Original Article

Characteristics and Mortality in High-, Intermediate-, and Low-Risk Acute Pulmonary Embolism Patients in the Emergency Department

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Background: Acute pulmonary embolism (APE) is a life-threatening condition. However, most APE patients have non-specific signs and symptoms. In 2019, the European Society of Cardiology published guidelines classifying the severity of APE, but no study has yet been conducted in the Thai population based on those guidelines.

Objective: To study characteristics and mortality in hospital, at 30 days, and at 1 year in APE patients classified by disease severity.

Materials and Methods: This was a retrospective descriptive study. The population consisted of patients diagnosed with acute pulmonary embolism at the emergency department of Khon Kaen University's Srinagarind Hospital from January 1, 2008 to November 30, 2018. Data were collected by reviewing hospital information program, medical charts, and PACS. Statistical analysis was performed using a Fisher's exact test to study the characteristics of patients and the death rate among these patients.

Results: A total of 110 patients had confirmed diagnoses of APE, 60.91% who were female. In terms of risk level, 2.72%, 35.45%, and 3.63% of patients were high-, intermediate-, and low-risk, respectively. Immobilization was significantly associated with high- and intermediate-risk, and high-sensitivity cardiac troponin t-test (hs-cTnT), N-terminal pro b-type natriuretic peptide (NTproBNP) levels, and RV dilatation were significantly associated with disease severity. Most patients received medical treatment. Mortality in hospital, at 30 days, and at 1 year was 9.09%, 11.81%, and 31.81%, respectively.

Conclusion: Some patient characteristics were associated with the disease severity. The mortality rate was high in the intermediate-risk group. This differed from the results of other studies, which found higher mortality rates in high-risk patients. Due to the small population in this study (especially high-risk patients) further research is necessary.

Keywords: Acute pulmonary embolism, ESC PE guideline 2019, Emergency department

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Acute pulmonary embolism (APE) is a life-threatening emergency condition. It has a worldwide incidence of 39 to 115 people per 100,000 population[1-7]. The incidence in Asian populations (Taiwan, Korea, and Hong Kong) has been reported to be 13.8 to 19.9 people per 100,000 population[8]. A study at Ramathibodi Hospital in Thailand, found the incidence of venous thrombosis to be 0.5 to 0.7% in in-hospital patients[9].

In 2014, The European Society of Cardiology (ESC)[10] studied the risk stratification of APE and found that some characteristics were common in high-risk patients but rare or absent in low-risk patients such as low blood pressure, a right ventricle enlargement, and cancer. A study at Siriraj Hospital from 2001 to 2005[11] found that the characteristics of APE patients in Thailand did not differ from those found in European countries and that malignancy was a risk factor for APE. The 2019, the European Society of Cardiology published guidelines for the diagnosis and treatment of acute pulmonary embolism, in which patients were classified according to severity (high, intermediate, and low). This classification is associated with mortality and informs treatment guidelines. However, there has yet been no study of the characteristics of patients with acute pulmonary embolism according to this severity classification. The objective of this study was thus to identify the characteristics of patients with varying levels of APE severity and the mortality rate over time in a Thai university hospital.

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Materials and Methods

This was a retrospective descriptive study. The sample consisted of 110 patients over 18 years of age who had been diagnosed with APE at the Srinagarind Hospital emergency department from January 2008 to November 2018. The exclusion criterion was incomplete medical data from the electronic medical chart program. Ethics approval was

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provided by the Khon Kaen University Ethics Committee for Human Research (HE621415).

The sample size was calculated based on estimation of a population with specified absolute precision which use interesting symptoms that was dyspnea. We used 0.939, 0.05, and 5 as the prevalence number, absolute precision, and alpha, respectively. We determined that a sample size of 101 would be required.

The primary outcome was the characteristics of patients diagnosed with acute pulmonary embolism at the emergency department according to severity of disease. The secondary outcomes were the mortality rate in hospital, at 30 days, and at 1 year in these patients and adverse effects (rehospitalization with cardiovascular symptoms within 1 year).

Statistical analysis was performed using STATA version 19.0.2. Categorical data were presented as percentages, and continuous data were presented using mean and standard deviation. Data analysis was performed using a Fisher's Exact test for data relationships between the two groups.

Results

One hundred ten subjects were examined. Three were high-risk, 32 were intermediate-high-risk, 71 were intermediate-low-risk and 4 were low-risk according to the 2019 ESC guidelines regarding severity of acute pulmonary embolisms.

Most of the patients were female in all groups. In the intermediate-high-, intermediate-low-, and low-risk groups, 65.63%, 50.70%, and 75%, respectively, were between 50 and 75 years of age. In terms of co-morbid diseases, bedridden status was significantly associated with disease severity (Table 1).

