The Egyptian Journal of Hospital Medicine (July 2022) Vol. 88, Page 4101- 4105

Predictors of Short-Term Mortality in Patients with Acute Pulmonary Embolism

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ABSTRACT

Background: Pulmonary embolism (PE) is associated with short- and long-term adverse events including mortality. Prompt diagnosis, risk stratification and treatment can improve the outcome. The objective of the present study is to determine the predictors of early death within 30 days in the course of acute pulmonary embolism (APE). **Patients and methods:** One hundred patients with APE were recruited from both inpatients department and ICUs at Cardiothoracic Minia University Hospital .All patients subjected to detailed history, general and local chest examination. Laboratory investigation included CBC, Hs-CRP, troponin and D-dimer. CT pulmonary angiogram (CTPA) with calculation of pulmonary artery obstructive index (PAOI) using Qandali Score and measurement of right ventricle to left ventricle (RV/LV) ratio, Echo with measurement of pulmonary artery systolic pressure (PASP) were done for all patients. Patients were monitored for 30 days from the onset of symptoms to assess the mortality. **Results:** Patients classified according to outcome into survivors, 80 (80%) patients and 20 (20%) non-survivors patients. Po2 and Sao2 were significantly higher in survivors (P values 0.0001 and 0.05, respectively). Pulmonary Embolism Severity Index (PESI) was significantly higher in the non-survivor group (P value 0.001). PAOI and RV/LV ratio were higher in non survivors with (P value 0.001 and 0.001, respectively). Also central location of emboli was higher in non survivors representing. PASP was higher in non survivors (P value 0.001). **Conclusion:** The non-survivor group showed decrease Po2 and Sao2, higher PESI, PAOI, RV/LV ratio, and dilated RV compared with the survivor group. Thus these parameters could be predictors for poor patient outcome.

Keywords: Predictors factors, mortality, acute pulmonary embolism, Minia University, pulmonary embolism severity index.

INTRODUCTION

Venous thromboembolism is a heterogeneous disease with various presentations and prognoses. The key to appropriate therapy is therefore risk stratification to identify patients at high risk of death who should receive specific therapeutic management [(1)]. Pulmonary embolism (PE) is the most serious manifestation of venous embolism and is a potentially life-threatening condition [(2)]. It is associated with short and long term adverse events including mortality. Fatal PE has variable incidence in different studies ranging from <1% to 29% [(3,4, 5,6)].

We aimed to determine the predictors of early death within 30 days in the course of acute pulmonary embolism (APE)

PATIENTS AND METHODS

Our study was a prospective study of all patients with APE who were admitted at Cardiothoracic Minia University Hospital during the period between October 2019 and July 2021. Diagnosis of PE was confirmed by CT pulmonary angiogram (CTPA).

All patients were subjected to detailed history including risk factors, clinical presentation, and general and local chest examination. Routine Laboratory investigation included CBC, liver and renal function tests were done to all patients. Also for all patients arterial blood gases (ABG) with measurement of PO2 and calculation of A-a gradient was done. Measurement of serum troponin, D- dimer and high sensitive CRP (Hs-CRP) were done for all patients.

Transthoracic echocardiography was done to all patients with evaluation of pulmonary artery systolic pressure (PASP) and for the presence or absence of right ventricle dilatation.

CTPA images were revised by senior radiologist to evaluate the right ventricle to left ventricle ratio (RV/LV ratio) and assessment of pulmonary artery obstructive index (PAOI) [(7)].

Patients were followed up for 30 days from the onset of symptoms to assess the mortality that was attributed to the embolic event.

Ethical consent:

The nature of the present study was explained to all patients. The laboratory and radiological procedures represented standard care and posed no ethical conflicts. All patients agree to participate in the study. The agreement of the Research Ethics Committee of Minia Faculty of Medicine was obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi-square test ($\chi 2$) was done to calculate difference between two or more groups of qualitative

Received: 19/4/2022
Accepted: 16/6/2022

variables. Quantitative data were expressed as mean ± SD (standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value <0.05 was considered significant.

RESULTS

One hundred patients with acute PE are included in the study; 80 patients survived the 4 weeks follow up period **(Group I),** and the remaining 20 patients died within 4 weeks of presentation **(Group II).**

Table 1 showed that there was no significant difference between survivors and non-survivors regarding demographic characteristics.

Table (1): Demographic characteristic and comorbidities in the studied groups.

Variable	Survivors N= 80	Non survivors N= 20	P value
Gender Male	32 (40%)	6 (30%)	0.3
Age	47.37 ± 16.3	54.3 ± 14.5	0.1
DM	16 (20%)	5 (25%)	0.6
Hypertension	10 (12.5%)	2 (10%)	0.4

(DM) diabetes mellitus, (this sentence was deleted)

Table 2 showed that Po2 and Sao2 and was significantly higher in survivors (P values 0.0001 and 0.05, respectively). Pulmonary Embolism Severity Index (PESI) was significantly higher in the non-survivor group (P= 0.001).

