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Editorial Board Member of *World Journal of Clinical Cases*, Moises Rodriguez-Gonzalez, MD, Adjunct Professor, Senior Researcher, Department of Pediatric Cardiology, Hospital Universitario Puerta del Mar, Cadiz 11009, Spain. doctormoisesrodriguez@gmail.com

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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Case Control Study

Plasma brain natriuretic peptide, platelet parameters, and cardiopulmonary function in chronic obstructive pulmonary disease

Hai-Jian Guo, Feng Jiang, Chu Chen, Jia-Yu Shi, Ya-Wen Zhao

ORCID number: Hai-Jian Guo 0000-0002-0108-4213; Feng Jiang 0000-0002-4406-2129; Chu Chen 0000-0002-9689-3151; Jia-Yu Shi 0000-0003-3627-8314; Ya-Wen Zhao 0000-0002-7976-6433.

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Hai-Jian Guo, Feng Jiang, Chu Chen, Jia-Yu Shi, Ya-Wen Zhao, Department of Cardiology, Affiliated Hospital of Nantong University, Nantong 226001, Jiangsu Province, China

Corresponding author: Feng Jiang, MM, Attending Doctor, Department of Cardiology, Affiliated Hospital of Nantong University, No. 20 Xisi Road, Nantong 226001, Jiangsu Province, China. jiangfengjf53@163.com

Abstract**BACKGROUND**

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease with worldwide occurrence and high disability and mortality rate. It occurs mostly in the elderly population with pulmonary heart disease, type II respiratory failure, and other serious complications.

AIM

To investigate the correlation of plasma brain natriuretic peptide (BNP) and platelet parameters with cardiac function and pulmonary hypertension in patients with COPD and pulmonary heart disease.

METHODS

From June 2016 to June 2019, 52 patients with COPD-pulmonary heart disease (pulmonary heart disease group), 30 patients with COPD (COPD group), and 30 healthy individuals (control group) in our hospital were enrolled in the study. The pulmonary heart disease group was further divided into subgroups according to cardiac function classification and pulmonary artery pressure. Plasma BNP and platelet parameters were estimated and compared among each group and subgroup. The correlation of plasma BNP and platelet parameters with cardiac function classification and pulmonary artery pressure was then analyzed.

RESULTS

In the pulmonary heart disease group, the COPD group, and the control group, the levels of plasma BNP, platelet distribution width (PDW), and mean platelet volume (MPV) showed a decreasing trend ($P < 0.05$), while an increasing trend was found in platelet count (PLT) and plateletcrit (PCT) levels among the three groups ($P < 0.05$). In the pulmonary hypertension mild, moderate, and severe subgroups, the levels of plasma BNP, PDW, and MPV showed an increasing trend ($P < 0.05$), while a decreasing trend was observed in PLT levels ($P < 0.05$); however, PCT levels showed no significant difference among the three subgroups

study are available from the corresponding author upon reasonable request.

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($P > 0.05$). In the cardiac function grade I, II, III, and IV subgroups, the levels of plasma BNP, PDW, and MPV showed an increasing trend ($P < 0.05$), while a decreasing trend was noted in PLT and PCT levels among the four subgroups ($P < 0.05$). Correlation analysis showed that the levels of plasma BNP, PDW, and MPV in patients with pulmonary heart disease were positively correlated with their pulmonary artery pressure ($P < 0.05$), while PLT was negatively correlated with their pulmonary artery pressure ($P < 0.05$). Moreover, plasma BNP, PDW, and MPV levels were positively correlated with cardiac function grade ($P < 0.05$) of these patients, while PLT and PCT levels were negatively correlated with their cardiac function grade ($P < 0.05$).

CONCLUSION

Plasma BNP and PLT parameters are significantly correlated with the cardiac function and pulmonary hypertension in patients with COPD and pulmonary heart disease, indicating that these parameters have high clinical relevance in reflecting the health condition of these patients and for guiding their treatment.