The most common chief complaints, symptoms, and signs in all groups were dyspnea and tachypnea. However, there was no statistically significant relationship between chief complaints, symptoms, and signs and disease severity (Table 2).

The authors found hypoxemia from arterial blood gas in all groups. However, there was no statistically significant relationship between arterial blood gas and the severity of disease. All patients in the high-risk group had positive age-adjusted D-dimer results. Fifty-eight patients underwent NTproBNP testing, 40 of whom had NTproBNP >600 ng/L. NTproBNP was significantly correlated with disease severity. Most of the patients had sinus tachycardia and normal sinus rhythm on the ECG. Chest x-rays revealed most of the patients to have pulmonary parenchymal lesions. Only 7% of patients in the intermediate-risk group had Westermark's sign and only 2% in the low-risk group had Hampton's sign. Right ventricle dysfunction was the most common echocardiographic finding in all groups. Right ventricle dilatation and left ventricle D shape were significantly correlated with disease severity. Most of the patients in the intermediate-high-risk group had main pulmonary lesions according to a CT pulmonary angiogram (CTPA), but most in the intermediate-low- and low-risk groups had segmental lesions (Table 3).

In terms of treatment, most of the patients received medication. Only one patient from the intermediate-low-risk group underwent surgical thrombectomy. All patients in the high-risk group received low molecular weight heparin treatment. In terms of outcome, 100 of 110 patients survived (90.9%). The in-hospital mortality rate was 9.09% (6.36%

Table 1. Patient characteristics classified by severity of disease

The patient characteristics (n = 110)	High risk (n = 3)	Intermediate risk		Low risk (n = 4)	*p*-value
		Intermediate High (n = 32)	Intermediate Low (n = 7)		
Sex (%)					
Male	1 (33.33)	15 (46.88)	26 (36.62)	1 (25)	0.775
Female	2 (66.67)	17 (53.13)	45 (63.38)	3 (75)	
Age (year) (%)					
18 to 49	2 (66.67)	6 (18.75)	15 (21.13)	0	0.629
50 to 75	1 (33.33)	21 (65.63)	36 (50.70)	3 (75)	
>75	0	5 (15.63)	20 (28.17)	1 (25)	
Co-morbid disease (n)					
Cancer	1	15	37	0	0.233
Hypertension	0	11	21	1	0.830
Diabetes	0	6	10	1	0.718
Coronary disease	1	4	10	1	0.433
Stroke	0	1	5	1	0.376
Bedridden	1	3	1	0	0.044*
Oral contraceptive	1	1	2	0	0.185
Other	2	12	33	3	0.441

* Statistical significance

Table 2. Chief complaints, symptoms, and signs classified by severity of disease

Chief complaints, symptoms and signs (n = 110)	High risk (n = 3)	Intermediate		Low (n = 4)	*p*-value
		Intermediate High (n = 32)	Intermediate Low (n = 71)		
Chief complaints (%)					0.734
Dyspnea	3 (100)	26 (81.25)	56 (78.87)	3 (75.00)	
Leg swelling	0	3 (9.38)	7 (9.86)	0	
Chest pain	0	1 (3.13)	3 (4.23)	0	
Syncope, near syncope	0	2 (6.25)	2 (2.82)	0	
Other	0	0	3 (4.23)	1 (25)	
Symptoms (n)					
Dyspnea	3	30	59	3	0.283
Leg edema	0	13	19	0	0.217
Cough	0	5	12	0	>0.999
Chest pain	0	4	9	1	0.759
Orthopnea	0	4	8	0	>0.999
Palpitation	0	3	5	0	0.827
Syncope, near syncope	0	3	3	0	0.580
Signs (n)					
Tachypnea (RR >20/min)	2	25	47	1	0.143
Tachycardia (HR >100/min)	1	18	37	0	0.172
Pitting edema	1	25	35	1	0.826
Hypoxemia (O_2 sat <90% room air)	1	17	34	0	0.251
Fever	0	2	3	0	0.746
Decreased mental status	0	1	3	1	0.307

in the intermediate-low-risk group). Mortality at 30 days was 11.81%, most cases of which were in the intermediate-risk group. The mortality rate at 1 year was 31.81%, with most cases in the intermediate-low-risk group. The rate of rehospitalization with cardiovascular disease within 1 year was 39.09%, most cases of which were in the intermediate-low-risk group (Table 4).

