

# D-dimer-to-platelet Ratio as a Novel Marker of in-hospital Adverse Outcomes Among Patients With Acute Pulmonary Embolism: a Single-center Retrospective Study

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## Research Article

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# Abstract

**Background:** This retrospective study aimed to evaluate the value of D-dimer to platelets ratio (DPR) in predicting the in-hospital prognosis of patients with acute pulmonary embolism (APE).

**Methods:** We retrospectively reviewed the medical records of 237 patients with APE admitted from January 2016 to August 2020. The associations between the DPR and other predictors and serious adverse events were analyzed with univariate and multivariate analyses.

**Results:** A total of 134 (56.5%) patients were categorized into the low DPR group (DPR <4.55) and 103 (43.5%) in the high DPR group (DPR  $\geq$ 4.55) according to the cut-off value for the DPR of 4.55 with a sensitivity of 87.5% and a specificity of 62.0%, respectively. The model that included DPR revealed a significant improvement in the accuracy of the predictive value compared with the sPESI score alone (AUC: 0.721 [95% CI: 0.636-0.807]; P <0.001 vs AUC: 0.607 [95% CI: 0.496-0.718]; P=0.085; respectively. Multivariate analysis showed that DPR (P=0.001) and the pulmonary embolus position (P=0.011) were independent factors of serious adverse events (SAEs) of APE inpatients. The in-hospital SAEs rate was significantly higher in the high DPR group compared with the low DPR group.

**Conclusion:** Our findings showed that DPR is seemed to be a novel marker of risk stratification in patients with APE. This parameter may be used to identify these patients at higher risk for clinical adverse events, and individualization of therapeutic interventions should be timely considered.

## Introduction

Acute pulmonary embolism (APE), an acute cardiopulmonary vascular disease, is considered to be one of the worst conditions in the venous thromboembolism (VTE). Despite advancements in both diagnostic and therapeutic approaches, the mortality rate of APE is still high[1, 2], it is very important to carry out accurate risk stratification and timely treatment for patients with APE.

Plasma D-dimer, as a degradation product of simplified fibrin, is elevated in the presence of thrombotic clots by simultaneous activation of coagulation and fibrinolysis and has been proven to be an important diagnostic parameter for APE[3, 4]. In recent years, the D-dimer levels not only has been demonstrated to be significantly associated with thrombus burden or severity status of APE[5–7], but also related to the prognosis outcomes[8, 9]. However, the D-dimer assay is not specific. Levels increase in patients with myocardial infarction, pneumonia, sepsis, cancer, and the postoperative state and those in the second or third trimester of pregnancy[1, 10]. Therefore, the prognostic value of D-dimer alone in APE is controversial[11, 12].

Platelet activation and inflammation have been shown to play an important role in the pathophysiology of PE[13, 14]. Due to excessive platelet activation and apoptosis[13], the decrease of platelet count may be used as a biomarker of the severity and poor prognosis of APE that has been found in some recent studies[15–17]. However, due to the limitation of research and the heterogeneity between studies, the role

of platelet indexes in diagnosing PE is uncertain. Therefore, we aimed to evaluate the value of D-dimer to platelets ratio (DPR) in predicting the in-hospital prognosis of patients with APE.

## Methods

### Patients

The medical records of all patients who were diagnosed as PE and received treatment from January 2016 to August 2020 in the respiratory and critical care ward of the Second Affiliated Hospital of Harbin Medical University were retrospectively reviewed. Patients were enrolled in the present study if they were the first time to be diagnosed with APE. The exclusion criteria were as follows: the duration of related symptoms of APE did not exceeded 14 days; the eastern cooperative oncology group performance status (ECOG PS) score of patients  $\geq 3$  who were pregnancy; patients with previous history of liver and kidney dysfunction, autoimmune or hematological diseases; patients who did not have complete clinical data. Patients with severe pneumonia and acute myocardial infarction at the beginning of the hospitalization were also excluded.

### Data collection

Clinical demographics (including age, gender, etc.), history of smoking, comorbidities (diabetes, hypertension, etc.), laboratory test results and lower extremity ultrasound and CTPA were recorded for all APE patients. The blood samples including blood cells, coagulogram, NT-proBNP and cardiac troponin I (cTn I) were collected and processed within 24 h. The DPR was calculated by dividing the D-dimer ( $\mu\text{g/L}$ ) level by the platelet ( $\times 10^9 / \text{L}$ ) level.

### The Study End Points

The study end point comprised in-hospital serious adverse events (SAEs) defined as: death, hemodynamic instability requiring admission to the intensive care unit for invasive mechanical ventilation or remedial thrombolysis. The present study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Harbin Medical University (KY2021-005).