Key Words: Chronic obstructive pulmonary disease; Pulmonary heart disease; Plasma brain natriuretic peptide; Platelet parameter; Cardiac function; Pulmonary hypertension; Correlation analysis

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Core Tip: In this study, we estimated and compared the plasma brain natriuretic peptide (BNP) and platelet count parameters among different groups and subgroups. We found that plasma BNP and platelet parameters in patients with chronic obstructive pulmonary disease (COPD) and pulmonary heart disease clearly differed from those of the subjects in the COPD and healthy control groups. Moreover, with the increase in pulmonary arterial pressure and grading of heart function classification in the pulmonary heart disease group, plasma BNP and platelet-associated indices showed an apparent trend. Therefore, our study showed that plasma BNP and platelet parameters are correlated with the classification of pulmonary arterial pressure and cardiac function in patients with combined COPD and pulmonary heart disease, which indicate that these parameters have high relevance in reflecting the patients' health condition and in guiding their clinical treatment.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by irreversible airflow limitation. As COPD develops in patients, they begin to show increased pulmonary circulation resistance, abnormally enhanced vascular intimal function, occurrence of vascular fibrosis and occlusion, and reshaping of the pulmonary circulation structure, which lead to pulmonary arterial hypertension (PAH) and further induces chronic pulmonary heart disease (pulmonary heart disease)[1]. Hence, for properly guiding clinical treatment, it is crucial to screen appropriate biochemical indices for patients diagnosed to have combined COPD and pulmonary heart disease. Platelets are known to contribute to thrombus formation, and pulmonary artery thrombosis is the main factor that leads to death in patients with COPD complicated with pulmonary heart disease. Plasma brain natriuretic peptide (BNP) is a sensitive marker of cardiac insufficiency[2,3]. To study the effect of plasma BNP and platelet parameters on assessing the health condition of patients with COPD and pulmonary heart disease, we conducted the present research.

MATERIALS AND METHODS

Subjects and samples

Inclusion criteria: In this cross-sectional study, COPD was diagnosed according to the guidelines for the diagnosis and management of COPD (Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease Guide)[4], while pulmonary heart disease was diagnosed based on the diagnostic criteria published in the seventh edition of Internal Medicine[5]. Exclusion criteria: Patients with bronchial asthma and bronchial dilation and those with other lung diseases such as severe tuberculosis were excluded.

From June 2016 to June 2019, 52 patients with COPD and pulmonary heart disease, 30 patients with COPD, and 30 healthy volunteers in our hospital were enrolled in this cross-sectional study. The patients were grouped according to their diagnosis as follows: The first group: 52 patients with COPD and pulmonary heart disease were included in the pulmonary heart disease group according to the diagnostic criteria for COPD complicated with pulmonary heart disease. This group included 30 males and 22 females, with an age range of 66-84 years and mean age of 74.67 ± 11.23 years. The second group: 30 patients with COPD alone were included in the COPD group as they were diagnosed to have only COPD but not pulmonary heart disease. This group included 17 males and 13 females, with an age range of 63-79 years and mean age of 72.67 ± 10.27 years. The third group: 30 healthy volunteers with healthy heart, liver, and kidney function; no chronic respiratory diseases; and no history of diabetes, cancer, allergies, and immune disorders were included in the control group.

Detection of plasma BNP

To estimate plasma BNP levels, 5 mL fasting venous blood was collected from each patient and centrifuged at 3000 rpm for 5 min to isolate the plasma. The plasma was then tested for BNP levels by chemiluminescence enzyme-linked immunosorbent assay with an E test TOSOH II BNP kit (Tosoh Corp., Tokyo, Japan).

Examination of platelet parameters

The blood samples were collected in disposable vacutainers coated with EDTA-K₂ and an anticoagulant, and the following parameters were assessed by an automatic blood cell analyzer (SYSMEX-XT-2000i): Platelet count (PLT), platelet distribution width (PDW), plateletcrit (PCT), and mean platelet volume (MPV).

