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Outpatient treatment of pulmonary embolism: sPESI score and highly sensitive troponin may prove helpful

M Kartal, A Unal, E Goksu, D Yilmaz, F Gungor

Introduction: Despite advances in therapeutic and diagnostic options, acute pulmonary embolism (PE) is associated with high morbidity and mortality. Risk classification is important in deciding how and where to treat patients This study aimed to investigate simplified pulmonary embolism severity index (sPESI) scores and highly sensitive troponin levels to predict 30-day clinical outcomes. ***Methods:*** Patients with the symptoms of dyspnoea, chest pain, and haemoptysis were included in the study. Multiple detector computed tomography (CT) examinations were performed. If the patients' glomerular filtration rate levels were less than 60 ml/min/1.73 m^2, then the ventilation/perfusion (V/Q) scan was the preferred imaging modality. Venous blood samples were collected to test for highly sensitive troponin T levels (Elecsys troponin T high sensitive, Roche diagnostics). All patients were examined by two-dimensional bedside echocardiography for detection of right ventricular dilatation. Patients' baseline characteristics (sex, ages, etc.) were recorded along with co-morbidities, symptoms, haemodynamic conditions, all-cause mortality rates during hospitalisation, the duration of hospital stay, radiographic test results, and laboratory findings, and electrocardiography were also obtained during emergency department admission. Primary outcome measure was defined as death in a month. Logistic regression model was created to reveal the associated parameters related to mortality within a month of the emergency department visit. ***Results:*** One hundred and seventy patients suspected of PE underwent either a CT angiogram or pulmonary V/Q scan. In total 70 patients were diagnosed with PE and included in the study. The logistic regression model was created in order to assess poor prognosis markers. In addition to the troponin levels and sPESI scores commonly used for pulmonary embolism prognosis, right ventricular dilatation, heart rate, systolic blood pressure and oxygen saturation using logistic regression models were created. Positive troponin level (odds ratio: 5.23 and 95% confidence interval [CI] 1.03 to 26.51) and negative sPESI score (odds ratio 2.14 and 95% CI 1.00 to 4.60) were found to be significant. ***Conclusions:*** Some scoring systems, including PESI and sPESI score, can be used for predicting mortality in patients with pulmonary embolism. If sPESI score is zero, and troponin levels are negative, the patient can be discharged safely. (Hong Kong j.emerg.med. 2017;24:132-137)

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Introduction

Despite advances in therapeutic and diagnostic options, acute pulmonary embolism (PE) is associated with high morbidity and mortality. The clinical course of a pulmonary thromboembolism may follow a variable pattern, from asymptomatic clinical course to sudden death. While the mortality rate is <1% in some patients, it may be as high as 9% in patients with massive PE.[1] Haemodynamic parameters, including systemic blood pressure and heart rate, and associated co-morbidities such as malignancy, heart failure, or

pulmonary diseases, are important prognostic factors in the decision to admit patients with pulmonary thromboembolisms.[1-4] Therefore, risk classification is important in deciding how and where to treat patients. In this context, the use of the pulmonary embolism severity index (PESI)/simplified (sPESI) models, biomarkers, and imaging-based risk models is widely accepted (Table 1).[5,6]

The sPESI model includes six equally weighted variables: age in excess of 80 years; a history of cancer; a history of chronic cardiopulmonary disease; heart rate greater than 110 beats per minute; systolic blood pressure less than 100 mmHg, and arterial oxyhaemoglobin saturation at less than 90%. For patients with low risk based on the sPESI score, low molecular weight heparin (LMWH) treatment and outpatient follow up were suggested, and no significant difference was observed in the efficacy and safety of treatment relative to inpatient treatment.[7,8]

A meta-analysis conducted in the previous year compared both evaluation systems. PESI has discriminative power to predict the short-term death and adverse outcome events in patients with acute PE, the PESI and the sPESI have similar accuracy, while sPESI is easier to use.[9] Highly sensitive troponin-T (hsTnT) combined with the simplified PESI improves the prediction in 30-day short term clinical outcomes for PE patients.[10]

Table 1. Pulmonary embolism severity index (PESI) and simplified pulmonary embolism severity index (sPESI) score

