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Analysis of the Occurrence of Acute Pulmonary Embolism in the ICU Ward and Related Risk Factors Predicting Its Severity

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ABSTRACT

Objective: To investigate the occurrence of acute pulmonary embolism in the intensive care unit (ICU) and analyze the related risk factors for predicting its severity.

Methods: From January 2016 to December 2020, 83 patients with acute pulmonary embolism in the intensive care unit of Peking University People's Hospital were selected as the research subjects, including 34 males (40.96%) and 49 females (59.04%), with an average age of 62.06±16.83 years. The patients were divided into a high-risk group (N = 31), medium-risk group (N = 32), and low-risk group (N = 20), according to the guidelines for diagnosis and treatment of acute pulmonary embolism issued by ASH in 2020. The clinical characteristics, treatment, and prognosis of the three groups were summarized, and the severity of the patients could be predicted and the related risk factors affecting prognosis were analyzed.

Results: There were significant statistical differences in respiratory rate, syncope as the first symptom, bilateral pulmonary embolism, and APACHE-II score among the three groups ($P < 0.05$). There were significant statistical differences in the laboratory indexes, such as BNP, cTnI and D-dimer before and immediately after APE among the three groups ($P < 0.05$). There were significant statistical differences in cTnI and D-dimer among the three groups ($P < 0.05$). By pairwise comparison, it was found that there were significant statistical differences between the high-risk and low-risk groups in the immediate test indexes of APE, such as BNP, D-dimer, lower extremity vascular ultrasound abnormalities, and ECG abnormalities ($P < 0.05$), while there was no significant statistical difference between the medium-risk and low-risk groups in the immediate test indexes of APE ($P > 0.05$). However, in the medium-risk group, the laboratory indexes tended to increase, in terms of treatment and outcome, thrombolysis rate, and inferior vena cava filter implantation rate. ICU stay (> 2 weeks) of the high-risk group was significantly higher than those of the other two groups, with significant statistical difference ($P < 0.05$). Logistic regression analysis showed that respiratory rate (or = 1.778,95% CI 1.043-3.032, $P = 0.034$), D-Dimer (or = 1,95% CI 1.0-1.0, $P = 0.006$), and APACHE-II score (or = 1.879,95% CI 1.398-2.527, $P = 0.000$) were independent risk factors for predicting the severity of APE patients in the ICU ward.

Conclusion: Acute pulmonary embolism (APE) is a critical disease in ICU. By monitoring BNP, cTnI and D-dimer, we can identify critical patients with APE early. In addition, we found that respiratory rate, D-dimer, and APACHE-II score were independent risk factors for predicting the severity of APE patients in the ICU. Clinically, APE can be identified early. The diagnosis, treatment rate, and prognosis can be improved by monitoring these indicators.

INTRODUCTION

Acute pulmonary embolism (APE) is a pathophysiological syndrome that blocks the main stem or branch of pulmonary artery by many endogenous or exogenous emboli. It is a common clinical cardiovascular disease. Its incidence rate is only inferior to coronary heart disease and hypertension [Sendama 2018]. With the continuous improvement of clinical diagnosis and treatment level, the detection rate of APE gradually has increased, especially the continuous improvement of the understanding of patients with sudden acute dyspnea after surgery and long-term bedridden patients in ICU. APE has become one of the common diseases in the ICU ward. This study retrospectively analyzed 83 patients with APE in our department, in order to explore and analyze the incidence of APE in the ICU ward, predict its severity and related risk factors affecting its prognosis, and guide clinical practice.

DATA AND METHODS

Research subjects: A total of 83 patients with acute pulmonary embolism (APE) diagnosed in the intensive care unit of Peking University People's Hospital from January 2016 to December 2020 were selected as the research subjects, including 34 males (40.96%) and 49 females (59.04%), with an average age of 62.06 ± 16.83 years. According to the 2020

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guidelines for the diagnosis and treatment of APE issued by ASH, all cases were diagnosed as pulmonary embolism by pulmonary CT angiography, which met the diagnostic criteria. Direct signs included low density filling defect in pulmonary artery, and no development of distal pulmonary vessels. Indirect signs included wedge-shaped shadow in the lung field, banded high-density area, discoid atelectasis, dilation of central pulmonary artery, and reduction or disappearance of distal vascular branches. Patient inclusion criteria: Those with confirmed APE and age ranged from 18 to 75 years. Exclusion criteria: acute coronary syndrome; all kinds of cardiomyopathy; idiopathic pulmonary hypertension; and aortic dissection. According to the 2020 guidelines for diagnosis and treatment of acute pulmonary embolism issued by ASH, the patients were divided into three groups: high-risk group (N = 31), medium-risk group (N = 32), and low-risk group (N = 20). The clinical characteristics, treatment, and prognosis of the three groups were summarized, and the risk factors that can predict the severity grade of patients and affect prognosis were analyzed.

