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Research article

Comparison of platelet volume indices in acute coronary syndrome

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ABSTRACT

Aim: To compare the parameters showing the platelet volume index in unstable angina pectoris (USAP), non-ST elevation myocardial infarction (non-STEMI) and ST elevation myocardial infarction (STEMI).

Methods: The platelet volume indices of 94 USAP, 161 non-STEMI and 86 STEMI cases with a total of 341 patients (245 men, 96 women) were compared. The patients between March 2015 and October 2018 who admitted to Bolu Abant Izzet Baysal University Hospital with the diagnosis of acute coronary syndrome were compared using platelet distribution width (PDW), PDW to platelet ratio (PPR), mean platelet volume (MPV), MPV to platelet ratio (MPR).

Results: No significant difference was found between the 3 groups in terms of PDW ($p = 0.26$), PPR ($p = 0.87$), MPV ($p = 0.41$) and MPR ($p = 0.78$) values.

Conclusion: In our study, there was no statistically significant difference between the types of acute coronary syndrome and platelet volume indices.

Keywords: Acute coronary syndromes, mean platelet volume, platelet distribution width, platelet volume indices.

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Introduction

Coronary artery disease is one of the most important health problems in both developed and developing countries [1]. Coronary artery disease may be in a wide range of stable angina pectoris and acute coronary syndrome including USAP (unstable angina pectoris), non-STEMI (non-ST elevation myocardial infarction) and STEMI (ST elevation myocardial infarction) and their prognosis and course vary widely [2]. Acute coronary syndromes are an important cause of hospitalization, mortality and morbidity worldwide [3]. Destruction and rupture of a stable plaque is also a stimulant for thrombogenesis and triggers a loss of function in the myocardial area of the coronary artery, whose flow is impaired in the acute coronary

syndrome, as well as the loss of cell death, ischemia-induced arrhythmias, and sudden cardiac death [4]. The importance and place of platelets and other hematological parameters in both acute and stable coronary artery diseases have been shown in many studies [5]. When the relationship between the activity and size of platelets is examined, it is known that thrombogenic activity of platelets increases in their size to the increase of thrombogenic granules on the platelets and of the receptors on the surface [6]. PDW (platelet distribution width), PPR (PDW to platelet ratio), MPV (mean platelet volume), MPR (MPV to platelet ratio) values are parameters that show the size and activity of platelets [7,8,9]. These parameters, which are indirect indicators of platelet activation, have been studied in a wide variety of disease groups such as cancer, inflammatory diseases, rheumatologic diseases, hypertension, diabetes, dyslipidemia and obesity and the effects of them on the diagnosis, follow-up and prognosis of diseases were shown in the literature [10,11].

The aim of our study is to compare the platelet volume indices using PDW, PPR, MPV and MPR values in patients with acute coronary syndrome.

Methods

Between March 2015 and October 2018, a total of 341 patients (245 men, 96 women) with 94 USAP, 116 non-STEMI and 86 STEMI who admitted to our hospital with the diagnosis of acute coronary syndrome were evaluated with coronary angiography results and hemogram parameters.

Age, gender, drugs, smoking, hypertension, hyperlipidemia, diabetes and family history, height and weight data were recorded in all patients. Hypertension diagnosed in patients with systolic blood pressure > 140 mmHg and/or diastolic blood pressure > 90 mmHg or presently receiving anti-hypertensive treatment. Diabetes was defined as fasting blood glucose > 126 mg/dl or related drug intake. Hyperlipidemia was defined as total cholesterol > 200 mg/dl or triglyceride > 150 mg/dl.

Patients with acute chest pain and persistent (>20 min) ST-segment elevation were defined as STEMI. Patients with acute chest pain but no persistent ST-segment elevation (transient ST-segment elevation, persistent or transient ST-segment depression, T-wave inversion, flat T waves or pseudo-normalization of T waves or normal ECG) and a clue for myocardial necrosis defined as NSTEMI. Unstable angina was defined as myocardial ischemia at rest or minimal exertion in the absence of cardiomyocyte necrosis [12].

The criteria for ST segment elevation were taken as follows: 1) At least 1 mm ST segment elevation in at least two successive leads, 2) 2.5 mm in men under 40 years of age, 2 mm in men over 40 years and 1.5 mm ST segment elevation in women in V2 and V3, 3) 0.5 mm ST segment elevation in V7-V9 (at least 2 consecutive lines), 4) 0.5 mm ST segment elevation in V3R and V4R (1 mm in men under 40).

Coronary angiography was performed by femoral or radial route using Seldinger technique. Coronary angiograms were evaluated by at least two cardiologists who were experienced and blinded to the independent study.