Variable	PESI score[A]	sPESI score[B]
Age >80	Age in years	1
Male sex	+10	–
History of cancer	+30	1
History of heart failure	+10	1[c]
History of chronic lung disease	+10	–
Pulse rate ≥110/minute	+20	1
Systolic blood pressure <100 mmHg	+30	1
Respiratory rate ≥30/minute	+20	–
Temperature <36°C	+20	–
Altered mental status	+60	–
Oxygen saturation <90%	+20	1

A: PESI score were defined as 65 or less class 1; 66-85 class 2; 86-105 class 3; 106-125 class 4; more than 125 class 5. Patients in risk classes 1 and 2 are defined as being low risk; B: 0 low risk, 1 or more high risk; C: The variables combined into a single category of chronic cardiopulmonary disease

This study aimed to investigate sPESI scores and highly sensitive troponin levels to predict 30-day clinical outcomes.

Methods

This was a prospective study, performed between May 2012 and November 2013, in the emergency department (ED) of a tertiary care facility with 90,000 annual ED patient visits. The study has been approved by the institutional review board.

Study population

Patients with the symptoms of dyspnoea, chest pain, and haemoptysis were included in the study. Patients were informed prior to the study. Arrest patients, pregnant women, computed tomography-angiography (CT angiography) or ventilation/perfusion scan (V/Q scan) patients with unknown pulmonary hypertension, imaging suboptimal patients, and those who did not want to participate were excluded from the study. Multiple detector computed tomography examinations were performed either according to the clinical gestalt of the physician, or Well's criteria. If the patients' modification of diet in renal disease glomerular filtration rate levels were less than 60 ml/min/1.73 m^2, then the V/Q scan was the preferred imaging modality. All patients were examined by two-dimensional bedside echocardiography for the purpose of detecting right ventricular dilatation. Right ventricular dilatation was defined as right/left ventricular dilatation with a ratio ≥1 from the subcostal or apical view. In each case, the echocardiography was performed by a senior or attending emergency physician. Before the study, all senior residents and attending physicians were trained with the standard education program for detecting right ventricular dilatations with echocardiography.

Venous blood samples were collected to test for highly sensitive troponin T levels (Elecsys troponin T high

sensitive, Roche diagnostics) and the test was accepted as positive if the highly sensitive troponin level was >14 picogram/ml (pgr/ml). Patients' baseline characteristics (sex, ages, etc.) were recorded along with co-morbidities, symptoms, haemodynamic conditions, all-cause mortality rates during hospitalisation, the duration of hospital stay, radiographic test results, and laboratory findings, and electrocardiography were also obtained during emergency department admission.

Study protocol

The patients with PE diagnosis in the ED were consulted by the pulmonologist for inpatient or outpatient treatment. In conjunction with standard care, those with stable vital signs, negative troponin levels and negative sPESI scores were discharged. All patients had been seen at the hospital outpatient pulmonology unit by the following day. Pulmonologist was informed for study hypothesis. After one month, all patients were contacted by phone to ascertain if death had occurred. Before discharge, LMWH (1 mg/kg enoxaparin) was administered to each patient and warfarin was started. LMWH was continued two times a day until the international normalised ratio measured between two and three. In the study period, patients continued their use of warfarin.

Outcome measures

Primary outcome measure was defined as death in a month.

Statistical analysis

The parameters related to mortality were compared with the Chi Square (for parameter fit to a normal distribution) and Mann Whitney U tests. For 80% power and 0.05 confidence interval (CI) the sample size was calculated as 65 patients. A logistic regression model was created to reveal the associated parameters related to mortality within a month of the ED visit. A p-value of less than 0.05 was regarded as statistically significant. For Well's score, median and interquartile range (IQR) was used.

Results

During the study period 170 suspected PE patients underwent either a CT angiogram or pulmonary V/Q scan. In total 70 patients were diagnosed with PE, and those were included in the study. Two patients who could not be reached by phone were excluded (There was no official record of these two patient deaths within a month). The statistical analysis was therefore performed with a total of 68 patients (Figure 1).

