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Brief communication (Original)

Clinical factors associated with death from acute pulmonary embolism in Thailand

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Background: Acute pulmonary embolism (APE) is under diagnosed and may be fatal. Computed tomographic pulmonary angiography (CTPA) showing right ventricular failure is associated with mortality in APE. In resource-limited facilities, clinical factors are crucial.

Objectives: We studied clinical factors that were associated with death from APE.

Methods: We enrolled patients with APE proven by CTPA between January 1, 2007 and July 31, 2011 at Khon Kaen University. Clinical factors associated with death from APE were studied by multiple logistic regression analysis. An online tool to assess risk of death from APE was also used.

Results: There were 81 eligible patients in the study. Of those, 20 patients (25%) died within 3 months. Clinical factors significantly associated with death were low systolic blood pressure (SBP), high pulse rate, and low oxygen saturation at presentation.

Conclusions: Initial systolic blood pressure, pulse rate, and oxygen saturation are associated with mortality from APE.

Keywords: Clinical factors, mortality, online tool, predictors, pulmonary embolism

Acute pulmonary embolism (APE) is a challenging condition and may be fatal if the diagnosis is delayed or missed. At autopsy, 23.6% of surgical patients had pulmonary emboli [1]. Clinical diagnosis of APE is difficult because of nonspecific clinical features. Computed tomographic pulmonary angiography (CTPA) is considered the criterion standard as an investigative tool for diagnosis of APE [2, 3]. CTPA can be used to predict mortality and outcome of patients with APE [4-6].

Right ventricular (RV) pressure overload is an important predictor of death from APE [4]. A right ventricular/left ventricular ratio of >1 as determined by CTPA indicates RV dysfunction and is significantly related to mortality from APE.

Thailand and other developing countries face the problem of limited resources. Diagnosis, based on clinical signs, is more practical and realistic in this setting. We studied clinical factors associated with death from APE.

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Methods

The study included all APE patients diagnosed between January 1, 2007 and July 31, 2011, by CTPA at Khon Kaen University Hospital in Thailand. CTPA techniques and findings are described elsewhere [7]. Baseline characteristics and clinical factors were retrospectively extracted from medical charts retrospectively. The study protocol was approved by the Ethics Committee for Human Research, Khon Kaen University, Khon Kaen, Thailand (HE541214). The committee allowed the authors to publish all data of the study.

Clinical factors included age, sex, grading of APE, causes of APE, body weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate, hematocrit and serum creatinine levels, international normalized ratio (INR) value, oxygen saturation level,

and electrocardiographic (ECG) findings. All factors were routinely recorded during hospital admission or on presentation of APE.

Patients were divided into two groups: survivors and those who died. Clinical factors of the groups were compared by descriptive statistics. Wilcoxon rank-sum and Fisher's exact tests were used to compare differences in numbers and proportions, respectively, between the two groups. Differences where $P < 0.05$ were considered significant.

Univariate logistic regression analyses were used to calculate the crude odds ratio (OR) for each variable for APE mortality. All variables with $P < 0.20$ in univariate analysis were included in subsequent multivariate logistic regression analyses. Variables with $P > 0.25$ in the multivariate mode were excluded using a stepwise approach. The final model retained all variables with $P < 0.25$. Analytical results were presented in terms of crude OR, adjusted OR, and 95% confidence interval (CI). Nagelkerke's R^2 was calculated to identify the proportion of explained variance in the model. All data analyses were performed on a personal computer using Stata software version 10.1 (StataCorp, College Station, TX, USA).

Results

There were 251 possible cases of pulmonary embolism during the study period; 81 patients (32.3%) with CTPA met the study criteria. Of those, 20 patients (25%) died within three months. The death group had a significantly higher proportion of patients with cancer and having a RV strain pattern on the ECG (**Table 1**). SBP, DBP, hematocrit, and oxygen saturation were also significantly less in patients who died, while the pulse rate and INR levels were significantly higher (**Table 1**). The median SBP and pulse rate of patients who died were 97.5 (range 90–110) mmHg and 113 (range 102–128) beats/min. The minimum SBP and highest pulse rate of APE patients who survived were 118 mmHg and 92 beats/min.

Systolic blood pressure of <110 mmHg and pulse rate of >92 beats/min were associated with death, using multiple logistic regression analysis. There were 4 clinical factors remaining in the final mode, derived by stepwise methods: age, oxygen saturation, RV strain pattern on the ECG, and hematocrit level (**Table 2**). Only oxygen saturation was significantly associated with death from APE (adjusted OR 0.21; 95% CI 0.06, 0.78). The R^2 value for the final model was 0.77. An online tool for calculating the risk of pulmonary embolism mortality is available at *http://202.28.94.20/pulmonary*.

