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Original Contribution

Diagnostic value of platelet indexes for pulmonary embolism☆

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ABSTRACT

Aim: The aims of the study are to investigate the changes in platelet indexes, including platelet count, platelet distribution width (PDW), and mean platelet volume (MPV), in patients with pulmonary embolism (PE) and to evaluate their diagnostic values in relation to this disease.
Methods: The study included 70 patients with PE as the observation group and 75 patients without PE as the control group. The differences in platelet count, PDW, MPV, D-dimer, and other indicators between the 2 groups were retrospectively analyzed.
Results: Platelet distribution width and MPV were significantly higher in patients with PE than in the controls (16.40% [13.70%-16.85%] vs 16.00% [11.28%-16.60%], $P = .023$; 9.91 ± 1.40 fL vs 8.84 ± 1.68 fL, $P < .001$, respectively). Multivariate logistic regression analysis showed that MPV and D-dimer were independent influencing factors for the diagnosis of PE. Receiver operating characteristic curve analysis showed that MPV (with the cut-off value set at 8.45 fL) had a sensitivity of 88.7%, negative predictive value of 78.7%, specificity of 50.0%, and positive predictive value of 61.9%. D-Dimer (with the cut-off value set at 835.5 μg/L) had a sensitivity of 80.6%, negative predictive value of 77.8%, specificity of 62.1%, and positive predictive value of 66.7%. The combination of D-dimer and MPV resulted in an increase in the area under the curve (0.799; 95% confidence interval, 0.724-0.874; $P < .001$).
Conclusion: Higher PDW and MPV levels are noticed in patients with PE. The combined application of MPV can improve the diagnostic value of D-dimer for PE.

1. Introduction

Pulmonary embolism (PE) is a clinical and pathophysiological pulmonary circulation disorder syndrome caused by partial or complete occlusion of the pulmonary artery. The existing literature has discussed the value of multiple biomarkers, such as D-dimer, brain natriuretic peptide (BNP), and troponin, in the diagnosis of PE and in making a prognosis, but these biomarkers could not be used as the foundation for diagnosis [1]. Among these biomarkers, D-dimer is widely used, but its poor specificity has limited its diagnostic yield. It is important to explore other laboratory parameters, such as platelet indexes. Thrombocytosis, defined by a platelet count (PLT) greater than 500×10^9/L, has been associated with an increased risk of symptomatic acute PE [2]. Gunay et al [3] reported that the mean values of mean platelet volume (MPV), platelet distribution width (PDW), and PLT were higher in PE groups than in controls ($P < .05$). However, Hilal et al [4] found that MPV did not correlate with the diagnosis of acute PE. Therefore, the role of platelet indexes in diagnosing PE is uncertain. The aim of this study is to investigate the diagnostic value of platelet indexes for PE.

2. Materials and methods

2.1. Patients and study design

The study retrospectively enrolled 145 consecutive patients who were admitted to our hospital between September 2009 and January 2014. According to the European Society of Cardiology guidelines [5], PE was confirmed by computed tomography pulmonary angiography (CTPA). Based on the CTPA results, these 145 patients were divided into 2 groups: 70 (32 males and 38 females) with PE as the observation group, aged from 20 to 86 (60.37 ± 13.75) years and 75 (43 males and 32 females) without PE as the control group, aged from 15 to 83 (56.84 ± 16.04) years. Age and sex distributions in the patients were similar between the 2 groups ($P > .05$).

Exclusion criteria included acute coronary syndrome, hematological disorders such as thrombocytosis and idiopathic thrombocytopenic purpura, severe hepatic and renal diseases, chronic pulmonary hypertension, diabetes mellitus, malignancy, and anticoagulation therapy used.

2.2. Computed tomography pulmonary angiography

All patients underwent CTPA using a 64-row multiple detector computed tomography scanner (LightSpeed VCT; GE Healthcare, Waukesha, WI). The imaging result of each patient was reported based on the consensus of 2 radiological technicians who were blinded to the plasma results.