The mean age of the study population was 60.34±17.49 years. Thirty (44.1%) patients were male, while 38 (55.9%) were female. The demographic characteristics of the patients are shown in Table 2.

Among the study population, 15 patients (22%) died, while 53 patients (78%) alive after the diagnosis of PE. When death-related parameters were considered, highly sensitive troponin levels (p=0.0025) and sPESI score (p=0.0001) were seen to be significant.

The logistic regression model was created in order to assess poor prognosis markers. In addition to the

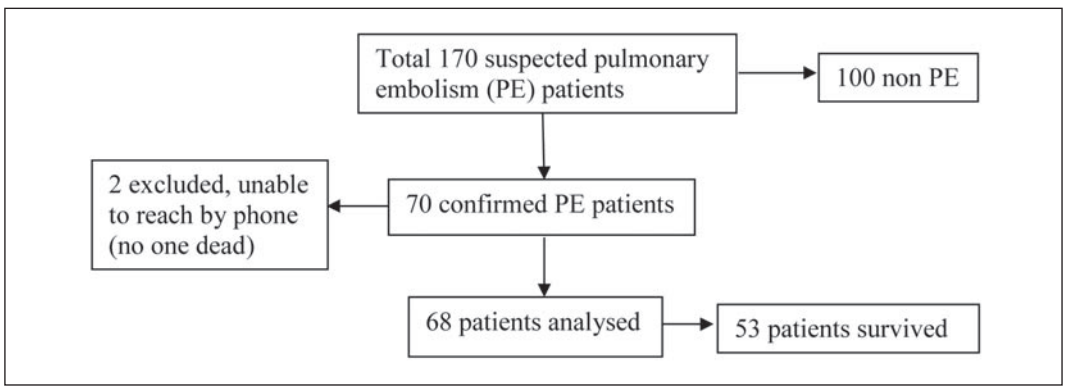


Figure 1. Patient flow chart.

troponin levels and sPESI scores commonly used for pulmonary embolism prognosis, right ventricular dilatation, heart rate, systolic blood pressure and oxygen saturation using logistic regression models were created. Positive troponin level (odds ratio: 5.23 and 95 CI% 1.03 to 26.51) and negative sPESI score (odds ratio 2.14 and 95% CI 1.00 to 4.60) were found to be significant.

When the patients who had died were studied, three patients were not defined with positive troponin levels, an odds ratio of five. On the other hand, all patients who had died were defined by the sPESI scores, but the odds ratio was found to be two (Table 3). No discharged patient died (Table 4).

Discussion

According to the results of the current study, patients with the diagnosis of PE and a sPESI score of zero may be safely discharged. Another result of this study is that high-sensitive troponin-positive patients should be reassessed in terms of requiring hospitalisation before being discharged from the ED.

For patients with acute symptomatic pulmonary embolism, accurate and objective models of prognosis could help clinicians to determine the appropriateness of early hospital discharge or completely ambulatory treatment. The PESI scoring system is a method for this purpose.[6] The accuracy and general applicability of the original PESI are now supported by derivation and validation in more than 17,000 patients from over 300 teaching and non-teaching hospitals across the United States and Europe.[7-11] For outpatient treatment of patients with pulmonary embolism, a PESI scores validation study has stated that PE patients can be treated as outpatients if the PESI score is 1-2.[12] However, the original PESI uses 11 clinical variables with different assigned weights, and its scoring depends on calculations that may be difficult to apply in the clinical setting. The PESI score was later simplified; this simplification increased adherence to its use among physicians.[6] It now includes only six variables (age >80 years, a history of cancer, a history of chronic cardiopulmonary disease, pulsations ≥110 beats per min, systolic blood pressure <100 mmHg and arterial oxyhaemoglobin saturation <90%) of equal weight (one point per variable). The score corresponds to the following classifications: 0 points = low risk; 1 or more points = high risk. This study indicated that the simplified PESI successfully predicts 30-day mortality after acute symptomatic PE. Therefore, the simplified PESI may be considered accurate in identifying low-risk patients with acute PE in real-world clinical situations.