### Statistical analysis

The categorical variables were described as the number/total number (%), and continuous variables were described by the mean with standard deviation (SD) or median with interquartile range (IQR) values. The receiver operating characteristic (ROC) curve analysis was applied to estimate the predictive value of DPR for prognosis. The Kolmogorov–Smirnov test was used to examine the data for the normality of the distribution. The means for continuous variables were compared according to the independent group t-tests, when the data were normally distributed. Otherwise, the Mann–Whitney test was used. The categorical data were compared by  $\chi^2$  test or Fisher's exact test. The use of other special methods will be noted in the article. Univariate and multivariate analyses of prognosis were performed using the Kaplan–

Meier product-limit method with the log-rank test and the Cox proportional hazards model, respectively. All the statistical analyses were performed using SPSS Statistics 25 (IBM SPSS). Bilateral test was used, and  $P < 0.05$  was considered statistically significant.

## Results

According to the inclusion and exclusion criteria, A total of 237 APE patients were finally included into the present study. A total of 24 patients (10.1%) had SAEs. Among them, 12 died in hospital, 8 were admitted to the intensive care unit for invasive mechanical ventilation because of hemodynamic instability and 4 received remedial thrombolysis. The median age of all patients was 64 years, and 144 (60.8%) patients were male.

### Clinical characteristics

Based on the results of the ROC curve analysis (Fig. 1), we divided the patients with APE into 2 groups according to the cut-off value for the DPR of 4.55 with a sensitivity of 87.5% and a specificity of 62.0%, respectively. A total of 134 (56.5%) patients were categorized into the low DPR group ( $DPR < 4.55$ ) and 103 (43.5%) in the high DPR group ( $DPR \geq 4.55$ ). The demographic and clinical characteristics associated with the DPR are presented in Table 1. The DVT ( $P < 0.001$ ) and the central embolus ( $P = 0.001$ ) were more prevalent in patients in the high DPR group. Moreover, symptoms of chest pain and tachycardia ( $> 110$  times/min) are also significantly more common in the high DPR group ( $P = 0.044$  and  $P = 0.001$ , respectively).

Table 1  
Clinical features of APE patients associated with DPR

| Clinical features   | Total patients | DPR ≥ 4.55      | DPR < 4.55      | P value |
|---|----------------|-----------------|-----------------|---------|
|   | (n = 237)      | (n = 103,43.5%) | (n = 134,56.5%) |         |
| Age (y), median (IQR)   | 64 (53–70)     | 65 (53–70)      | 64 (51–70)      | 0.601   |
| >80   | 6 (2.5)        | 1/103 (1.0)     | 5/134 (3.7)     | 0.237   |
| ≤80   | 231 (97.5)     | 102/103 (99.0)  | 129/134 (96.3)  |         |
| Gender  |                |                 |                 | 0.336   |
| Male  | 144/237 (60.8) | 59/103 (57.3)   | 85/134 (63.4)   |         |
| Female  | 93/237 (39.2)  | 44/103 (42.7)   | 49/134 (36.6)   |         |
| Smoking history   |                |                 |                 | 0.300   |
| Never smoked  | 150/237 (63.3) | 69/103 (67.0)   | 81/134 (60.4)   |         |
| Past or current smoker  | 87/237 (36.7)  | 34/103 (33.0)   | 53/134 (39.6)   |         |
| Comorbidity   |                |                 |                 |         |
| Atrial fibrillation   | 17/237 (7.2)   | 8/103 (7.8)     | 9/134 (6.7)     | 0.756   |
| Malignance  | 44/237 (18.6)  | 21/103 (20.4)   | 23/134 (17.2)   | 0.527   |
| Pleural effusion  | 82/237 (34.6)  | 37/103 (35.9)   | 45/134 (33.6)   | 0.707   |
| Pneumonia   | 129/237 (54.6) | 62/103 (60.2)   | 67/134 (50.0)   | 0.118   |
| CVD   | 66/237 (27.8)  | 28/103 (27.2)   | 38/134 (28.4)   | 0.842   |
| Diabetes mellitus   | 21/237 (8.9)   | 12/103 (11.7)   | 9/134 (6.7)     | 0.185   |
| Hypertension  | 55/237 (23.2)  | 25/103 (24.3)   | 30/134 (22.4)   | 0.733   |
| COPD  | 32/237 (13.5)  | 11/103 (10.7)   | 21/134 (15.7)   | 0.265   |
| Clinical feature  |                |                 |                 |         |
| Chest pain  | 105/237 (44.3) | 38/103 (36.9)   | 67/134 (50.0)   | 0.044   |
| Hemoptysis  | 57/237 (24.1)  | 23/103 (22.3)   | 34/134 (25.4)   | 0.587   |
| Dyspnea   | 190/237 (80.2) | 85/103 (82.5)   | 105/134 (78.4)  | 0.425   |
| Hypotension (< 100mmHg)   | 16/237 (6.8)   | 9/103 (8.7)     | 7/134 (5.2)     | 0.285   |
| Tachycardia (> 110 times/min)   | 38/237 (16.0)  | 26/103 (25.2)   | 12/134 (9.0)    | 0.001   |
| Abbreviations: APE, acute pulmonary embolism; DPR, D-dimer to platelet ratio; IQR, inter-quartile range; CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease;DVT, deep venous thrombosis; sPESI, simplified PE severity index. |                |                 |                 |         |