Discussion

Most of the patients in this study were female, which is consistent with previous studies in Asian populations[11-14]. A study of Barrios et al[15] found that male and female patients had different disease characteristics, with more female patients being older, bedridden, and experiencing syncope. They also had higher NTproBNP values than their male counterparts, but lower rates of COPD and cancer. Most of the patients in the present study were 50 to 75 years old, which is consistent with a 2019 ESC study[1] that found that the incidence of APE increases with age. In terms of co-morbid diseases, we found that bedridden status was correlated with disease severity, in that all bedridden patients were in the intermediate- and high-risk groups. In terms of laboratory results, the authors found that NTproBNP level was significantly associated with disease severity, which is consistent findings by the ESC[1] that NTproBNP >600 ng/L is associated with poor disease prognosis. Only one patient in the high-risk group submitted to NTproBNP examination, with a result of 419 ng/L. That patient had not died after 1 year. In the intermediate-risk group, 68.96% of patients had NTproBNP >600 ng/L. Sinus tachycardia was the most common ECG finding, which is consistent with a previous study[12]. Although the S1Q3T3 pattern is specific to APE, it was not found in the high-risk patients. We found that RV dysfunction was associated with disease severity, which is consistent with previous studies[1,10,11].

In terms of the patient outcomes, the intermediate-low-risk patients had the highest rate of in-hospital mortality (6.36%), followed by the intermediate-high- and low-risk groups (1.81% and 0.9%, respectively). However, it was not possible to analyze the probability of death in the high- and low-risk groups due to their small populations. The mortality rate found in this study differs from the 22% found in high-risk patients by the ESC in 2014[10]. A possible limitation in this study is that some related diseases were not studied[16-20].

Conclusion

The present study found that bedridden status, NT-proBNP, and RV dysfunction were significantly correlated with APE severity at the emergency department. However, the mortality rate in this study was lower than in previous studies (especially in high-risk patients) due to the small population.

What is already known on this topic?

Acute pulmonary embolism is a life-threatening condition, requiring highly suspicious of doctor to make a diagnosis. Recent studies have examined patient characteristics,

Table 3. Laboratory and imaging results classified by severity of disease

Laboratory results	High risk (n = 3)	Intermediate risk		Low risk (n = 4)	*p*-value
		Intermediate high (n = 32)	Intermediate low (n = 71)		
Arterial blood gas (n = 70)					
Hypoxemia (PaO^2 <80 mmHg)	2	16	25	3	0.166
Respiratory alkalosis	1	10	18	2	0.639
Metabolic acidosis	0	1	2	0	>0.999
Respiratory acidosis	0	0	1	0	>0.999
Normal acid base	2	12	20	1	0.410
Age-adjusted D-dimer (n = 110)					
Positive	3	31	60	3	0.166
hs-cTnT (n = 72)					
Positive >14	3	32	25	0	<0.001*
NTproBNP (n = 58)					
>600 ng/L	0	17	23	0	0.042*
Positive	0	12	22	1	0.753
EKG (n = 110)					
Sinus tachycardia	1	17	37	0	0.220
Normal sinus rhythm	2	14	32	4	0.152
S1Q3T3	0	15	15	1	0.037*
Inverted T wave	0	4	4	0	0.565
Right bundle branch block	0	5	1	0	0.045*
Other	0	3	6	1	0.637
CXR (n = 110)					
Pulmonary parenchymal lesion	2	16	32	2	0.884
Pleural effusion	0	11	31	2	0.438
Cardiomegaly	0	7	22	1	0.728
Westermark's sign	0	4	4	1	0.248
Prominent pulmonary trunk	0	2	2	0	0.683
Hampton's hump sign	0	1	1	1	0.157
Echocardiogram (n = 64)					
RV dilatation	1	19	11	0	<0.001*
LV D shape	2	13	8	0	0.001*
Intracardiac mass or clot	0	0	2	0	>0.999
Pulmonary hypertension	0	3	3	0	0.580
Pericardial effusion	0	1	1	0	0.585
CTPA (n = 110)					
RV dysfunction	1	12	6	0	0.003*
Lesion at segment branch	1	14	45	1	0.105
Lesion at main pulmonary trunk	2	18	26	3	0.105
Lung infarction	0	6	16	1	0.958

* Statistical significance

Table 4. Patient outcomes classified by severity of disease

The outcome (n = 110)	High Risk (n = 3)	Intermediate risk		Low risk (n = 4)
		Intermediate high (n = 32)	Intermediate low (n = 71)	
Survival to discharge (%)	3 (100)	30 (27.27)	64 (58.18)	3 (2.72)
In-hospital death	0	2 (1.81)	7 (6.36)	1 (0.90)
Death within 30 days	1 (0.90)	6 (5.45)	6 (5.45)	0
Death within 1 year	0	5 (4.54)	29 (26.36)	1 (0.90)
Re-admission within 1 year	0	11 (0.1)	31 (28.18)	1 (0.90)

but have not been able to use them to predict severity of disease.

What this study adds?