Venous blood samples were taken within the first 6 h of admission to hospital. Glucose, creatinine and lipid profiles were determined by standard methods. MPV and PDW values were studied in tri-potassium EDTA (Ethylenediaminetetraacetic acid) tubes. The PPR was calculated by dividing the PDW

value by the number of platelets and MPR was calculated by dividing the MPV value by the number of platelets. Patients who were diagnosed with acute coronary syndrome in the last 6 months, patients with coronary bypass history, decompensated heart failure, atrial fibrillation, cardiomyopathy or congenital heart disease, inflammatory disease, renal or hepatic failure, cancer, septicemia, pregnancy and thrombocytopenia were excluded from the study. The study was approved by the Local Ethics Committee of Bolu Abant Izzet Baysal University Hospital, Turkey.

Statistical analysis

Analyses were carried out using SPSS 16.0 Statistical Package Program for Windows (SPSS Inc, Chicago, Illinois, USA). Quantitative variables are expressed as mean± standard deviation (SD), and qualitative variables as numbers and percentages. Differences between independent groups was assessed by Student t-test for normally distributed quantitative variables and Mann-Whitney's U-test for variables without normal distribution and Chi-square test for qualitative variables. All results were considered statistically significant at the level of $p \leq 0.05$.

Table 1. General characteristics of the study groups.

Baseline characteristics	USAP (n=94)	Non-STEMI (n=161)	STEMI (n=86)	*p*
Age (mean±SD) (years)	63 (38-93)	69 (35-91)	69 (33-92)	*0.055*
Body mass index (kg/m2)	26 (19-34)	27 (19-40)	29 (20-38)	*0.004*
Male/female	73/21	106/55	66/20	*0.060*
Hypertension (%)	60 (64%)	98 (61%)	35 (41%)	*0.002*
Smoking (%)	41 (44%)	55 (34%)	24 (28%)	*0.082*
Family history (%)	16 (17%)	16 (10%)	7 (8%)	*0.124*
Diabetes mellitus (%)	33 (35%)	53 (33%)	21 (24%)	*0.257*
Acetyl salicylate (%)	40 (42%)	50 (31%)	23 (27%)	*0.059*
Clopidogrel (%)	16 (17%)	18 (11%)	6 (7%)	*0.107*
Statin (%)	22 (23%)	32 (20%)	12 (14%)	*0.269*
Calcium channel blocker (%)	13 (14%)	33 (20%)	9 (10%)	*0.096*
ACE inhibitor (%)	22 (23%)	25 (15%)	13 (15%)	*0.220*
ARB (%)	19 (20%)	27 (17%)	4 (5%)	*0.008*
Beta-blocker (%)	40 (42%)	47 (29%)	14 (16%)	*0.001*

ACE: angiotensin-converting enzyme, ARB: angiotensin receptor blocker, SD: standard deviation, USAP: Unstable angina pectoris, Non-STEMI: non-ST elevation myocardial infarction, STEMI: ST elevation myocardial infarction.

Results

Baseline patient demographics, including age, sex and clinical risk factors, were compared between the groups. While demographic factors of age, gender, smoking, family history and presence of diabetes were not statistically significant among the 3 groups, body mass index was the lowest in the USAP group and the highest in the STEMI group (*p=0.004*). The presence of hypertension was the lowest in the STEMI group and the highest in non-STEMI group (*p=0.002*). Previous medications were also comparable between the three groups.

While the use of acetylsalicylate, clopidogrel, statin, calcium channel blocker and ACE (angiotensin-converting enzyme) inhibitor were not significantly different between groups; ARB (angiotensin receptor blocker) and beta-blockers were found to be the lowest in the STEMI group and the highest in the non-STEMI group (*p=0.008* and *p=0.001*) (Table 1).

When blood parameters of patients were examined, no significant difference was found between creatinine, LDL-cholesterol, HDL-cholesterol, triglyceride, total cholesterol,

Table 2. Laboratory data of the study cohort.

Parameters	USAP (n=94	Non-STEMI (n=161)	STEMI (n=86)	*p*
Creatinine (mg/dl)	0.9 (0.5-1.8)	1.0 (0.6-1.9)	0.8 (0.6-1.7)	*0.58*
Fasting plasma glucose (mg/dL)	111 (52-361)	121 (75-412)	124 (53-399)	*0.02*
LDL-cholesterol (mg/dL)	107 (39-337)	110 (37-233)	111 (32-299)	*0.52*
HDL-cholesterol (mg/dL)	41 (27-75)	42 (21-82)	40 (25-67)	*0.84*
Triglyceride (mg/dL)	140 (40-538)	117 (43-820)	115 (33-524)	*0.06*
Total cholesterol (mg/dL)	182 (88-410)	183 (110-322)	177 (116-400)	*0.88*
Hematocrit (%)	42 (29-51)	41 (24-53)	41 (26-51)	*0.34*
Hemoglobin (g/dL)	14 (8.7-17.1)	13.5 (8.1-17.9)	13.7 (8.6-18.1)	*0.79*
Platelet counts (K/uL)	208 (56-432)	219 (91-612)	216 (93-450)	*0.91*
PDW (GSD)	17.6 (15.9-21.2)	17.8 (15.4-23.0)	17.5 (15.4-20.5	*0.26*
PPR	0.08 (0.04-0.30)	0.08 (0.03-0.24)	0.08 (0.04-.19)	*0.87*
MPV (fL)	7.6 (5.9-11.3)	7.6 (5.2-12.3)	7.3 (5.3-13.8)	*0.41*
MPR	0.04 (0.01-0.14)	0.03 (0.01-0.12	0.04 (0.01-0.09)	*0.78*