| Clinical features  | Total patients | DPR $\geq$ 4.55 | DPR < 4.55     | P value |
|--|----------------|-----------------|----------------|---------|
| DVT  | 113/196 (57.7) | 62/82 (75.6)    | 51/114 (44.7)  | < 0.001 |
| Proximal   | 36/113 (31.9)  | 23/62 (37.1)    | 13/51 (25.5)   | 0.199   |
| Distal   | 77/113 (68.1)  | 39/62 (62.9)    | 38/51 (74.5)   |         |
| Embolus position   |                |                 |                | 0.001   |
| Central type   | 48/237 (20.3)  | 31/103 (30.1)   | 17/134 (12.7)  |         |
| Peripheral type  | 189/237 (79.7) | 72/103 (69.9)   | 117/134 (87.3) |         |
| sPESI  |                |                 |                | 0.302   |
| 0  | 94/237 (40.1)  | 37/103 (35.9)   | 57/134 (42.5)  |         |
| $\geq$ 0   | 143/237 (59.9) | 66/103 (64.1)   | 77/134 (57.5)  |         |
| Abbreviations: APE, acute pulmonary embolism; DPR, D-dimer to platelet ratio; IQR, inter-quartile range; CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease; DVT, deep venous thrombosis; sPESI, simplified PE severity index. |                |                 |                |         |

The initial laboratory indicators of these two groups are presented in Table 2. The leucocytes ( $8.80 \times 10^9/L$  vs.  $7.40 \times 10^9/L$ ,  $P = 0.021$ ), neutrophils ( $6.78 \times 10^9/L$  vs.  $5.43 \times 10^9/L$ ,  $P = 0.024$ ), NT-proBNP counts ( $1343.00\text{pg/mL}$  vs.  $174.50\text{pg/mL}$ ,  $P < 0.001$ ) and D-dimer ( $1629.00\text{ug/L}$  vs.  $414.50\text{ug/L}$ ,  $P < 0.001$ ) were significantly higher in the high DPR group, but the platelet counts ( $181.00 \times 10^9/L$  vs.  $220.00 \times 10^9/L$ ,  $P < 0.001$ ) was significantly lower. Furthermore, elevated NT-proBNP and cTnI levels were more prevalent in patients in the high DPR group.

Table 2  
The laboratory examination of APE patients associated with DPR

| Clinical features  | Total patients          | DPR $\geq$ 4.55           | DPR < 4.55             | P value |
|--|-------------------------|---------------------------|------------------------|---------|
|  | (n = 237)               | (n = 103 ,43.5%)          | (n = 134 ,56.5 %)      |         |
| White blood cells, $\times 10^9$ /L  | 8.00 (5.90–11.20)       | 8.80 (6.40–12.00)         | 7.40 (5.60–10.10)      | 0.021   |
| Neutrophil, $\times 10^9$ /L   | 5.82 (3.96–8.56)        | 6.78 (4.52–9.30)          | 5.43 (3.83–8.03)       | 0.042   |
| Lymphocytes, $\times 10^9$ /L  | 1.48 (1.09–1.99)        | 1.48 (1.07–1.91)          | 1.49 (1.12–2.03)       | 0.571   |
| Platelets, $\times 10^9$ /L  | 202.00 (151.00-253.50)  | 181.00 (126.00-218.00)    | 220.00 (178.00-271.00) | < 0.001 |
| Monocyte, $\times 10^9$ /L   | 0.42 (0.28–0.60)        | 0.41 (0.28–0.63)          | 0.42 (0.29–0.58)       | 0.963   |
| D-dimer, ug/L  | 728.00 (372.50-1446.50) | 1629.00 (1042.00-3967.00) | 414.50 (213.00-645.50) | < 0.001 |
| Fibrinogen, g/L  | 4.02 (3.00-5.15)        | 3.80 (2.73–5.06)          | 4.05 (3.13–5.35)       | 0.057   |
| DPR  | 3.68 (1.80–7.47)        | 8.83 (5.90–24.80)         | 1.92 (0.96–2.87)       | < 0.001 |
| NT pro-BNP counts, pg/mL   | 394 (79-2721)           | 1343.00 (258.00-4903.50)  | 174.50 (39.75-1588.75) | < 0.001 |
| $\geq$ 125 pg/mL   | 111/159 (69.8)          | 63/73 (86.3)              | 48/86 (55.8)           | < 0.001 |
| <125 pg/mL   | 48/159 (30.2)           | 10/73 (13.7)              | 38/86 (44.2)           |         |
| cTn I, ug/L  |                         |                           |                        | 0.023   |
| $\geq$ 0.056 ug/L  | 35/147 (23.8)           | 23/72 (31.9)              | 12/75 (16.0)           |         |
| <0.056 ug/L  | 112/147 (76.2)          | 49/72 (68.1)              | 63/75 (84.0)           |         |
| Abbreviations: APE, acute pulmonary embolism; DPR, D-dimer to platelet ratio; cTn I, cardiac troponin I. |                         |                           |                        |         |