Bedridden status, NT-proBNP, and RV dysfunction are correlated with disease severity. The mortality rate in the present study was lower than in previous studies, especially in the high-risk group. Further studies should be conducted with larger populations in each group.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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ลักษณะผู้ป่วยและอัตราการเสียชีวิตในผู้ป่วยโรคลิ่มเลือดอุดกั้นในหลอดเลือดปอดเฉียบพลันในแผนกฉุกเฉินที่มีความเสี่ยงสูง กลาง และต่ำ

กมลวรรณ เอี้ยงฮง, กอบกาญจน์ กุลสุจริต, กรกฎ อภิรัตน์วรากุล, ดนุ เกษรศิริ, ฐปนวงศ์ มิตรสูงเนิน, วัชรพงศ์ พุทธิสวัสดิ์

ภูมิหลัง: โรคลิ่มเลือดอุดกั้นในหลอดเลือดปอดเฉียบพลันเป็นภาวะที่ทำให้เกิดอันตรายถึงชีวิต อย่างไรก็ตามผู้ป่วยโรคลิ่มเลือดอุดกั้นในหลอดเลือดปอดเฉียบพลันส่วนใหญ่มีอาการและอาการแสดงไม่ชัดเจนในปี พ.ศ. 2562 สมาคมโรคหลอดเลือดหัวใจแห่งยุโรป ได้เผยแพร่แนวทางการแบ่งระดับความรุนแรงของผู้ป่วยโรคลิ่มเลือดอุดกั้นในหลอดเลือดปอดเฉียบพลัน แต่การศึกษานี้ไม่ได้ศึกษาในประชากรไทย

วัตถุประสงค์: เพื่อศึกษาลักษณะผู้ป่วยและอัตราการเสียชีวิตในโรงพยาบาลในระยะเวลา 30 วันและ 1 ปี ในผู้ป่วยโรคลิ่มเลือดอุดกั้นในหลอดเลือดปอดเฉียบพลันโดยแบ่งตามระดับความรุนแรงของโรค

วัสดุและวิธีการ: การศึกษาแบบพรรณนาย้อนหลัง ประชากรศึกษาคือประชากรที่ได้รับการวินิจฉัยโรคลิ่มเลือดอุดกั้นในหลอดเลือดปอดเฉียบพลันที่แผนกฉุกเฉินมหาวิทยาลัยขอนแก่น โรงพยาบาลศรีนครินทร์ ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2551 ถึง วันที่ 30 พฤศจิกายน พ.ศ. 2561 ข้อมูลรวบรวมจากโปรแกรมข้อมูลโรงพยาบาลเวชระเบียนทางการแพทย์ และระบบจัดเก็บรูปภาพทางการแพทย์ การวิเคราะห์ข้อมูลเชิงสถิติเพื่อศึกษาลักษณะผู้ป่วยและอัตราการเสียชีวิตในผู้ป่วยเหล่านี้

ผลการศึกษา: ผู้ป่วยทั้งหมด 110 ราย ที่ได้รับการวินิจฉัยโรคลิ่มเลือดอุดกั้นในหลอดเลือดปอดเฉียบพลันเป็นเพศหญิงร้อยละ 60.91 ผู้ป่วยความเสี่ยงสูงร้อยละ 2.72 ความเสี่ยงปานกลางร้อยละ 35.45 ความเสี่ยงต่ำร้อยละ 3.63 ภาวะนอนติดเตียงมีความสัมพันธ์ทางสถิติกับผู้ป่วยที่มีระดับความเสี่ยงสูงและปานกลาง ระดับเอนไซม์หัวใจขาดเลือดชนิดโทรโปนินที ระดับเอนไซม์โปรบีเอนพีและภาวะหัวใจห้องล่างขวาโตมีความสัมพันธ์กับระดับความรุนแรงของโรค ผู้ป่วยส่วนใหญ่ได้รับการรักษาด้วยยา อัตราการเสียชีวิตในโรงพยาบาลที่ 30 วัน และ 1 ปี คิดเป็นร้อยละ 9.09, 11.81 และ 31.81 ตามระดับ

สรุป: ลักษณะผู้ป่วยบางประเภทมีความสัมพันธ์กับระดับความรุนแรงของโรค อัตราการเสียชีวิตสูงในกลุ่มความเสี่ยงปานกลาง ซึ่งผลการศึกษาแตกต่างจากการศึกษาก่อนหน้าที่พบว่ามีอัตราการเสียชีวิตในกลุ่มผู้ป่วยที่มีความเสี่ยงสูง เนื่องจากในกลุ่มความเสี่ยงสูงในการศึกษานี้มีจำนวนประชากรน้อย การศึกษาต่อไปจึงมีความจำเป็น