Table (2): Comparison between the two groups regarding the vital signs and ABG at admission.

Variable	Survivors N= 80	Non survivors N= 20	P value
Temperature	37.36 ± 0.56	37.39 ± 0.29	0.8
RR	26.2 ± 5.7	26.3 ± 6.7	0.9
HR	90 ± 19.4	100.8 ± 23.8	0.09
DBP	73.9 ± 10.7	74.2 ± 9.9	0.9
SBP	117 .7 ± 17	113.1 ± 13	0.4
PH	7.37 ± 0.38	7.43 ± 0.056	0.6
Paco2	34.12 ± 6.3	32.87 ± 6.4	0.5
Hco3	24.34 ± 4.06	21.69 ± 0.74	0.02
PO2	72.3 ± 12.1	60.4 ± 12.5	0.0001 *
SaO2	91.2 ± 8.57	85.9 ± 9.8	0.05 *
PESI	1.7 ± 0.7	3.6 ± 0.7	0.001 *

(PO2) partial pressure of oxygen, (A-a gradient) The alveolar-arterial gradient, (PESI) Pulmonary Embolism Severity Index. (*) P <0.05 significant.

Table 3 shows that Hs-CRP was significantly higher in the non-survivor group (p value 0.02).

Table (3): Comparison of laboratory findings between survivors and non survivors.

Variable	Survivors N= 80	Non survivors N= 20	P value
HB (g/dL)	11.86 ± 1.98	12.06 ± 1.49	0.7
WBC (mcL)	9.82 ± 2.9	9.2 ± 2.6	0.5
Urea (mg/dL)	39.25 ± 3.4	42.3 ± 5.1	0.4
Creatinine (mg/dL)	0.88 ± 0.2	0.99 ± 0.2	1.1
ESR (mm/hr)	36.89 ± 3.35	35.3 ± 8.6	0.19
Albumin (g/L)	4.04 ± 0.57	4.13 ± 0.53	0.58
PNL count	8.8 ± 2.3	9.5 ± 2.03	0.3
Lymphocyte%	28.3 ± 1.8	29.7 ± 5.4	0.9
Hs-CRP (mg/dL)	29.7 ± 1.4	41.1 ± 5.2	0.02*
D-dimer (ng/mL)	642.1 ± 96.3	679.7 ± 124.3	0.4
Troponin (ng/mL)	0.10 ± 0.01	0.11 ± 0.01	0.9

(hs-CRP) The high-sensitivity C-reactive protein.. (*) P <0.05 significant.

Table 4 shows that (some words are deleted) CTPA, PAOI and RV/LV ratio were significantly higher in non survivors (p values 0.001 and 0.001, respectively). PASP was elevated in both groups with more significant elevation in the non-survivors group (P= 0.001). Also dilated right ventricle was present in 90% in the non-survivors (P= 0.03).

Table (4): Comparison of CTPA and transthoracic Echocardiographic findings in both groups.

Variable	Survivors N= 80	Non survivors N= 20	P value
RV/LV ratio	0.9 ± 0.2	1.5 ± 0.3	0.001 *
PAOI	19.1 ± 15.1	48.9 ± 11.9	0.001 *
ECHO Dilated right ventricle	32 (40%)	18 (90%)	0.03 *
PASP	41.3 ± 13.1	53.2 ± 13.67	0.001 *

RV/LV ratio Right Ventricle-to-Left Ventricle Diameter Ratio, (PAOI) pulmonary artery obstruction index, (PASP) Pulmonary arterial systolic pressure. (*) P <0.05 significant.

Table 5 shows that in the majority of the non-survivor group (70%) the embolus were located in the main pulmonary artery either alone or with lobar, segmental or sub segmental involvement. In the

majority of the survivors the emboli were located in the lobar, segmental or sub segmental arteries (77.5%).

Table (5): Location of embolus in CTPA in survivors and non survivors.

Affected artery	Survivors N= 80	Non survivors N= 20	P value
Main pulmonary artery only ± lobar, segmental or sub-segmental affection	18 (22.5%)	14 (70%)	0.001*
Isolated lobar/ segmental/ Sub segmental	62 (77.5%)	6 (30%)	0.001*

(*) P <0.05 significant.

DISCUSSION

PE is associated with short and long term adverse events including mortality. Fatal PE has variable incidence in different studies ranging from <1% to 29% [3,4,5,6,8]. In the current study, 20% of patients died within the first month of onset of symptoms. The variability in mortality rates could be attributed to the differences in studies populations and the type of patients studied.

Vital signs including O2 saturation, respiratory rate, and heart rate provide immediate feedback on acute physiological changes in emergency department patients [9]. Abnormal vital signs, such as respiratory rate and O2 saturation, which indicate compromised hemodynamics, have been demonstrated to predict ICU admission and in-hospital mortality in patients with PE [10,11].

Our results revealed that Pao2 and Sao2 were significantly lower in the non-survivors patients. In the current study sPESI was significantly higher in the non-survivors group. In a study conducted by **Wu *et al.*** [12] they found that sPESI and D-dimer were associated with in-hospital death from PE. Combining both sPESI and D-dimer level can significantly improve the specificity of predicting in-hospital death for patients with PE.