### Correlation analysis of DPR

In correlation analysis, DPR levels on addition was shown to be significantly and positively correlated with NT-pro BNP ( $r = 0,331$ ,  $p < 0.001$ ), cTnI levels ( $r = 0.187$ ,  $p = 0.023$ ) and central thrombus ( $r = 0.215$ ,  $p = 0.001$ ) (Table 3).

Table 3  
Correlation analysis of DPR

| parameter  | DPR level     |           |
|--|---------------|-----------|
|  | R-coefficient | P-value*  |
| NT-pro BNP levels ( $\geq 125$ pg/mL vs $< 125$ pg/mL)                                       | 0.331         | $< 0.001$ |
| cTn I levels ( $\geq 0.056$ ug/L vs $< 0.056$ ug/L)  | 0.187         | 0.023     |
| Embolus position (central vs peripheral)   | 0.215         | 0.001     |
| *: Spearman correlation analysis; DPR, D-dimer-to-Platelet Ratio; cTn I, cardiac troponin I; |               |           |

### ROC curve analysis of DPR and sPESI

To assess the value of integrating DPR to the simplified PE severity index (sPESI) score to predict prognosis in patients with APE,  $DPR \geq 4.55$  was regarded as 1 point and added to the patient's sPESI score. The model that included DPR revealed a significant improvement in the accuracy of the predictive value compared with the sPESI score alone (AUC: 0.721 [95% CI: 0.636–0.807];  $P < 0.001$  vs AUC: 0.607 [95% CI: 0.496–0.718];  $P = 0.085$ ; respectively. (Fig. 2)

### Univariate analysis

Univariate analysis indicated the tachycardia that  $> 110$  times/min (Crude HR: 2.394 [95% CI: 0.990–5.788];  $P = 0.053$ ), DPR (Crude HR: 9.472 [95% CI: 2.824–31.767];  $P < 0.001$ ) and the pulmonary embolus position (Crude HR: 4.121 [95% CI: 1.839–9.235];  $P = 0.001$ ) may be the risk factors of the SAEs. (Table 4)

Table 4  
Univariate and multivariate analysis for risk factors of SAEs with APE

| Clinical characteristics   | Univariate analysis  | Multivariate analysis |                      |         |
|--|----------------------|-----------------------|----------------------|---------|
|  | Crude HR (95%CI)     | P-value               | Adjusted HR (95%CI)  | P-value |
| Age (years)  | 1.009;(0.977-1,041)  | 0.600                 |                      |         |
| Gender   | 0.862;(0.577-1.287)  | 0.467                 |                      |         |
| COPD   | 3.908;(0.527-28.961) | 0.182                 |                      |         |
| Pleural effusion   | 1.627;(0.726-3.648)  | 0.237                 |                      |         |
| Pneumonia  | 1.134;(0.503-2.558)  | 0.762                 |                      |         |
| Tachycardia<br>(> 110 times/min)   | 2.394;(0.990-5.788)  | 0.053                 | 1.708;(0.694-4.201)  | 0.244   |
| Hypotension (< 100mmHg)  | 1.452;(0.338-6.227)  | 0.616                 |                      |         |
| DPR ( $\geq 4.55$ vs < 4.55)   | 9.472;(2.824-31.767) | < 0.001               | 7.469;(2.195-25.413) | 0.001   |
| DVT (Yes vs No)  | 1.993;(0.634-6.259)  | 0.238                 |                      |         |
| Embolus position   | 4.121;(1.839-9.235)  | 0.001                 | 2.900;(1.282-6.560)  | 0.011   |
| Abbreviations: SAEs, serious adverse events; APE, Acute pulmonary embolism; COPD, Chronic obstructive pulmonary disease; DPR, D-dimer-to-Platelet Ratio; DVT, deep venous thrombosis |                      |                       |                      |         |

### Multivariate analysis

After the univariate analyses of prognostic factors affecting the hospital time poor prognosis of APE, the tachycardia, DPR and the pulmonary embolus position were finally incorporated in the multivariate Cox regression. It's shown that only DPR (Adjusted HR:7.469 [95% CI: 2.195-25.413]; P = 0.001) and the pulmonary embolus position (Adjusted HR:2.900 [95% CI: 1.282-6.560]; P = 0.011) were independent factors of SAEs of APE inpatients (Table 4)

Figure 3 represents the Kaplan–Meier curves for the in-hospital SAEs of the patients according to DPR cut-off level of 4.55. The in-hospital SAEs rate was significantly higher in the high DPR group compared with the low DPR group (log-rank = 19.967, P < 0.001).