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2.3. Laboratory examination

All blood samples were drawn from the antecubital vein upon admission. For measurements of platelet indexes, blood was analyzed in an automated blood cell counter (SYSMEX XS-1000i; SYSMEX Corporation, Kobe, Japan) containing EDTA-K_2 as an anticoagulant. The normal values of PLT, PDW, and MPV are 100 to 300 × 10^9/L, 11.0% to 17.1%, and 7.5 to 11.0 fL, respectively. Plasma D-dimer levels were measured by an immunoturbidimetric assay (ACL TOP; Instrumentation Laboratory, Fullerton, CA). The normal values of D-dimer are 0 to 1000 μg/L. Other indicators were detected at the same time, including N-terminal pro-brain natriuretic peptide (NT-proBNP), troponin I (TNI), red blood cell count (RBC), hemoglobin (Hgb), red cell distribution width (RDW), fibrinogen (Fib), C-reactive protein (CRP), serum creatinine (SCr), and low-density lipoprotein cholesterol (LDL-C). All assays were performed by laboratory technicians who were blinded to the CTPA results.

2.4. Data processing

Data including clinical characteristics such as age, gender, medical history, CTPA results, and plasma results were compiled into spreadsheet format (Microsoft Office Excel 2003; Microsoft Corp, Seattle, WA) for subsequent analysis.

2.5. Statistical analysis

Statistical analysis was performed using the SPSS package (version 20.0; SPSS for Windows, Chicago, IL). Descriptive statistics were reported, including the mean, SD, median, interquartile range, and percentage. The Student *t* or Mann-Whitney *U* test was used for comparisons between 2 groups, depending on whether the data accorded with the normal distribution.

Variables with categorical data were statistically compared using the χ^2 or Kruskal-Wallis test. Logistic regressions were used to perform multivariate analyses. Receiver operating characteristic (ROC) curves were analyzed to assess the optimal cut-off values of the influence factors. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated for the chosen cut-off values. $P < .05$ was considered statistically significant.

The κ statistic was used to evaluate the interrater reliability of CTPA results between the 2 radiological technicians.

3. Results

There were no significant differences in PLT between the 2 groups (205.0 [157.5-289.8] × 10^9/L vs 224.0 [167.0-261.0] × 10^9/L, $P = .582$). Platelet distribution width was higher in the patients with PE than in the patients without PE (16.40% [13.70%-16.85%] vs 16.00% [11.28%-16.60%], $P = .023$). Mean platelet volume was significantly higher in patients with PE than in the controls (9.91 ± 1.40 fL vs 8.84 ± 1.68 fL, $P < .001$). The differences in Fib, TNI, D-dimer, and NT-proBNP between the 2 groups were also statistically significant ($P < .05$) (Table 1). The κ value was .812.

Univariate logistic regression analysis showed that factors in the diagnosis of PE included PDW, MPV, TNI, D-dimer, and NT-proBNP (Table 2).

Including PDW, MPV, TNI, D-dimer, and NT-proBNP as variables, multivariate logistic regression analysis showed that MPV and D-dimer were independent factors for the diagnosis of PE (Table 3).

D-Dimer, MPV, and D-dimer + MPV were analyzed for ROC curves. The results indicated that the area under the curve (AUC) of D-dimer was larger than the AUC of MPV, and combining D-dimer and MPV resulted in an increase in the AUC (0.799; 95% confidence interval [CI], 0.724-0.874; $P < .001$) (Table 4 and Figure), suggesting that the diagnostic value of D-dimer for PE was increased by the combination. Taking the maximum Youden's index (sensibility + specificity − 1) as standard, the optimal cut-off values were assessed. Sensitivity, specificity, NPV, and PPV were calculated for the chosen cut-off values (Table 5). When the cut-off value was set at 8.45 fL, MPV had a sensitivity of 88.7%, NPV of 78.7%, specificity of 50.0%, and PPV of 61.9%. D-Dimer had a sensitivity of 80.6%, NPV of 77.8%, specificity of 62.1%, and PPV of 66.7% when the cut-off value was set at 835.5 μg/L. The combination of MPV and D-dimer had increased specificity (90.9%) and PPV (84.6%).