Subgrouping

Patients were subgrouped according to their pulmonary artery pressure: On the basis of the 2009 European Society of Cardiology Guidelines[6] and the echocardiography results for pulmonary artery systolic pressure (PASP), the patients in the pulmonary heart disease group were divided into mild ($35 \text{ mmHg} \leq \text{PASP} < 50 \text{ mmHg}$), moderate ($50 \text{ mmHg} \leq \text{PASP} < 70 \text{ mmHg}$), and severe ($\text{PASP} \geq 70 \text{ mmHg}$) subgroups.

According to the World Health Organization criteria for evaluating cardiac function in patients with PAH[7] (Table 1), the patients were divided into cardiac function I, II, III, and IV subgroups.

Comparison of parameters

The following comparisons were made in this study: (1) Comparison of plasma BNP and platelet parameters among the pulmonary heart disease, COPD, and control groups; (2) Comparison of plasma BNP and platelet parameters among the different pulmonary artery pressure subgroups; (3) Comparison of plasma BNP and platelet parameters among the different heart function classification subgroups; and (4) Analysis of the correlation of plasma BNP and platelet parameters with pulmonary arterial pressure and cardiac function in patients with COPD and pulmonary heart disease.

Statistical analysis

Statistical analysis was performed using SPSS software version 19.0 (Armonk, NY, United States). The measurement data were expressed as mean \pm SD. One-way analysis of variance was used to compare the data between multiple groups, while least square difference was used as a comparative analysis for within group comparison. Case presentation was used to enumerate data, and the results were compared between the two groups by the χ^2 test. Spearman's correlation analysis was used to determine correlation, and *P* values of less than 0.05 were regarded as statistically significant.

Table 1 World Health Organization criteria for evaluating cardiac function in patients with pulmonary arterial hypertension

Grade	Symptom
I	Daily manual activity is unrestricted.
II	Physical activity is mildly restricted, and the symptoms disappear after taking rest; symptoms of shortness of breath and fatigue gradually develop after performing daily general activities.
III	Physical activity is clearly constrained, and there are no apparent symptoms after taking rest; performing activities that require greater strength than that for daily activities could induce shortness of breath, fatigue, and palpitation.
IV	No physical activity is allowed, especially in those with right heart failure syndrome; resting can also trigger anhelation and fatigue symptoms, and any physical activity can aggravate the abovementioned symptoms.

RESULTS

Comparison of plasma BNP and platelet parameters among the pulmonary heart disease, COPD, and control groups

As shown in Table 2, the levels of plasma BNP, PDW, and MPV showed a statistically significant correlation with pulmonary heart disease and COPD condition ($P < 0.05$), while the PLT and PCT levels showed an opposite trend ($P < 0.05$).

Comparison of plasma BNP and platelet parameters among the different pulmonary artery pressure subgroups

As shown in Table 3, in the mild, moderate, and severe subgroups, the levels of plasma BNP, PDW, and MPV showed a gradual increasing trend ($P < 0.05$), although the PLT level exhibited a declining trend ($P < 0.05$). The PCT value showed no significant difference among the three groups ($P > 0.05$).

Comparison of plasma BNP and platelet parameters among the different heart function classification subgroups

As shown in Table 4, patients in cardiac function classification subgroups I, II, III, and IV showed increasing levels of plasma BNP, PDW, and MPV ($P < 0.05$) and declining levels of PLT and PCT ($P < 0.05$).

Correlation of plasma BNP and platelet parameters with pulmonary arterial pressure in the pulmonary heart disease group

As shown in Table 5, correlation analysis showed a positive correlation between plasma BNP, PDW, and MPV level and pulmonary arterial pressure in the pulmonary heart disease group ($P < 0.05$); however, a negative correlation was noted between PLT and pulmonary arterial pressure ($P < 0.05$).