### Discussion

The present study demonstrated rising DPR was associated with SAEs in APE. To the best of our knowledge, this is the first paper to explore the value of DPR in predicting prognosis in APE. Furthermore, a significant increase in the area under the ROC curve has been observed when  $DPR \geq 4.55$  as 1 point

added to patients' sPESI scores, suggesting more precise risk categorization compared to that of the sPESI score alone. These findings demonstrated the DPR may be a potential biomarker that may help identify patients with APE who are at higher risk of poor prognosis upon initial presentation. Furthermore, other meaningful findings worth being noted were as follows: First, NT-proBNP ( $r = 0,331$ ,  $p < 0.001$ ) and cTnI levels ( $r = 0.187$ ,  $p = 0.023$ ) were observed to be significantly correlated with DPR. Besides, our findings also demonstrated the pulmonary embolus position were correlated with DPR levels. Based on these findings, we postulated that the higher DPR value may be associated with the larger thrombus burden of APE patients. Second, the DPR and the pulmonary embolus position were proved to be independent predictors of in-hospital prognosis.

Elevated DPR can be regarded as increased D-dimer and a low platelet count status. Elevated D-dimer and thrombocytopenia have been observed to be associated with poor prognosis of APE in recent studies[8, 9, 13, 15–19]. But so far, no research has been done to explore the value of DPR in predicting the prognosis of APE.

Plasma D-dimer, as a degradation product of cross-linked fibrin, can well reflect the state of coagulation and fibrinolysis[3]. The correlation between D-dimer levels and the burden of PE has been proved in recent studies[6, 7, 20]. Keller K, et al[6] also confirmed the level of D-dimer could be used as a biomarker to identify the patients with right ventricular dysfunction (RVD) in normotensive APE. The cause of this phenomenon could be attributed to the position of the embolus[21, 22]. Therefore, it can be speculated that patients with higher D-dimer may have more embolus burden of APE, leading to higher SAEs that was confirmed by Lobo JL, et al[23] and Song ZK, et al[24] studies. In addition, as an effective biomarker, D-dimer could significantly improve the predictive value of clinical predictive model[25, 26]. However, the D-dimer assay is not specific. Levels increase in patients with myocardial infarction, pneumonia, sepsis, cancer, and the postoperative state and those in the second or third trimester of pregnancy[1, 10]. Therefore, the prognostic value of D-dimer alone in SAEs is controversial[11, 12]. Geissenberger F, et al [11] found D-dimer could predict the severity of disease but not the prognosis in APE.

It's well known that systemic inflammatory and hypercoagulable state play an important role in the pathophysiology of APE. Platelet hyperactivation can interact with inflammation and coagulation reaction, resulting in adverse prognostic events in patients with APE[13, 27]. Whether platelet count can be used as a marker of activation is currently controversial. Ozcan Cetin E, et al[28] reported that increased platelet was closely correlated with the RVD and disease severity in APE patients that are consistent with Telo S' research[29]. Contrarily, decreased platelet count has been shown to reflect an aggravated thrombocyte activity and that lead to destructive thrombotic response[30]. In clinical practice, Yordan T, et al[15] found the platelet significantly decreased in massive PE patients compared to low-risk groups and to be associated with RVD. The relationship between massive PE leading to cardiopulmonary resuscitation and increased D-dimer and decreased platelets has been confirmed by Leitner J, et al[17]. In this study, we found the elevated DPR caused by increased D-dimer and decreased platelets was associated with SAEs in APE. The reasons for this phenomenon may be attributed to the following aspects: first, we found that elevated DPR was significantly correlated with DVT and central thrombus, to

a certain extent, reflecting thrombus burden in APE patients. Second, the correlation between DPR and NT-pro BNP was also confirmed. Elevated troponin and NT-pro BNP have been demonstrated to reflect the functional status of the right heart and be related to the prognosis in patients with APE[1, 18, 31]. Due to the limited number of cardiac ultrasound and taking into account the differences in the level of sonographers, this study cannot effectively reflect the state of right heart function by cardiac ultrasound. However, we excluded patients with a clear diagnosis of acute myocardial infarction and acute heart failure reducing impact on right heart function to a certain extent. Therefore, The DPR, as a simple, inexpensive and available index of prothrombotic status, seemed to be a potential predictor of in-hospital serious adverse outcomes.

