has been investigated before.[22-24] Earlier retrospective studies have identified the clot burden score to be predictive of short-term mortality. Van der Meer reported 11–fold increase risk of dying within 3 months, if the obstruction index was 40% or higher.[22] In contrast, two large prospective studies that included patients with symptomatic acute PE did not find significant association of obstruction score with 30-day all cause, death, clinical deterioration or 12-month all cause-mortality rate.[23,24] The findings of the current study are in agreement with these last reports.

It is worth noting that in the present study, LMWH was used in the management of most of our patients with PE. This practice is supported by many earlier studies and meta-analysis that showed equal efficacy of LMWH and UFH in the management of PE.[25-27] In addition, LMWH has the advantage of not requiring monitoring, easy administration and lower incidence of heparin induced thrombocytopenia and this is in accordance with the guidelines of the European Society of Cardiology.[25] However, we noted with much interest that patients who died were more likely to have received UFH than those who survived. This can be attributed to the fact that these patients were unstable and up to date, there are no studies supporting the use of LMWH in this group of high risk PE.[25-27]

Limitations to our study include the small number of patients and therefore our findings need to be verified by studies with larger number of patients. This may help in a better understanding of the clinical and radiological presentation of PE in our population and identify high risk patients who require more frequent monitoring and more aggressive therapeutic intervention.

Conclusion

Patients with PE in our center present at younger age and their mortality rate is lower than reported in studies elsewhere. The presence of concomitant cardio-respiratory diseases and the clinical presentation with palpitation and tachypnea in addition to the presence of RV dysfunction were found to be associated with increased mortality.

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