Research method: The general data (gender, age, etc.), laboratory indexes immediately before APE (including myocardial injury markers, BNP, D-dimer, CRP, PO2, pCO2, oxygenation index, etc.), echocardiographic results (such as right ventricular enlargement, decreased right ventricular wall motion, tricuspid regurgitation, etc.), and past history were collected (smoking, drinking history, history of fracture, DVT, hypertension, diabetes, etc.). The guidelines for diagnosis and treatment of acute pulmonary embolism (2020) issued by ASH were divided into a high-risk group (N = 31), medium-risk group (N = 32), and low-risk group (N = 20). Three groups, summarize the clinical characteristics, treatment and prognosis of the three groups, and analyze the risk factors that can predict the severity grade of patients and affect the prognosis.

Observation index: The general data, laboratory indexes, imaging results, treatment, and outcome of the three groups before and immediately after APE were recorded and compared. The related risk factors for predicting the severity classification of the patients were analyzed.

Statistical method: SPSS 22.0 statistical software was used to process the data. The measurement data of normal distribution were expressed by mean ± standard deviation (x ± s), and t-test or analysis of variance were used for inter-group comparison; The measurement data of non-normal distribution are represented by M (Q1, Q3), and the comparison between two groups adopts the nonparametric test. The use case (percentage) of count data is used for comparison between the two groups χ 2 inspection. Binary regression analysis was used to predict the risk factors related to the severity classification of patients. The difference was statistically significant with $P < 0.05$.

RESULTS

Comparison of general data of three groups of patients: There was no significant difference in gender, age, BMI, smoking, drinking, hypertension and diabetes, history of DVT, and history of cancer in the three groups ($P > 0.05$). There were significant statistical differences in respiratory rate, syncope as the first symptom, bilateral pulmonary embolism, and APACHE-II score ($P < 0.05$). (Table 1)

The three groups of patients before and immediately after APE were compared.

There were significant statistical differences in the laboratory indexes, such as BNP, cTnI and D-dimer before and immediately after APE among the three groups ($P < 0.05$). (Table 2)

Comparison of various laboratory indexes of the three groups immediately after APE: There were significant statistical differences in the laboratory indexes, such as cTnI and D-dimer immediately after APE among the three groups ($P < 0.05$). It was found there were significant differences in the immediate test indexes of APE between the high-risk group and low-risk group ($P < 0.05$), such as BNP, D-dimer, lower extremity vascular ultrasound abnormalities and ECG abnormalities. There was no significant difference in the immediate test indexes of APE between the medium-risk group and low-risk group ($P > 0.05$), However, the test indexes of patients in the medium-risk group showed an aggravating trend. (Table 3) (Table 4) (Table 5)

Treatment and prognosis of the three groups: In terms of treatment and outcome of the three groups, the thrombolysis rate, inferior vena cava filter implantation rate, and ICU hospitalization time (> 2 weeks) in the high-risk group were significantly higher than the other two groups ($P < 0.05$). (Table 6)

Analysis of independent risk factors for predicting the severity of APE patients in ICU: Through logistic binary regression analysis, we found that respiratory rate (or = 1.778, 95% confidence interval 1.043 ~ 3.032, $P = 0.034$), D-Dimer (or = 1,95% confidence interval 1.0 ~ 1.0, $P = 0.006$), and APACHE-II score (or = 1.879,95% confidence interval 1.398 ~ 2.527, $P = 0.000$) were independent risk factors for predicting the severity of APE patients in the ICU ward. (Table 7)

DISCUSSION

APE is a clinical syndrome caused by thrombosis of the pulmonary artery and its branches from the human venous system or right heart. It is mainly a pathological and physiological feature of blood circulation, hemodynamic changes, and respiratory dysfunction. It is a common clinical cardiovascular emergency with high incidence rate and mortality. Current research has found that among many cardiovascular diseases, APE is the third leading cause of death after acute myocardial infarction and stroke [Righini 2017; Serhal 2017; Agnelli 2010; Vinson 2016]. Although great progress has been made in the diagnosis, treatment, and prevention of APE in the past two decades, the mortality still is very high. According to research, the mortality in the first 30 days of onset is about 9%-11% [Konstantinides 2015]. This study analyzed the occurrence of APE in the ICU ward of our hospital and the relevant risk factors for predicting its