Analysis of correlation of plasma BNP and platelet parameters with cardiac function in the pulmonary heart disease group

As shown in Table 6, correlation analysis revealed a positive correlation between plasma BNP, PDW, and MPV levels and heart function classification in the pulmonary heart disease group ($P < 0.05$); however, PLT and PCT levels were negatively correlated with heart function classification ($P < 0.05$).

DISCUSSION

Timely and accurate diagnosis of patients with COPD and pulmonary heart disease is important in guiding their clinical treatment and for improving prognosis. Our present study showed that plasma BNP and platelet parameters in patients with COPD and pulmonary heart disease clearly differed from those of the subjects in the COPD and healthy control groups. Moreover, with the increase in pulmonary arterial pressure and grading of heart function classification in the pulmonary heart disease group, plasma BNP and platelet-associated indices showed an apparent trend, thus suggesting that plasma BNP and platelet parameters could serve as markers of the incidence and development of COPD with pulmonary heart disease as well as enable to assess efficiently intervention methods.

Table 2 Comparison of plasma brain natriuretic peptide and platelet parameters among the pulmonary heart disease, chronic obstructive pulmonary disease, and control groups

Index	PAH group (n = 52)	COPD group (n = 30)	Controls (n = 30)	F	P value
Plasma BNP (pg/L)	59.93 ± 25.77	32.66 ± 6.45 ^a	14.13 ± 2.46 ^{a,c}	65.484	0.000
PLT (×10 ⁹ /L)	122.93 ± 27.25	161.26 ± 32.25 ^a	198.46 ± 43.69 ^{a,c}	49.040	0.000
PDW (fL)	19.78 ± 4.96	14.62 ± 2.69 ^a	9.79 ± 1.62 ^{a,c}	69.027	0.000
PCT (%)	0.17 ± 0.04	0.21 ± 0.05 ^a	0.26 ± 0.04 ^{a,c}	37.817	0.000
MPV (fL)	19.08 ± 5.21	14.65 ± 3.12 ^a	10.03 ± 2.02 ^{a,c}	48.422	0.000

^aP < 0.05 vs the pulmonary heart disease group.

^cP < 0.05 vs the chronic obstructive pulmonary disease group.

BNP: Brain natriuretic peptide; COPD: Chronic obstructive pulmonary disease; PLT: Platelet count; PDW: Platelet distribution width; PCT: Plateletcrit; MPV: mean platelet volume.

Table 3 Comparison of the plasma brain natriuretic peptide and platelet parameters in the different pulmonary artery pressure subgroups

Index	Mild group (n = 16)	Moderate group (n = 23)	Severe group (n = 13)	F	P value
Plasma BNP (pg/L)	34.75 ± 11.14	61.18 ± 18.77 ^a	88.72 ± 16.55 ^{a,c}	39.806	0.000
PLT (×10 ⁹ /L)	138.39 ± 21.75	122.39 ± 28.66 ^a	104.86 ± 19.65 ^{a,c}	6.637	0.003
PDW (fL)	16.78 ± 2.69	19.22 ± 4.2 ^a	24.47 ± 5.15 ^{a,c}	13.149	0.000
PCT (%)	0.19 ± 0.04	0.17 ± 0.05	0.16 ± 0.03	1.319	0.277
MPV (fL)	14.70 ± 3.64	19.08 ± 4.12 ^a	24.46 ± 3.29 ^{a,c}	23.827	0.000

^aP < 0.05 vs the mild group.

^cP < 0.05 vs the moderate group.

BNP: Brain natriuretic peptide; PLT: Platelet count; PDW: Platelet distribution width; PCT: Plateletcrit; MPV: mean platelet volume.

