Does platelet indices play a role in the distinction of pulmonary embolism clinical forms?

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Abstract

Aim: The aim of this study is to investigate the changes in platelet indexes, including mean platelet volume (MPV), platelet distribution width (PDW) and platelet count (PC), in patients with acute pulmonary embolism (PE), in addition to evaluating the diagnostic value in clinical forms.

Material and methods: The study consisted of 84 patients with PE and the control group consisted of 40 healthy subjects. PE patients were divided into two groups in accordance with the clinical forms as 60 submassive and 24 nonmassive. The differences in platelet count, MPV, PDW, PC, D-dimer, and other indicators were analyzed between the two groups. Venous peripheral blood samples to measure the MPV, PDW and PC were acquired on admission.

Results: MPV levels were found to be statistically higher in the submassive group compared to the nonmassive group and the control group (p<0.01 and p<0.001, respectively). PDW levels were found to be statistically higher in the submassive group compared to the non-massive group and control group (p=0.027 and p<0.001, respectively). PC was significantly lower in the submassive group compared to the non-massive group and control group (p=0.022 and p<0.001, respectively). It was determined that a positive correlation existed between the MPV and right ventricular diameter (RVD) (r=0.27, p<0.01).

Conclusion: High MPV and PDW levels and low PC may be indicators of the severity of acute PE. Also, the correlation between the MPV and RVD suggests that MPV can be used as a marker of right ventricular function.

Keywords: Pulmonary Embolism; Platelet İndices; Right Ventricular Diameter.

INTRODUCTION

Pulmonary embolism (PE) is a clinical and pathophysiological pulmonary circulation disorder syndrome, which is caused by partial or complete occlusion of the pulmonary artery (1). PE is a common and sometimes fatal disease, with a wide diversity of presenting symptoms, ranging from no symptoms at all to shock or sudden death (2). Acute PE affects both the circulation and gas exchange. The right ventricular (RV) failure caused by pressure overload is considered as the primary cause of death in severe PE (3). RV dysfunction can be assessed by echocardiography in patients with acute PE (4). Thrombosis commences with the aggregation of erythrocytes, fibrin, and platelets. Platelets have a major role in the pathogenesis of thromboembolic disease (5). Mean platelet volume (MPV), a measurement of platelet size, which is available in every blood count, is progressively recognized as a significant marker of platelet activity (6). Increased platelet volume is linked with increased platelet reactivity, reduced bleeding time, and increased platelet aggregation ex vivo (7). Platelet distribution width (PDW)

indicates the variability in platelet size and is another marker of platelet activation. Platelet volume indices are simple, low-cost tests, which are examined as part of the complete blood counts and are a simple way of accurately evaluating platelet functions (8). It was determined that only one or two studies were conducted concerning the role of platelet index in the distinction of clinical forms of subjects with PE. The aim of this study is to investigate the changes in the platelet index, which includes MPV, PDW, and platelet count (PC), in patients with PE and to examine the diagnostic values in the distinction of the clinical forms of submassive and nonmassive.

MATERIALS and METHODS

Study design

The study group comprised of 84 consecutive patients with acute PE, who were admitted to our university hospital between January 2016 and April 2016. This study was carried out in accordance with the Helsinki Declaration and approved by the local ethics committee of Firat University (Number:1116 / 2016.16.14).

The diagnosis of pulmonary embolism was confirmed by evaluating the computed tomography pulmonary angiography results. Submassive and nonmassive PE groups were determined according to the European Society of Cardiology Guidelines, based on systemic systolic blood pressure on admission and the presence of right ventricular (RV) dysfunction, which was determined by echocardiography and, the serum troponin and BNP levels. Submassive (hemodynamically stable with a presence of impaired right ventricular function on echocardiography or elevated serum troponin I and BNP levels); and nonmassive (hemodynamically stable without an evidence of right ventricular dysfunction and normal serum BNP, troponin I levels). The patients with PE were divided into two groups as 60 submassive and 24 nonmassive. 40 healthy control subjects were included in the study.

Exclusion criteria involved acute coronary syndromes, hematological disorders, severe hepatic and renal diseases, chronic pulmonary hypertension, diabetes mellitus, hypothyroidism, chronic inflammatory diseases, malignancy, pregnancy and anticoagulation therapy. Control group comprised of 40 healthy subjects who were admitted to our chest diseases outpatient clinic and did not have any pathology according to the laboratory findings and physical examinations.