Table 1. Patients' characteristics

Item	High-risk group (*N* = 31)	Medium-risk group (*N* = 32)	Low-risk group (*N* = 20)	*P*-value
Age (years)	60.45±17.58	61.16±17.45	66.0±14.69	0.485
Gender (female)	19 (61.3)	19 (59.4)	11 (55.0)	0.904
BMI	25.34±3.24	25.61±4.57	25.34±3.90	0.955
Smoking history	5 (16.1)	9 (28.1)	5 (0.25)	0.509
Drinking history	4 (12.9)	3 (9.4)	5 (0.25)	0.283
Temperature ( )	36.8±0.8	36.8±0.68	36.5±0.37	0.143
Heart rate (times/minute)	85.19±17.96	87.0±15.90	80.40±19.46	0.143
Respiratory rate (times/minute)	20.87±3.85	19.0±2.57	18.25±4.15	0.022
Systolic pressure (mmHg)	124.87±22.64	128.03±18.93	130.15±16.39	0.634
Diastolic pressure (mmHg)	73.71±13.62	73.66±14.01	74.3±8.77	0.982
First symptoms (syncope)	11 (35.48)	3 (9.375)	1 (5)	0.006
First symptoms (chest tightness and wheezing)	17 (54.84)	24 (75)	14 (70)	0.22
Imaging examination: Bilateral pulmonary embolism	20 (64.52)	18 (56.25)	5 (25)	0.018
History of diabetes mellitus	5 (16.13)	8 (25)	8 (40)	0.16
History of hypertension	13 (41.94)	12 (37.5)	14 (70)	0.057
Combined with tumor history	3 (9.68)	9 (28.13)	5 (25)	0.164
History of trauma/fracture	8 (25.81)	3 (9.375)	1 (5)	0.069
DVT history	23 (74.19)	26 (81.25)	11 (55)	0.115
APACHE-II score	30.39±4.03	23.59±3.33	19.05±3.10	0.000

BMI, body mass index. *Statistically significant

Table 2. The three groups of patients before and immediately after APE were compared

Item	Before APE	APE time	*P*-value
High-risk group			
BNP	180 (84, 271)	632 (460, 1124)	0.000*
cTnI	0.0055 (0.0023, 0.019)	0.12 (0.045, 1.16)	0.000*
D-Dimer	585 (338, 1019)	10681 (3371.75, 22712.75)	0.000*
Medium-risk group			
BNP	79 (34, 146)	695 (339, 1058)	0.004*
cTnI	0.005 (0.002, 0.014)	0.052 (0.027, 0.094)	0.011*
D-Dimer	407 (254.5, 855)	3158 (1018, 11120.25)	0.000*
Low-risk group			
BNP	84 (30.9, 118.25)	334.5 (236.25, 665)	0.008*
cTnI	0.003 (0.002, 0.004)	0.049 (0.018, 0.175)	0.012*
D-Dimer	303.5 (130.5, 574)	2088 (878.5, 3371.25)	0.000*

severity and prognosis evaluation, so as to further strengthen the attention to the disease and guide relevant clinical practice.

In this study, we found that the basic clinical characteristics of the three groups were respiratory rate and syncope as the first symptom. Imaging showed there were significant statistical differences in bilateral pulmonary embolism and APACHE-II score ($P < 0.05$), compared with the other two groups. Patients in the high-risk group had a faster respiratory rate, higher proportion of syncope as the first symptom, higher proportion of pulmonary artery CT

Table 3. Comparison of various laboratory indexes of the three groups immediately after APE

Item	High-risk group (*N* = 31)	Medium-risk group (*N* = 32)	Low-risk group (*N* = 20)	*P*-value
BNP	632 (460, 1124)	695 (339, 1058)	334.5 (236.25, 665)	0.097
CRP	32.51 (10.375, 76.57)	70.6 (20.15, 123.12)	41.87 (4.69, 96.97)	0.392
cTnI	0.12 (0.045, 1.16)	0.052 (0.027, 0.094)	0.049 (0.018, 0.175)	0.038
PH value	7.47 (7.44, 7.48)	7.48 (7.46, 7.50)	7.47 (7.46, 7.49)	0.078
PO2	76.0 (62.0, 98.4)	77.05 (62.25, 86.5)	83.0 (73.23, 91.75)	0.106
PCO2	32.0 (28.0, 34.3)	32.0 (31.0, 33.0)	33.0 (31.25, 35.0)	0.557
Oxygenation index	187.0 (152.0, 261.7)	158.0 (132.8, 201.5)	186.0 (162.5, 238.5)	0.128
D-Dimer	10681 (3371.75, 22712.75)	3158 (1018, 11120.25)	2088 (878.5, 3371.25)	0.002
EF%	68.5 (62.25, 73.13)	68.5 (63.0, 71.63)	64.93 (60.13, 69.38)	0.293
Abnormal echocardiography	24 (77.42)	18 (56.25)	14 (70)	0.193
Lower extremity vascular ultrasound abnormalities	27 (87.1)	26 (81.25)	12 (60)	0.063
Abnormal ECG	27 (87.1)	26 (81.25)	12 (60)	0.063