Table 4 Comparison of plasma brain natriuretic peptide and platelet parameters among the different heart function classification subgroups

Index	I (n = 16)	II (n = 14)	III (n = 13)	IV (n = 9)	F	P value
Plasma BNP (pg/L)	31.15 ± 5.46	53.58 ± 7.49 ^a	78.99 ± 15.44 ^{a,c}	93.46 ± 12.05 ^{a,c,e}	88.199	0.000
PLT (×10 ⁹ /L)	143.16 ± 19.45	131.16 ± 20.41 ^a	107.46 ± 23.58 ^{a,c}	96.52 ± 20.11 ^{a,c,e}	12.866	0.000
PDW (fL)	15.66 ± 2.13	17.99 ± 3.33 ^a	22.16 ± 2.68 ^{a,c}	26.45 ± 4.52 ^{a,c,e}	27.386	0.000
PCT (%)	0.20 ± 0.04	0.17 ± 0.04 ^a	0.15 ± 0.03 ^{a,c}	0.13 ± 0.02 ^{a,c,e}	6.817	0.001
MPV (fL)	14.03 ± 2.44	18.16 ± 3.07 ^a	22.15 ± 4.05 ^{a,c}	24.05 ± 3.74 ^{a,c,e}	26.531	0.000

^aP < 0.05 vs group I.

^cP < 0.05 vs group II.

^eP < 0.05 vs group III.

BNP: Brain natriuretic peptide; PLT: Platelet count; PDW: Platelet distribution width; PCT: Plateletcrit; MPV: mean platelet volume.

During the progression of COPD, PAH increases in patients and right ventricular function is decompensated. As the disease progresses further, patients show right ventricular enlargement, hypoxia, relative increase in blood flow, and persistent permissive hypercapnia, which induce ventricular hypertrophy and gradually lead to the development of pulmonary heart disease[8,9]. Plasma BNP is a common biological diagnostic marker of left ventricular dysfunction, and its level is affected by multiple factors such as right atrial pressure, pulmonary vascular resistance, and right ventricular hypertrophy[10]. BNP is associated with multiple physiological processes, where it can selectively relax the renal arteries, increase glomerular filtration rate, and

Table 5 Analysis of correlation of plasma brain natriuretic peptide and platelet parameters with pulmonary arterial pressure in patients with chronic obstructive pulmonary disease and pulmonary heart disease

Index	<i>r</i>	<i>P</i> value
Plasma BNP (pg/L)	0.783	0.000
PLT ($\times 10^9/L$)	-0.471	0.000
PDW (fL)	0.566	0.000
PCT (%)	-0.216	0.124
MPV (fL)	0.726	0.000

BNP: Brain natriuretic peptide; PLT: Platelet count; PDW: Platelet distribution width; PCT: Plateletcrit; MPV: mean platelet volume.

Table 6 Analysis of correlation of plasma brain natriuretic peptide and platelet parameters with cardiac function classification in the pulmonary heart disease group

Index	<i>r</i>	<i>P</i> value
Plasma BNP (pg/L)	0.929	0.000
PLT ($\times 10^9/L$)	-0.670	0.000
PDW (fL)	0.806	0.000
PCT (%)	-0.553	0.000
MPV (fL)	0.814	0.000

BNP: Brain natriuretic peptide; PLT: Platelet count; PDW: Platelet distribution width; PCT: Plateletcrit; MPV: mean platelet volume.

retain diuretic natriuretic function. It can also relax vascular smooth muscle, inhibit smooth muscle hyperplasia, expand peripheral arteries, reduce cardiac afterload, and adjust myocardial remodeling, thus effectively improving ventricular functions[11,12].

In the present study, plasma BNP levels in the pulmonary heart disease group were clearly higher than those in the COPD and healthy control groups. The mechanism underlying this finding might be related to the increase in ventricular overload and stimulation of BNP secretion from the left and right ventricular muscle in the pulmonary heart disease group. The study also showed that, with the increase in pulmonary arterial pressure and grading of heart function classification in the pulmonary heart disease group, plasma BNP levels gradually showed an upward trend, and significant differences in the BNP levels were noted between the groups. This finding suggests that increase in pulmonary arterial pressure and decline in cardiac function may be caused by increased levels of plasma BNP. Correlation analysis also showed a positive correlation of plasma BNP levels with pulmonary arterial pressure and heart function classification grade.