Additionally, we sought to integrate DPR to the sPESI score to determine whether its prognostic utility could be enhanced with additional criteria reflective of prothrombotic status. Our integrative model demonstrated an increase in the area under the ROC curve for assessing SAEs (AUC: a), suggesting improved predictive value compared to that of the sPESI score alone. The sPESI model had been demonstrated to successfully predicts 30-day mortality in APE[32, 33]. We did not observe such a substantial improvement according to the sPESI score alone. We speculated the difference was caused by the following reasons: first, remedial thrombolysis and admission to the intensive care unit for invasive mechanical ventilation as adverse events were also included into SAEs that were only discussed during hospitalization, which may slightly underestimate the incidence of adverse events, while other studies looked at the mortality within 30 days[32]. On the other hand, cigarette smoking is an established risk factor for COPD[34], an important part of SPESI, but not all patients with a history of smoking were tested for lung function our study that may weaken the prediction accuracy of sPESI. But our integrative model can still accurately identify high-risk patients, showing that DPR is a potential effective predictor.

## **Clinical Implications**

Considering that DPR is associated with the poor prognosis of acute PE, this parameter may be a useful indicator for identifying patients at high risk of adverse events. In our study, adding DPR to the sPESI score seems to play a contributive role in predicting in-hospital serious adverse events, and may provide a more accurate risk classification. Therefore, for patients with elevated DPR, we need to strengthen clinical monitoring and formulate individualized treatment plans in a timely manner based on changes in the patient's condition.

Although it is necessary for further evaluation in prospective randomized trials, DPR should still be considered in the process of patient risk stratification and monitoring of treatment effects.

## **Limitations**

There are several limitations in the present study. First, it is a retrospective single-center study. Our analysis involved a simple baseline determination from the beginning of the hospitalization that may not reflect the patient's status over-long periods. Second, the patients only limited to respiratory ward are not representative of the entire APE hospitalized patients. Finally, the sample size is relatively small,

prospective and controlled studies involving larger numbers of patients with APE are needed to further explore the DPR in the future.

## Conclusions

DPR, as a simple, inexpensive and available marker of prothrombotic status, is seemed to be a novel marker of risk stratification in patients with APE. This parameter may be used to identify these patients at higher risk for clinical adverse events, and individualization of therapeutic interventions should be timely considered.

## Declarations

### **Ethics approval and consent to participate:**

The present study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Harbin Medical University (KY2021-005).

### **Consent for publication:**

Not applicable

### **Availability of data and materials:**

Not applicable

### **Competing interests:**

Not applicable

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Not applicable

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### **Authors' contributions:**

Yi Yang, Menghan Wang, Yupeng Li and Xue Wang performed data collection. Xincheng Li, Yaowu He and Yu Shang performed data analysis and edited manuscripts. Xincheng Li, Yaowu He and Yu Shang prepared the first manuscript draft, validated data collection, refined the research idea, performed data analysis and edited manuscripts. Hong Chen and Junwei Wang developed the research idea, refined the

research idea, validated data collection and edited manuscripts. Hong Chen and Junwei Wang are the guarantor of the manuscript.