Table 2. Patient characteristics

	All	Dead	Alive	Ss*
Gender	68	15	53	p=0.16
Male	30 (44.1%)	9	21	
Female	38 (55.9%)	6	32	
Age (years)	60.3±17.5	61.93±15.51	59.89±18.13	p=0.69
Wells score (median-IQR)	4.5 (3,0-5,8)	4.5 (3.0-6.0)	4.5 (3.0-5.7)	p=0.44
Pulse rate/minute	101.3±18.9	112.67±24.85	98.11±15.70	p=0.06
Respiratory rate/minute (median-IQR)	28 (22-34)	34 (28-40)	26 (20-32)	p=0.002
Hypotension**	6	4	2	p=0.006
SpO_2 ≥90%	18	6	12	p=0.067
Right ventricular dilatation***	13 (19.1%)	4	9	p=0.4
SPESI ≥1	38 (55.9%)	15	23	p=0.279
Highly sensitive troponin (+)	29 (42.6%)	12	17	p=0.001

*Ss: Statistical significance; **Hypotension: if systolic blood pressure <100 mmHg; ***Right ventricular dilatation: if right/left ventricle >1
IQR=interquartile range; SPESI=simplified pulmonary embolism severity index

The value of cardiac troponins has been investigated previously. Ozsu et al investigated the role of troponins and sPESI score in predicting mortality. This prospective short study included 206 patients. 90-day mortality was identified as the endpoint. They found that patients with acute PE, low-risk sPESI, and negative troponin levels can be safely treated in outpatient settings. They used standard cardiac troponins.[10] Additionally, Akgullu et al investigated the role of troponins in predicting early mortality with other parameters. This retrospective study included 206 patients. The authors created a model to ascertain which parameters can indicate possible death. According to their findings, in addition to sPESI, creatinine and QTc intervals and troponin levels were significant.[11] In both studies, standard troponin levels were used; standard troponin level, in terms of cardiac effects, is a reliable parameter. However, high sensitivity of troponin levels, in terms of determining the cardiac effects, has been determined to be more effective.[10] Lankeit et al found a good parameter for the prognosis of high sensitivity troponin levels.[13] Furthermore, Ozsu et al investigated the efficacy of highly sensitive troponin as a predictor of survival in 121 patients. Normal high sensitivity troponin levels, coupled with the lowest score of the sPESI, were identified as predictors of low mortality. This is stated on the basis that the patient can be discharged.[10] Likewise, in the current study, highly sensitive troponin levels of pulmonary embolism were determined as being useful in predicting the prognosis.

Table 3. Logistic regression analysis about death

Parameter	Odds ratio	95% confidence interval
Highly sensitive troponin	5.23	1.03 to 26.51
sPESI score	2.14	1.00 to 4.60
Right ventricular dilatation	0.33	0.004 to 2.68
SpO_2 (%)	0.96	0.82 to 1.05
Hypotension	1.10	0.79 to 1.52
Pulse rate	0.008	0.02 to 0.67

Remarks: Highly sensitive troponin >0.14 picogram/ml; sPESI score was defined in Table 1; Right ventricular dilatation: right/left ventricle ratio >1; Hypotension: systolic blood pressure <100 mmHg; Pulse rate >100 beats/minute.

Table 4. sPESI score, troponin and death relationship

Parameter	Dead's	Total
sPESI = 0, Troponin(-)	0	23
sPESI ≥1, Troponin(-)	3	16
sPESI = 0, Troponin(+)	0	7
sPESI ≥1 , Troponin(+)	12	22

According to the current research, a troponin-based model was created when the deceased had been identified, although in three patients this could not be recognised. However, none of the patients died with sPESI at zero. On the other hand, the odds ratio for troponin in the analysis seems to be better. These two parameters might facilitate the decision to continue the treatment of patients who are either admitted or discharged. Studies with larger numbers of patients may give better information on the role of troponin in this regard.

Our study has several limitations. Firstly, our study population was relatively small. Secondly, our study had a relatively small outcome of interest (death number). Our analysis might therefore have been affected by the small number of deceased patients.

Conclusion

Pulmonary embolism in the emergency room is an often diagnosed and potentially fatal disease. Some scoring systems, including PESI and sPESI score, can be used for predicting mortality. If sPESI score is zero, and troponin levels are negative, the patient can be discharged safely.

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