Table 1. Clinical factors of acute pulmonary embolism patients, categorized by survival group

Variables	Survivors N = 61	Deaths N = 20	*P*
Age, years	52.97 (± 15.50)	52.05 (± 11.92)	0.71
Male gender, n (%)	35 (57)	10 (50)	0.57
Cancer, n (%)	28 (46)	10 (50)	0.80
Body weight, kg	62.03 (7.6)	59.35 (6.8)	0.12
SBP, mmHg	134 (10)	98 (7)	<0.001
DBP, mmHg	82.8 (5)	61.8 (9)	<0.001
Pulse rate, bpm	72.3 (11)	113.8 (8)	<0.001
Hematocrit, %	33.8 (3)	29.9 (3)	<0.001
Serum creatinine, mg/dL	0.99 (2.8)	1.41 (0.2)	<0.001
INR	0.99 (0.2)	1.13 (0.2)	0.02
Oxygenation, %	94.3 (3.0)	91.9 (5.4)	<0.001
ECG: RV strain, n (%)	8 (13)	11 (55)	<0.001

Data presented as mean (SD) unless indicated otherwise, SBP = systolic blood pressure, DBP = diastolic blood pressure, INR = international normalized ratio, ECG = electrocardiography, RV = right ventricle

Table 2. Factors associated with death, by multiple logistic regression analysis

Variables	Univariate odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Age	1.00 (0.96, 1.03)	1.08 (0.93, 1.26)
Oxygenation	0.32 (0.14, 0.71)	0.21 (0.06, 0.78)
ECG: right ventricle strain	8.10 (2.56, 25.64)	4.04 (0.40, 40.57)
Cancer	1.18 (0.43, 3.24)	3.02 (0.21, 44.39)

Discussion

The mortality rate of APE in this study was 25%, and all patients died within 3 months. From a previous report, predictors of in hospital prognosis in APE consisting of sudden onset of symptoms, overt right ventricular failure, hypoxemia at admission, low SBP and DBP, deranged liver function tests, conduction block [8]. In the present study, 3 significant clinical factors associated with death from APE were similar to those previously reported including low SBP, high pulse rate, and low oxygen saturation [8].

Both SBP and pulse rate were dramatically associated with mortality from APE. All patients who died had SBP at presentation of APE <110 mmHg and pulse rate of >92 beats/min. Both factors may indicate massive APE and early signs of obstructive shock [2]. Prompt management and further investigation are necessary in these patients, particularly in a resource-limited setting. Physicians should be aware of a high mortality rate if these factors are present in APE patients. Emergency referral for CTPA or thrombolytic therapy may be warranted [2].

Oxygen saturation was another significant survival factor of APE in this study. It was negatively associated with mortality. In other words, patients with high oxygen saturation at APE presentation will have a low mortality rate. Every 1% increase in oxygen level lowers the mortality rate by 79%. Oxygen desaturation also indicated massive APE. Having low oxygen saturation (<90%) was shown to be related to worse outcome at 30 days [9, 10].

RV failure, as evidenced by CTPA, was previously shown to predict mortality in APE [4]. RV strain patterns on an ECG may be associated with increased RV pressure load. However, this was not associated with mortality from APE. To detect RV strain, ECG results may not be as sensitive as the RV/LV ratio from CTPA, which may show RV pressure load earlier than ECG changes. However, right ventricular dysfunction as determined by echocardiography was a predictor for 30-day mortality, with 19% sensitivity and 95% specificity [11]. Thus, ECG findings are less sensitive than echocardiography and CTPA in detecting RV strain.

The strength of this study is that all patients were diagnosed with APE by CTPA. Predictors in the analysis were clinical factors that can be practically applied. An online tool is also provided to evaluate patients at high-risk. Physicians therefore can choose appropriate management techniques, such as thrombolytic therapy, embolectomy or other interventions [7, 12].

Limitations of the study included the small number of patients included reducing its power, and that the results of this study may apply to only Thai or Asian populations. Pulmonary embolism in our hospital included 251 cases over 3.5 years or 71 patients a year. The rate of pulmonary embolism in Asian population after knee surgery was 0.01%–0.6% [13, 14], which was lower than that reported in western countries. The low rate of venous thromboembolism in Asians has been attributed to several factors including their lower prevalence of obesity, genetic factors, or dietary pattern [13].

In conclusion, low systolic blood pressure, high pulse rate, and low oxygen saturation at presentation were associated with mortality in patients with acute pulmonary embolism.

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Conflict of interest statement

The authors declare that there is no conflict of interest in this research.

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