Long-term hypoxia in patients with COPD leads to increased blood viscosity. Moreover, other influencing factors such as infection and acidosis could damage vascular endothelial cells and expose collagen tissue in these patients. This further results in the accumulation of platelets around the tissue, which subsequently activates coagulation and easily leads to thrombus formation and pulmonary arterial embolism [13]. Clinical data show that small pulmonary artery embolization is the leading cause of death in patients with COPD and pulmonary heart disease[14].

Platelet parameter is a set of markers that reflect blood coagulation function in patients. PLT effectively reflects platelet formation and decay, and its reduction is the main cause of bleeding. PDW indicates the variability in platelet size, while MPV reflects megakaryocyte and platelet generation. The parameters PDW, PCT, and MPV are markers of thrombopoiesis, wherein a high level of MPV was confirmed to be an independent risk factor of myocardial infarction in patients with coronary heart disease and thus can predict adverse cardiovascular events with high sensitivity[15, 16]. Our study revealed that PDW and MPV exhibited a declining trend in the pulmonary heart disease, COPD, and control groups, although PLT and PCT showed an increasing trend. With the constant increase in pulmonary artery pressure, PDW and MPV in the pulmonary heart disease group showed an upward trend, with a

decline in PLT. Moreover, with the increase in the grade of heart function classification, PDW and MPV increased, but PLT and PCT levels declined. Correlation analysis also showed a positive correlation between platelet parameters and pulmonary arterial pressure and cardiac function classification in the pulmonary heart disease group. This finding suggests the relevance of platelet parameters in reflecting the health condition of these patients.

CONCLUSION

In conclusion, in patients with combined COPD and pulmonary heart disease, plasma BNP and platelet parameters were found to be correlated with the classification of pulmonary arterial pressure and cardiac function, thus indicating that these parameters have high relevance in reflecting the patients' health condition and in guiding their clinical treatment. The number of subjects included in this study was small; therefore, in future studies, a larger sample size is needed to analyze further the relationship between plasma BNP and platelet parameters and pulmonary artery pressure and cardiac function classification. The mechanisms by which plasma BNP and platelet parameters affect pulmonary artery pressure and cardiac function should also be further studied.

ARTICLE HIGHLIGHTS

Research background

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease with worldwide occurrence and high disability and mortality rate. Following the development of COPD, patients begin to show increased pulmonary circulation resistance, abnormal enhancement of vascular intima function, development of vascular fibrosis and occlusion, and remodeling of pulmonary circulation structure.

Research motivation

This study could serve as an important reference to explain the correlation of plasma brain natriuretic peptide (BNP) and platelet parameters with pulmonary arterial pressure and cardiac function classification in patients with COPD complicated with cor pulmonale.

Research objectives

This study aimed to investigate the correlation of plasma BNP and platelet parameters with cardiac function and pulmonary hypertension in patients with COPD and pulmonary heart disease.

Research methods

Fifty-two patients with COPD-pulmonary heart disease, 30 patients with COPD, and 30 healthy individuals were enrolled in the study. Plasma BNP and platelet count (PLT) parameters were estimated and compared among different groups and subgroups.

Research results

In the pulmonary heart disease, COPD, and control groups, the plasma BNP, platelet distribution width (PDW), and mean platelet volume (MPV) levels showed a decreasing trend, while the PLT and PCT levels showed an increasing trend. In patients with pulmonary heart disease, the plasma BNP, PDW, and MPV levels were positively correlated, and the PLT level was negatively correlated with their pulmonary artery pressure and cardiac function grade.

Research conclusions

Plasma BNP and PLT parameters are significantly correlated with cardiac function and pulmonary hypertension in patients with COPD and pulmonary heart disease, and these parameters can be used to monitor patients' health status and recommend appropriate treatment.

Research perspectives

The mechanisms by which plasma BNP and platelet parameters affect pulmonary artery pressure and cardiac function should also be further studied.

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