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Mean platelet volume in ST elevation and non-ST elevation myocardial infarction

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SUMMARY

Platelet activation is thought to play a key pathogenetic mechanism in acute coronary syndromes. We investigated the mean platelet volume and platelet count in patients with both ST elevation myocardial infarction and non-ST elevation myocardial infarction. Fifty two patients with non-ST elevation myocardial infarction and 56 patients with ST elevation myocardial infarction were enrolled in the study. Age- and gender-matched 50 healthy subjects constituted the control group. Venous blood samples for whole blood analysis were drawn on admission and analyzed by an autoanalyser. The difference in mean platelet volume was statistically significant in ST elevation myocardial infarction and non-ST elevation myocardial infarction patients, which was 8.7±1 and 7.9±0.7 fl ($p<0.01$), respectively. However, the difference in mean platelet volume between non-ST elevation myocardial infarction and control group was not significant (7.9±0.7 and 8.1±0.7 fl; $p=0.52$, respectively). Moreover, platelet counts of both ST elevation myocardial infarction and non-ST elevation myocardial infarction groups were significantly lower than the controls. Platelet counts in the ST elevation myocardial infarction and non-ST elevation myocardial infarction patients did not show any statistically significant difference. The underlying mechanism should be investigated in further studies, which may shed light on developing new therapeutic strategies for this particular acute coronary syndrome.

Key words: *Mean platelet volume, non-ST elevation myocardial infarction, ST elevation myocardial infarction*

ÖZET

ST elevasyonlu ve ST elevasyonsuz miyokard infarktüsünde ortalama trombosit hacmi

Akut koroner sendromların fizyopatolojik mekanizmasında trombosit aktivasyonunun anahtar rol oynadığı düşünülmektedir. Çalışmamızda ST elevasyonlu miyokard infaktüsü ve ST elevasyonsuz miyokard infarktüsü olgularında ortalama trombosit hacmi ve trombosit sayılarını araştırdık. ST elevasyonsuz miyokard infarktüslü 52 hasta ve ST elevasyonlu miyokard infaktüslü 56 hasta çalışmaya dahil edildi. Yaş ve cinsiyet uyumlu 50 sağlıklı olgu kontrol grubunu oluşturdu. Hastaların ilk kabullerinde venöz kan örnekleri alınarak otoanalizörde tam kan sayımları yapıldı. Ortalama trombosit hacmi ST elevasyonlu ve ST elevasyonsuz miyokard infarktüslü olgularda istatistiksel olarak anlamlı olacak şekilde (sırasıyla 8.7±1 ve 7.9±0.7 fl ($p<0.01$)) farklıydı. Ancak ST elevasyonsuz miyokard infarktüslü ve kontrol grubu olgular arasında ortalama trombosit hacmi açısından istatistiksel olarak anlamlı farklılık yoktu (sırasıyla 7.9±0.7 ve 8.1±0.7 fl; $p=0.52$). Bunun yanı sıra trombosit sayısı hem ST elevasyonlu, hem de ST elevasyonsuz miyokard infarktüslü olgularda kontrol grubuna göre daha düşüktü. ST elevasyonlu ve ST elevasyonsuz miyokard infarktüslü olgular arasında trombosit sayısı açısından istatistiksel olarak anlamlı farklılık yoktu. Akut koroner sendromların bu özel grubunda yeni tedavi stratejilerine yön verebilecek ve altta yatan mekanizmaların aydınlatılması için ileri çalışmalara ihtiyaç vardır.

Anahtar kelimeler: *Ortalama trombosit hacmi, ST elevasyonsuz miyokard infarktüsü, ST elevasyonlu miyokard infarktüsü*

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Introduction

The biological events that occur in the coronary artery system immediately preceding acute coronary syndromes are still unclear. However, platelets are definitely involved, and changes in platelet structure may be a causal factor in producing a thrombus in the coronary artery. All regional acute myocardial infarctions are caused by thrombosis developing on a culprit coronary atherosclerotic plaque. Thrombosis is also the major initiating factor in unstable angina, particularly when rest pain is recent and increasing in severity, frequency and duration. Platelet activation, by favoring thrombus formation and coronary artery occlusion, is thought to play a key pathogenetic role in acute myocardial infarction.

It has been shown that platelet size, measured as mean platelet volume (MPV), correlates with their reactivity (2). Circulating platelets are heterogeneous in size, density, and reactivity. Platelet age and size are independent determinants of platelet function. Mean platelet volume is positively associated with indicators of platelet activity including expression of glycoprotein Ib and glycoprotein IIb/IIIa receptors (3-7). Higher values of MPV characterize patients with myocardial infarction and unstable angina as compared to those with stable angina or noncardiac chest pain, and elevated MPV has been recognized as an independent risk factor for myocardial infarction and stroke (8-11). In acute states of platelet activation, increase in platelet volume might be a result of a change in the fragmentation pattern of megakaryocyte cytoplasm (12). An elevated MPV is associated with poor clinical outcome among survivors of myocardial infarction (13,14).

To the best of our knowledge, this property of MPV has only been studied in the context of comparing stable and unstable angina pectoris (USAP) as well as USAP and acute myocardial infarction (MI). This laboratory parameter has never been investiga-

ted in comparing ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI) patients in terms of understanding the pathophysiological difference between platelets in both clinical conditions. In this study, we aimed to investigate the MPV and platelet count for better understanding the pathophysiologic role of platelets in both STEMI and NSTEMI patients.