Table 4. Comparison of various laboratory indexes between high-risk group and low-risk group immediately after APE

Item	High-risk group (*N* = 31)	Low-risk group (*N* = 20)	*P*-value
BNP	632 (460, 1124)	334.5 (236.25, 665)	0.019*
CRP	32.51 (10.375, 76.57)	41.87 (4.69, 96.97)	0.696
cTnI	0.12 (0.045, 1.16)	0.049 (0.018, 0.175)	0.06
PH value	7.47 (7.44, 7.48)	7.47 (7.46, 7.49)	0.452
PO2	76.0 (62.0, 98.4)	83.0 (73.23, 91.75)	0.412
PCO2	32.0 (28.0, 34.3)	33.0 (31.25, 35.0)	0.211
Oxygenation index	187.0 (152.0, 261.7)	186.0 (162.5, 238.5)	0.802
D-Dimer	10681 (3371.75, 22712.75)	2088 (878.5, 3371.25)	0.001*
EF%	68.5 (62.25, 73.13)	64.93 (60.13, 69.38)	0.198
Abnormal echocardiography	24 (77.42)	14 (70)	0.553
Lower extremity vascular ultrasound abnormalities	27 (87.1)	12 (60)	0.026*
Abnormal ECG	27 (87.1)	12 (60)	0.026*

indicating bilateral pulmonary embolism, and APACHE-II score. Later, we found that the respiratory rate (or = 1.778, 95% confidence interval 1.043 ~ 3.032, P = 0.034) and APACHE-II score through logistic binary regression analysis (or = 1.879,95% confidence interval 1.398 ~ 2.527, P = 0.000) can be used as an independent risk factor for predicting the severity of APE patients in the ICU ward. Previous studies have found that the higher the APACHE-II score, the higher the risk of VTE and APE in ICU patients. APACHE-II score is one of the independent risk factors for VTE and APE in ICU patients [Malato 2015]. Our study also confirmed the correlation between APACHE-II score and APE, which is consistent with previous studies.

In recent years, cardiac biomarkers such as BNP and D-dimer, an index reflecting the state of coagulation function, are increasingly widely used in the early condition evaluation and prognosis guidance of APE [Winterton 2017; Liedl 2017]. As early as 2014, the European Heart Association suggested that the condition of APE should be graded according to the degree of myocardial injury. In case of early myocardial injury, it should be emphasized that timely thrombolytic or anticoagulant treatment can significantly reduce mortality. BNP is an amino acid polypeptide synthesized and secreted by cardiomyocytes and existing in the cytoplasm of cardiomyocytes. Under normal circumstances, when cardiomyocytes are damaged, BNP can be released into the blood to improve the level of BNP in peripheral blood. Animal experiments have confirmed that when the pulmonary artery pressure increases, the plasma BNP level also increases. In humans, with pulmonary hypertension, the plasma BNP level also significantly increased [Klok 2008]. Similar to previous studies, we found that the immediate BNP level of APE in

Table 5. Comparison of various laboratory indexes of patients in moderate risk group and low risk group immediately after APE

Item	Medium-risk group (*N* = 32)	Low-risk group (*N* = 20)	*P*-value
BNP	695 (339, 1058)	334.5 (236.25, 665)	0.145
CRP	70.6 (20.15, 123.12)	41.87 (4.69, 96.97)	0.168
cTnI	0.052 (0.027, 0.094)	0.049 (0.018, 0.175)	0.768
PH value	7.48 (7.46, 7.50)	7.47 (7.46, 7.49)	0.257
PO2	77.05 (62.25, 86.5)	83.0 (73.23, 91.75)	0.121
PCO2	32.0 (31.0, 33.0)	33.0 (31.25, 35.0)	0.1
Oxygenation index	158.0 (132.8, 201.5)	186.0 (162.5, 238.5)	0.054
D-Dimer	3158 (1018, 11120.25)	2088 (878.5, 3371.25)	0.142
EF%	68.5 (63.0, 71.63)	64.93 (60.13, 69.38)	0.261
Abnormal echocardiography	18 (56.25)	14 (70)	0.321
Lower extremity vascular ultrasound abnormalities	26 (81.25)	12 (60)	0.093
Abnormal ECG	26 (81.25)	12 (60)	0.093