PDW: platelet distribution width, PPR: PDW to platelet ratio, MPV: mean platelet volume, MPR: MPV to platelet ratio, USAP: Unstable angina pectoris, Non-STEMI: non-ST elevation myocardial infarction, STEMI: ST elevation myocardial infarction, fL: femtolitre.

hematocrit, hemoglobin and platelet counts while plasma glucose levels were highest in the USAP group; lowest in the STEMI group ($p = 0.02$). There was no statistically significant difference between the three groups in terms of platelet function tests which formed the aim of our study, PDW ($p=0.26$), PPR ($p=0.87$), MPV ($p=0.41$) and MPR ($p=0.78$) (Table 2).

Discussion

In this study, platelet volume indices PDW, PPR, MPV and MPR values were not significantly different among the patients with acute coronary syndrome. Atherosclerosis causing coronary artery disease (CAD) is a chronic process. After a silent period, a stable or unstable clinical picture may occur. Acute coronary syndrome (ACS) is a wide spectrum of exacerbation periods, including USAP, non-STEMI and STEMI. Inflammation and platelet activation are the cornerstones of both atherosclerosis and acute coronary syndromes. Platelets are important triggers in the atherothrombotic process with their direct inflammatory mediators as well as their direct effects on the inflammatory pathway [13]. Activated platelets initiate the free arachidonic acid pathway; prostaglandins produced in the process starting with this pathway, especially thromboxane A2 is the most potent vasoconstrictor and platelet activating substrate [14]. Large platelets are more enzymatic and metabolically more active due to the higher content of pro-aggregate mediators and more surface proteins (p-selectin, Glycoprotein -IIb/IIIa) [15,16]. The two most well-known parameters showing the platelet size are MPV and PDW, and these two values have been used in the literature for many times [7,19-30]. PDW is more specific in demonstrating activation; unlike MPV, it does not increase with simple platelet swelling [17]. An example might be the correlation between increased PDW and MPV with shortened bleeding time [18]. In addition to studying the prognostic significance of these markers in a wide variety of patient groups, patients with acute coronary syndrome were compared with stable coronary artery disease and non-cardiac patients [2]. The comparison between the 3 groups was not found in the existing literature and such a comparison of these values especially in the Turkish population constitutes a first study.

In the literature, platelet volume, PDW and P-LCR (platelet larger cell ratio) values were significantly higher in USAP and acute MI patients than in stable CAD and control group [19]. While these values were used for prognosis as well, PDW value was determined as a predictor in the patients who had saphenous vein occlusion [20]. In another study, STEMI patients were compared with the control group and as a result, PDW and MPV values were found to be significantly high and were associated with STEMI severity [7]. Following the literature there are studies in parallel with the results of our study, in which no significant relationship was observed. For example, in 1300 patients who underwent percutaneous coronary intervention, in the study that investigated the relationship between peri-procedural MI and PDW, patients were examined in 3 groups according to PDW value and it was concluded that the increase in PDW did not increase the risk of peri-procedural MI [21]. In another study, 2330 patients who underwent coronary angiography were divided into 3 groups. There was no significant relationship between CAD grade and carotid IMT (intima-media thickness), MPV and PDW [18]. Similar findings were also found in the studies of Tavil et al and Halbmayer et al [22-24]. In the literature, the

relation of MPR and PPR ratios of platelet volume indices with prognosis in various cancer types have been studied [25]. The correlation with the severity of coronary artery disease in patients with non-STEMI [26] and the relationship with disease severity in pediatric intensive care unit (PICU) [27] have been studied previously. However, in our study, these values were compared in 3 types of acute coronary syndromes.

In our study, we examined patients in 3 groups under the title of acute coronary syndrome and compared them with platelet volume index parameters, however we did not find any significant difference. Although these 3 clinical manifestations may present with different clinical and severity, the underlying pathophysiological events may overlap in a common pathway. In addition, circulating platelets have a life span of about 10 days [28]. Since, the blood samples were taken from the patients who were in the first 6 h of hospitalization, our calculation included the 90% of the platelets which are in fact independent of the acute coronary syndrome but already in the circulation at the time of measurement. Thus, this may explain the statistical insignificance between the groups. Although previous studies have shown that these values change with blood uptake in supine or sitting position [29], patients' positions during blood collection could not be standardized due to the retrospective design of our study. This deficiency may have affected statistical values. The fact that the study was conducted only in the Turkish population may prevent us to generalize the values that have been shown to be influenced by ethnic factors [30]. Single-center and the limited number of patients might be considered as the other limitations in our study.

Informed Consent: *Informed consent was obtained from all individual participants included in the study.*

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Research Ethics Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflicts of interest: *There are no conflicts of interest.*

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