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## Figures

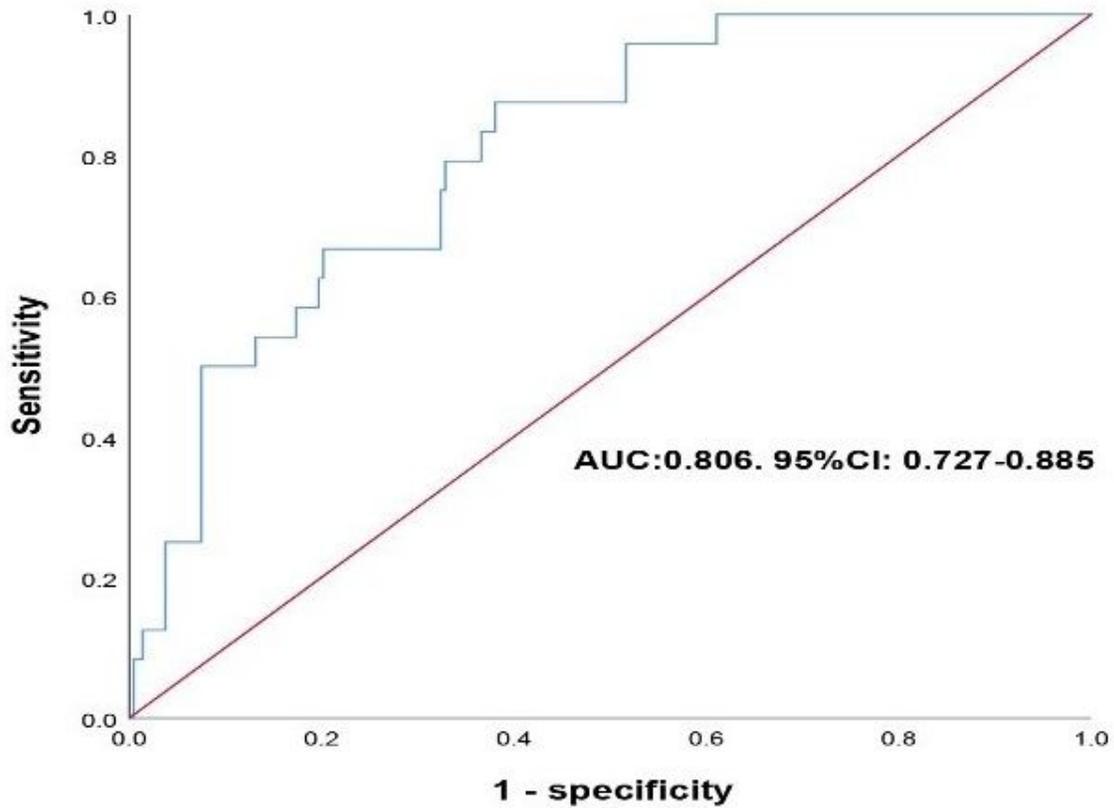
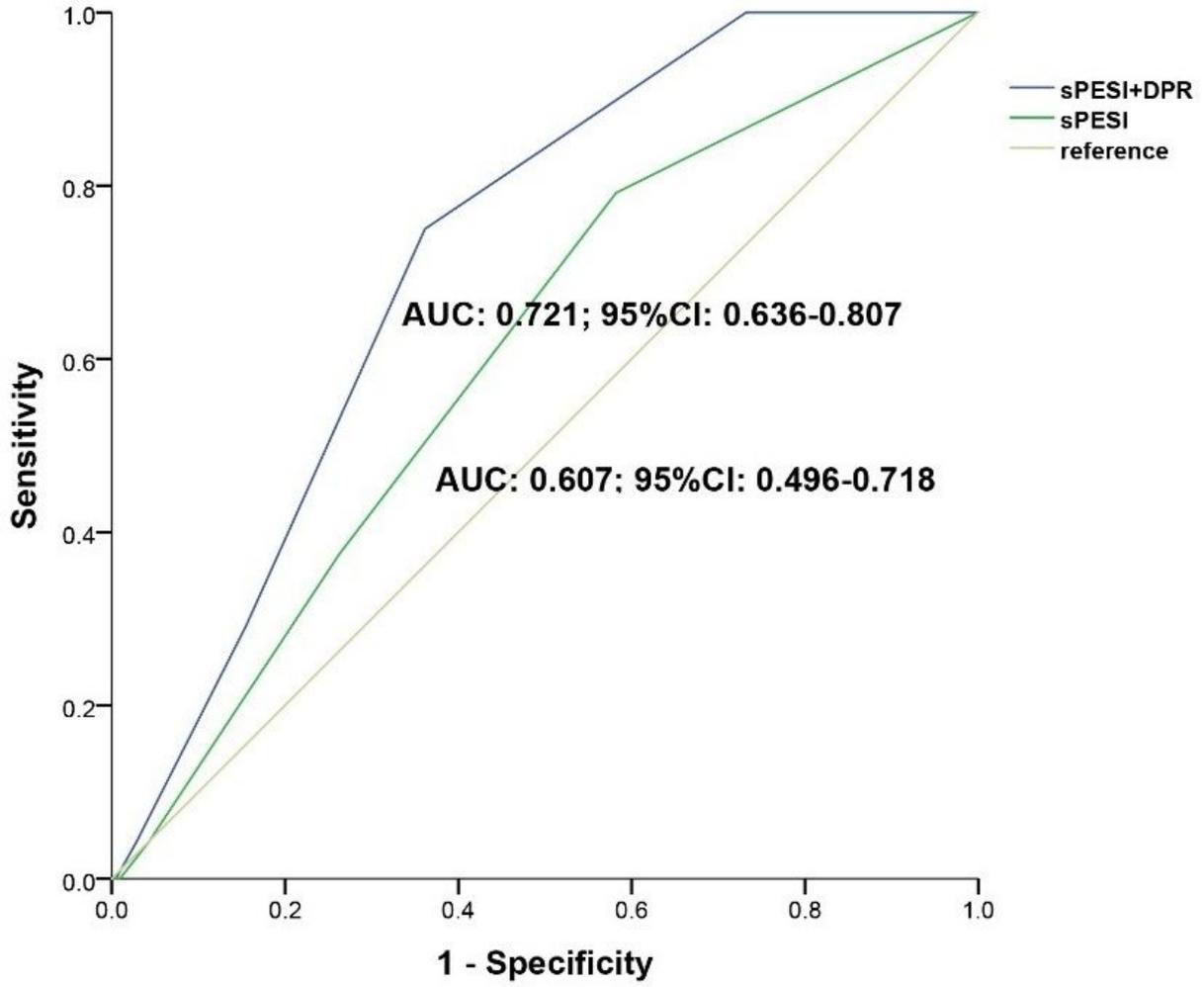