Biochemical analysis
We determined the platelet count, MPV, PDW, PC, D-Dimer, B-type natriuretic peptide (BNP), cardiac troponin I (cTnI) at the time of patient presentation. Blood samples were acquired within 2 hours of presentation before inducing any medication and were collected in tripotassium EDTA tubes (Vacuette). The MPV, PDW and PC measurements were carried out after 30 minutes following the blood sampling by an automatic blood counter (Siemens Advia 2120, Diagnostic Solutions, Milan, Italy). cTnI and BNP assays were carried out on the Siemens ADVIA Centaur XP immunoassay analyzer (Siemens Healthcare Diagnostics K.K. Tokyo, Japan). All D-dimer levels in plasma specimens were evaluated by using the BCS XP coagulation analyzer. D-dimer measurements were expressed in fibrinogen equivalent units (FEU), with a detection range of 0.17-4.40 mg/L.

Statistical analysis
In the present study, the IBM Statistical Product and Service Solutions version 21.0 (IBM SPSS Statistics 21 program, authorization code: d91314f638c364094170; Armonk, New York, USA) was used. Significant differences among groups were assessed with a Oneway Analysis of Variance (ANOVA) using least significant differences (LSD-test) to distinguish among groups. Results were expressed as the mean standard deviation. The P value less than 0.05 was deemed statistically significant. The $\chi 2$ test was used to compare differences in categorical values between the groups. Correlations between the variables were established by the Pearson's correlation.

RESULTS

60 patients with submassive PE were involved in the study (24 males, 36 females; mean age (61.85±17.41). 24 patients with nonmassive PE comprised of 10 males, 14 females with mean age of 55.66±16.05. The control group comprised of 40 patients as 20 males, 20 females with a mean age of 58.10±12.47. The baseline characteristics of the patients with PE and controls were demonstrated in Table 1. Significant differences were observed between submassive and nonmassive groups regarding the BNP, cTNI and RVD (p<0.001) (Table 1).

Table 1. Comparison of the clinical and laboratory characteristics of the patients with PE and controls			
Characteristics	Submassive PE, (n=60)	Non-massive PE, (n=24)	Control (n=40)	p value
Age, years	61.85±17.41	55.66±16.05	58.10±9.71	N.S.
Gender (M/F)	24/36	8/16	20/20	N.S.
Smoker, n	32	29	30	
Cigarettes (Pack-Year)	38.10±17.2	42.50±19.70	37.20±16.90	N.S.
BNP (pg/dl)	102.65±11.23	80.54±69.16	-	<0.001
cTnI (ng/ml)	0.10 ± 0.30	0.014 ± 0.022	-	<0.001
RVD (mm)	24.84±2.87	21.20±1.58	-	<0.001
D-Dimer (mg/L)	4.3±3.10	3.9±2.90		0.06
M/F, male to female; BNP, B-type natriuretic peptide; cTnI, cardiac troponin I; RVD, right ventricular diameter; NS, non-significant			

Significant differences were observed among MPV levels of submassive, nonmassive and control groups (9,27±0.7fL, 8,66±0.95fL and 8,29±0.53fL, respectively). MPV levels were found to be statistically higher in submassive group compared to nonmassive group and the control group (p<0.01 and p<0.001, respectively) and MPV levels were significantly higher in nonmassive group compared to control group (p=0.045) (Figure 1). There were significant differences between PDW levels of submassive, nonmassive and control

groups (54,83±7.26%, 51,1292±5.75 and 47,2250±6.83, respectively). PDW levels were statistically higher in submassive group compared to nonmassive group and control group (p=0.027 and p<0.001, respectively) and PDW levels were significantly higher in non-massive group compared to control group (p=0.029) (Figure 2). Additionally, significant differences were observed among PC levels of submassive, nonmassive and control groups (231,98±67.73, 267,54±67.74 and 281,92±54, respectively). PC was significantly lower in submassive group compared to non-massive group and control group (p=0.022 and p<0.001 respectively) (Figure 3). The correlation between MPV and with RDV in PE patients is presented in Figure 4. There was a positive correlation between the MPV and RVD (r=0.27, p<0.01) (Figure 4).
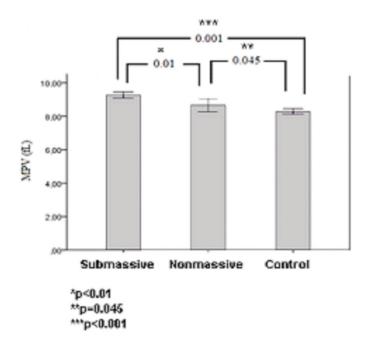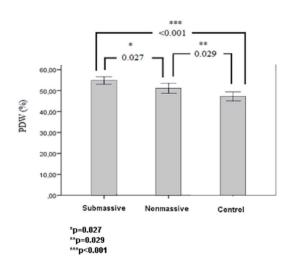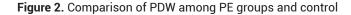

Figure 3. Comparison of PLT among PE groups and control
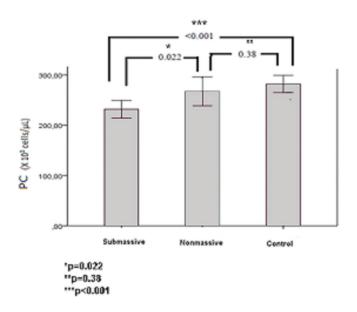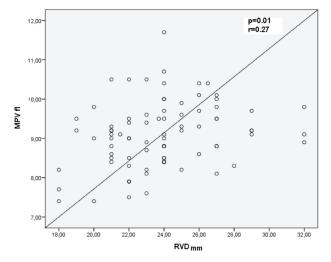

Figure1. Comparison of MPV among PE groups and control

Figure 4. Correlation between MPV and right ventricular diameter (RDV). MPV was correlated with RDV using Pearson correlation. (n=84; r=0.27 and p<0.01).