CRP is a well-known marker of inflammation and tissue damage. In the present study Hs-CRP was higher in non-survivors and this is agreement with **Araz *et al.*** [13] who found that changes in serum Hs-CRP levels can be a potential predictor of the outcomes for patients with PE. Also our results are in agreement with **Avci *et al.*** [14].

Abul *et al.* [15] explored the prognostic value of CRP in patients with acute PE and found that RV dysfunction was more frequent among the patients with elevated CRP levels when the patients were divided into groups according to CRP levels of less than 10 mg/L, (10–100 mg/L) and greater than 100 mg/L.

Jovanovic *et al.* [16] investigated the value of CRP at the time of hospital admission in predicting 30-day PE caused death in patients with spontaneous versus provoked PE. They found that CRP has a very good predictive value for spontaneous PE but is less valuable in provoked PE.

Prognosis of PE based on levels of D-dimer has shown mixed results, and data on in-hospital prognosis of stable patients are sparse.

Stein *et al.* [17] assessed in-hospital prognosis in 292 stable patients with PE. They found that markedly elevated levels of D-dimer did not indicate a high mortality from PE or all-cause mortality during hospitalization.

Our study found that there was no significant difference between survivors and non-survivors regarding serum D-dimer (P value 0.4), and this is supported by the results of **Lakhanpal *et al.*** [18].

In the current study, PAOI in non-survivors was significantly higher than in survivors (P= 0.001). In agreement with our finding, **Bazeed *et al.*** [19] found that PAOI is significantly higher in no-survivors. Our results are also supported by the findings of **Çildağ and Karaman** [20] who revealed a higher obstruction index in patients who had a poor prognosis. Similarly, **Bazeed *et al.*** [19] reported a significant difference in the PA obstruction index between survivors and non-survivors (P value <0.001).

Previous studies reported that the PAOI is a good predictor of the survival of patients with severe PE [12, 21, 22].

In our study the non-survivor had significantly higher incidence of central location of embolus either in main pulmonary artery only or main pulmonary artery with lobar, segmental or sub-segmental affection (70%), compared to survivors. **Al Otair *et al.*** [23] found that central location of emboli was higher in non-survivors (55.6%) compared to survivors (30.2%).

Vedovati *et al.* [24] concluded that in hemodynamically stable patients with acute PE, central emboli are associated with an increased risk for all-cause death or clinical deterioration. This risk is low in patients with segmental or subsegmental PE.

The importance of the assessment of right ventricle function in risk stratification of acute PE has been stressed by international guidelines. Right ventricle assessment may allow detection of high-risk patients before clinical deterioration. It was found that RV failure resulting from arterial obstruction is a good indicator for mortality in severe acute PE, as severe pulmonary hypertension develops, which produces RV dilatation [22,25]. Right ventricular dysfunction (RVD) can be assessed on CT by calculating right ventricular/left ventricular (RV/LV) diameter ratio. In a study that involved 32 patients with proven PE, the authors found that; CTPA findings that may predict short term mortality are the high grades of inferior vena cava reflux, RV/LV diameter ratio more than 1.2[26].

In our study, we found that RV/LV ratio was significantly higher in non-survivors, (P= 0.001). Our results are in agreement with several studies suggesting that an increased RVD/LVD ratio is a predictor of short-

term mortality after PE. **Collomb *et al.* [27], Ghaye *et al.* [28], Ghuysen *et al.* [29] Araoz *et al.* [30] and Meinel *et al.* [31]** reported RV/LV diameter ratio as the strongest predictor of the clinical outcome of PE. **Lim *et al.* [32]** found a RVD/LVD ratio of greater than 1 measured on axial sections indicative of RV strain at pulmonary CTA. In a study involved 635 patients with PE, multivariate analysis revealed that increase in RV/LV ratio more than 1 was independently associated with short-term mortality [33].

On the other hand **Stein *et al.* [34]** found no association between mortality and increased RV/LV ratio. The reason for this discrepancy in the literature may be due to the difference in the RV/LV ratio measurements) and diversity of CT acquisition (different CT scanner geometry).

In the current study, evaluation of the right ventricle by transthoracic echocardiography revealed that dilation of right ventricle was present in 90% of non-survivors whereas and only 40% of survivors had dilated right ventricle. **Dahhan *et al.* [35]** noticed RT ventricle dilatation in 50% of non-survivor in contrast to 42% of survivors.

Limitation: The study is limited by the small sample size in the early mortality group.

CONCLUSION

PE is a serious health problem with significant morbidity and mortality. Identification of patients at increased risk of early death from PE can facilitate allocation of patients who may benefit from ICU admission and more intensive therapy. High PESI, decreased oxygen tension, elevated hs-CRP, increased RV/LV ratio and PAOI and Elevated PASP can all predict short term mortality from PE.

Conflict of interest: The authors declare no conflict of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution: Authors contributed equally in the study.

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