Table 6. Treatment and prognosis of the three groups

Item	High-risk group (*N* = 31)	Medium-risk group (*N* = 32)	Low-risk group (*N* = 20)	*P*-value
Thrombolysis (cases)	27	13	0	0.000*
Bolt removal (example)	5	2	0	0.11
Inferior vena cava filter implantation (cases)	10	5	0	0.013*
APE after operation (cases)	10	9	4	0.632
Whether ventilator support (example)	9	5	2	0.194
ICU length of stay (> 2 weeks)	31 (100)	12 (37.5)	0 (0)	0.000*
Discharge (cases)	27	29	20	0.262
Hospital death (cases)	4	3	0	0.262

Table 7. Analysis of independent risk factors for predicting the severity of APE patients

	B vable	SE	Wals	df	Sig	Exp (B)	Lower limit of Exp(B) 95%	Upper limit of Exp(B) 95%
Respiratory rate	0.576	0.272	4.471	1	0.034*	1.778	1.043	3.032
D-Dimer	0.000	0.000	7.64	1	0.006*	1	1	1
APACHE-II score	0.631	0.151	17.434	1	0.000*	1.879	1.398	2.527

the three groups was significantly higher than in the previous group ($P < 0.05$). There was significant statistical difference between the high-risk group and low-risk group ($P < 0.05$), although there was no significant difference in the immediate BNP level between the medium-risk group and low-risk group ($P > 0.05$). The BNP level in the medium-risk group was significantly higher than in the low-risk group, which also confirmed the important significance of BNP in the early condition evaluation and prognosis guidance of APE.

D-dimer is a specific decomposition product formed by fibrinolytic hydrolysis of fibrin. It is a specific index of fibrinolysis process. When activated thrombosis occurs in blood vessels, the level of D-dimer significantly can be increased, so it has high specificity for the diagnosis of APE. At present, it is generally believed that APE can be basically excluded when D-dimer < 500ng/ml. Our study found that there was significant difference in the level of D-dimer before and immediately after APE among the three groups ($P < 0.05$). There was significant statistical difference in the level of D-dimer immediately after APE among the three groups ($P < 0.05$). It was found that there was significant difference in the level of D-dimer immediately after APE between the

high-risk group and low-risk group ($P < 0.05$). The results of logistic binary regression analysis showed that D-Dimer (or = 1.95% confidence interval 1.0 ~ 1.0, $P = 0.006$) was one of the independent risk factors for predicting the severity of APE patients in ICU ward, which was similar to the results of previous domestic related studies [Bi 2021; Shan 2021]. In conclusion, the higher the level of D-dimer, the more serious the condition of APE patients and the higher the corresponding risk of death.

In terms of treatment and prognosis of patients with APE, we found that the thrombolytic rate, the implantation rate of inferior vena cava filter, and the length of stay in ICU (> 2 weeks) were significantly higher than the other two groups, with significant statistical differences ($P < 0.05$). According to the 2020 guidelines for the diagnosis and treatment of acute pulmonary embolism issued by ASH, patients with high-risk APE should be given thrombolytic therapy in time, which can improve their condition and survival rate in a short time. Previous studies also have confirmed that early thrombolytic therapy for high-risk patients can significantly improve the prognosis of patients [St pniewski 2021; Kesselman 2017; Mostafa 2016]. The proportion of patients in the high-risk group in the ICU (> 2 weeks) is significantly higher than that in the other two groups, which also confirms the severity of the patient's condition.

CONCLUSION

We found that APE is an acute and severe disease in the ICU and the incidence rate is still high. BNP, cTnI and D-dimer, as early disease evaluation indexes of APE patients, have certain guiding significance in clinical work. In addition, we found that the respiratory rate, D-dimer, and APACHE-II scores can be used as independent risk factors to predict the severity of APE patients in the ICU ward. Because this study is a single-center retrospective study, there inevitably will be some bias, and the sample size is relatively small, and the statistical effectiveness will be affected to a certain extent. In the future, we need more centers, a larger sample size, and longer follow-up time to further verify our results.

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