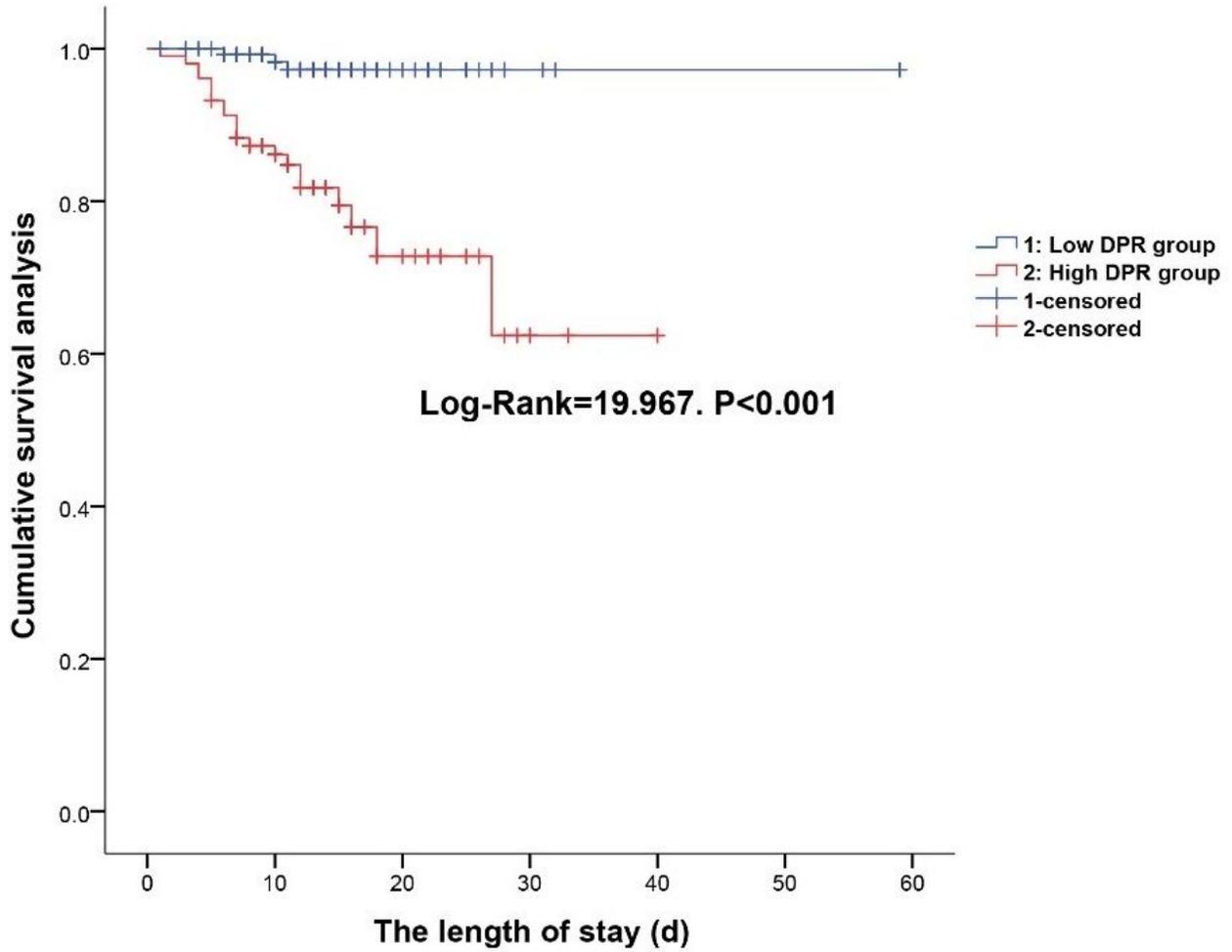
Figure 1

The ROC curve analysis of DPR. Abbreviations: AUC: area under the curve; DPR: D-dimer to Platelet ratio; ROC: receiver operating curve.



**Figure 2**

ROC curve analysis showing the predictive value of sPESI model and integrative model (DPR  $\geq 4.55$  + sPESI) for in-hospital adverse events. Abbreviations: AUC: area under the curve; DPR: D-dimer to Platelet ratio; ROC: receiver operating curve. sPESI: simplified PE severity index.



**Figure 3**

Kaplan-Meier survival curve demonstrating in-hospital adverse events among DPR groups. Abbreviations: DPR: D-dimer to Platelet ratio.