DISCUSSION

In our study, we determined that PDW and MPV levels were higher in submassive PE group compared to nonmassive and control group. PC was determined to be significantly lower among submassive PE patients compared to nonmassive and the control group. Also, there was positive correlation between MPV and RVD.

The MPV and PDW are platelet indices, which are easily assessed and also increase during platelet activation (9). Circulating platelets exhibit heterogeneity in terms of size, density and reactivity. Larger platelets, which are measured as the MPV, are possibly more reactive and possess a higher thrombotic potential. Additionally, higher MPV correlates well with an increased number of platelet-platelet aggregates, and the elevated MPV values are linked with a shortened bleeding time, increased thromboxane A2 and B2 per unit volume and expression

Figure 2. Comparison of PDW among PE groups and control

of the large amount of adhesion molecules, such as P-selectin glycoprotein 1b and glycoprotein IIb/IIIa (10). Larger platelets are probably younger, more reactive, and create more thrombogenic factors (11). Therefore, large platelets are more agreeable and, metabolically and enzymatically more active compared to small platelets and normal platelets (12). The MPV is known to be a clinical significance in thromboembolic diseases. The MPV is a notable predicting factor of mortality in acute myocardial infarction along with early death in acute pulmonary thromboembolism (13). Additionally, elevated levels of MPV were demonstrated to be associated with various kinds of diseases such as infective endocarditis, rheumatoid arthritis, and gestational diabetes (8). In previous studies, a relationship between the MPV and acute deep venous thrombosis was reported (DVT) (7,14,15). Several investigations evaluated the role of MPV in PE patients and significantly higher MPV levels were reported (1,16,17).

In contrast to our study, Hilal E et al. reported that the level of MPV had no considerable difference among the groups of patients with massive, submassive, and nonmassive PE. Nevertheless, they reported higher MPV levels in non-surviving PE patients compared to surviving patients (18).

Platelet distribution width (PDW) is a measurement of platelet heterogeneity, which in turn may occur due to the aging of platelets or heterogeneous demarcation of megakaryocytes (19). Researchers consistently reported that PDW may be related to increased platelet activation in patients with PE (1,20). Wang et al. reported that PDW was significantly higher in the chronic obstructive pulmonary disease (COPD) patients with PE compared to the COPD patients without PE and also reported that higher PDW significantly correlate with bilateral thrombus in pulmonary artery branches (2). Günay et al. reported that MPV, PDW levels, and platelet levels were higher in massive and submassive patient groups with PE compared to control subjects (20).

In our study, PC was determined to be significantly lower among submassive PE patients compared to nonmassive and the control group. This low PC in patients with submasivve PE might be caused by the consumption of the platelets. Similar to our results, Yardan et al. reported lower PC with higher MPV levels (5). Therefore, increased MPV could be related to accelerated blood coagulation and low platelet count and may also indicate the activation of the coagulation system. Low PC is known to be linked with increased glycoprotein VI and inflammatory markers in cardiovascular disease (13). Increased MPV levels and low PC may be interpreted as the consumption of small platelets and a compensatory production of larger reticulated platelets (5).

In our study there was positive correlation between MPV and RVD similar to before studies (5,21). Right ventricle enlargement with increased pulmonary artery pressure can be accepted as hemodynamic indicators and both of them can show the the severity of pulmonary arterial vasculature thrombotic occlusion (18). Moreover, platelet activation correlates with the RV dysfunction. Right ventricular dysfunction may directly promote platelet activation by impaired left ventricular filling and reduced cardiac output (22). Also, Günay et al. reported a positive correlation between CT pulmonary arterial obstruction index and MPV in patients with acute PE. They proposed that MPV could be utilized in the determination of disease severity and could pave the way to therapeutic strategies for PE patients (20).

The notable limitation of our study was the small number of patients with PE and the fact that we detected only four massive PE patients. Thus, we could not include a massive PE group.

CONCLUSION

In conclusion, we have demonstrated that MPV and PDW were significantly elevated in submassive patients compared with nonmassive patients and, the MPV was correlated with RVD. PC was found to be decreased in patients with PE. These findings suggest that platelet indices, MPV, and PDW, can be utilized in the determination of disease severity, and consideration of therapeutic strategies in pulmonary embolism patients.

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