Table 1
Comparison of the clinical and laboratory characteristics of the patients with PE and without PE

Index	PE (n = 70)	Non-PE (n = 75)	*P*
Age (y)	60.37 ± 13.75	56.84 ± 16.04	.158
Female, n (%)	38 (54.3%)	32 (42.7%)	.162
RBC (×10^{12}/L)	4.03 ± 0.86	4.17 ± 0.92	.340
Hgb (g/L)	124.84 ± 16.12	123.60 ± 16.49	.647
RDW (%)	13.95 (12.98-15.70)	13.70 (12.80-14.40)	.079
PLT (×10^9/L)	205.0 (157.5-289.8)	224.0 (167.0-261.0)	.582
PDW (%)	16.40 (13.70-16.85)	16.00 (11.28-16.60)	.023
MPV (fL)	9.91 ± 1.40	8.84 ± 1.68	<.001
CRP (mg/L)	28.10 (14.30-62.80)	11.60 (2.75-87.50)	.061
Fib (g/L)	5.56 ± 1.73	5.12 ± 2.15	.021
TNI (ng/mL)	0.095 (0.031-0.454)	0.016 (0.004-0.037)	<.001
D-Dimer (μg/L)	3860.0 (1038.0-6834.5)	583.0 (171.0-2583.0)	<.001
NT-proBNP (pg/mL)	787.50 (210.13-2355.50)	78.28 (22.72-251.10)	<.001
SCr (μmol/L)	81.35 (64.45-101.78)	76.40 (59.30-93.20)	.174
LDL-C (mmol/L)	1.92 ± 0.63	1.89 ± 0.71	.787

4. Discussion

Pulmonary embolism and deep venous thrombosis (DVT) are 2 manifestations of venous thromboembolism (VTE), and PE is commonly a consequence of DVT. The annual incidence of PE in the United States has been estimated at 600 000 cases. The main cause of death in the acute stage is acute right ventricular failure, and the acute case fatality rate ranges from 7% to 11%. Pulmonary embolism is responsible for more than 100 000 deaths per year in the United States alone [1,5].

Pulmonary embolism is a severe disease endangering the whole world, with poor prognosis and high mortality. Its clinical presentation is often atypical, and the final diagnosis still depends on CTPA or pulmonary angiography [5], which are often difficult to perform in a timely manner because of the acuteness of the disease or lack of available equipment. Thus, the discovery of easily available and rapid diagnostic markers for acute PE is necessary. The common blood markers include D-dimer, troponin, BNP, and others [1,5]. D-Dimer is a sensitive marker of thrombosis and secondary fibrinolytic activity. The specificity of D-dimer for VTE is poor because fibrin is produced in a wide variety of conditions, such as cancer, inflammation, pregnancy, and infection [5]. For example, the enzyme-linked immunosorbent assay and quantitative rapid enzyme-linked immunosorbent assay dominate the rank order

Table 2
Univariate logistic regression analysis of PE

Index	Regression coefficient	Wald	*P*	OR	95% CI
Age	0.016	1.983	.159	1.016	0.994-1.039
Female	0.467	1.949	.163	1.596	0.828-3.075
RBC	−0.182	0.913	.339	0.833	0.573-1.211
Hgb	0.005	0.213	.645	1.005	0.985-1.025
RDW	0.131	2.793	.095	1.140	0.978-1.329
PLT	0.000	0.021	.886	1.000	0.996-1.003
PDW	0.137	5.108	.024	1.147	1.018-1.291
MPV	0.443	14.251	<.001	1.558	1.238-1.961
CRP	−0.003	0.590	.443	0.997	0.991-1.004
Fib	0.115	1.758	.185	1.122	0.947-1.329
TNI	2.559	4.651	.031	12.921	1.263-132.224
D-Dimer	0.000	16.516	<.001	1.000	1.000-1.001
NT-proBNP	0.000	4.706	.030	1.000	1.000-1.001
SCr	0.009	2.279	.131	1.009	0.997-1.020
LDL-C	0.068	0.074	.785	1.071	0.655-1.750