Material and Methods

Fifty two consecutive patients with NSTEMI (mean age 69±14 years, 77% of them male) and 56 consecutive patients with STEMI (mean age 66±16 years, 68% of them male), thus a total of 108 acute coronary syndrome patients (mean age 68±16 years, 75% of them male) were enrolled in this study. Age- and gender-matched 50 healthy subjects (mean age 66±15, 74% of them male) without diabetes mellitus, hypertension, dyslipidemia and no history of bleeding diathesis constituted the control group. None of the subjects were smoker, under any medication, had any known platelet diseases and abnormal routine blood chemistry values.

Enrollment criteria required a clinical picture consistent with acute MI, with ongoing chest pain unresponsive to nitrates and lasting more than 30 minutes and elevated serum cardiac markers such as troponins, creatinin kinase and aspartate transaminase. Patients with cardiogenic shock, currently receiving antithrombotic therapy, stroke within 2 years, or any permanent residual neurologic defect were excluded. STEMI was defined as the presence of ST-segment elevation of at least 1 mm in 2 or more contiguous leads or new (or presumably new) left bundle branch block. NSTEMI criteria included other electrocardiographic patterns, such as ST-segment depression or T-wave inversion and required angiographic demonstration of a high-grade culprit stenosis with an associated segmental wall motion abnormality before enrollment.

In all cases, venous peripheral blood samples for the MPV measurement were drawn on admission. Blood samples were taken into standardized tubes containing dipotassium ethylenedinitro tetraacetic acid (EDTA) and stored in room temperature. All measurements were performed within 30 min after blood collection. A biochemical profile was obtained by automated analysis (R-A 1000, RA-XT autoanalyser, Technicon, Tarrytown, NY, USA) in the Department of Biochemistry. A Coulter MD II device (Coulter MD II Series Analyzer, Coulter Cooperation, Miami, FL, USA) was utilized for whole blood counts with appropriate calibration (15). The assessment of MPV was made without clopidogrel, heparin, or tirofiban on medication board.

In each case, coronary angiography was performed in standard projections for different coronary arteries (Integris H5000C, Philips Company, Netherlands). Digital angiograms were then analyzed by an experienced interventional cardiologist. All angiograms were assessed with a respect to Thrombolysis In Myocardial Infarction (TIMI) flow scale in infarct-related artery (16).

All patients received 300 mg acetylsalicylic acid before intervention and unfractioned heparin during PCI on a routine basis. Clopidogrel was given (600 mg loading dose, and subsequently 75 mg daily) to all stent implanted cases. Glycoprotein IIb/IIIa inhibitors (tirofiban) were administered during PCI, at the discretion of the operator. All specific drugs were started in the cardiac intensive care unit according to current guidelines (17,18).

In statistical analysis data were analyzed using SPSS for Windows statistical package version 15.0 (SPSS Inc., Chicago, IL). Quantitative data were presented as mean±standard deviation. Demographic characteristics were expressed by descriptive analysis. Independent samples t-test or Mann-Whitney U-test was used to compare continuous variables where appropriate. Statistical difference was defined by a p value below 0.05.

Results

There were no differences between the STEMI and NSTEMI groups in terms of age, smoking habits, hypertension, diabetes mellitus, blood lipid profile, whole blood count, sedimentation and leukocyte differential counts (Table I). Only the MPV comparison between STEMI and NSTEMI groups demonstrated a statistical significance in favor of higher MPV values for STEMI (p=0.001). When we compared the MPV values of both STEMI and NSTEMI patients individually with healthy controls, only the MPV values in the STEMI group were found to be significantly higher (8.7±1 vs 8.1±0.7, p=0.03 and 7.9±0.7 vs 8.1±0.7, p=0.52, respectively). Comparing STEMI and NSTEMI total platelet counts individually with those of healthy people demonstrated lower platelet counts for both STEMI and NSTEMI groups reaching statistical significance (221.2±69.9 vs 350.1±102.8; p=0.01 and 256.5±78 vs 350.1±102.8; p<0.001, respectively). Total platelet counts in the STEMI and NSTEMI patients did not show any statistical difference (p=0.2). All NSTEMI patients survived, but four STEMI patients (7%) died in the early 30-day period.

Table I. Characteristics of the study groups

	Control group (n=50)	*Non-ST elevation myocardial infarction group (n=52)*	*ST elevation myocardial infarction group (n=56)*	*p value**
Age (year)	67±14	69±14	66±16	0.11
Gender (male)	35 (70%)	40 (77%)	38 (68%)	0.29
Smoking	9 (18%)	9 (17%)	11 (20%)	0.75
Hypertension	11 (22%)	11 (21%)	14 (25%)	0.65
Diabetes mellitus	7 (14%)	6 (12%)	8 (14%)	0.67
Cholesterol/HDL	4.9±2.3	5.1±3.5	4.8±1.7	0.81
LDL (mg/dL)	122.1±48.6	121.8±53.8	122.3±46.8	0.90
HDL (mg/dL)	43.1±14.7	43.9±15.4	42.9±14.3	0.88
VLDL (mg/dL)	26±22	24±19	35±29	0.23
Triglyceride (mg/dL)	173±114	168.3±94	181.3±148	0.10
White blood count (10^9/L)	8.7±4	11.4±6	11.2±4	0.93
Neutrophil (%)	58.1±19.4	73.3±20	62.8±20	0.10
Lymphocyte (%)	27.5±12	20.2±9	26.4±19	0.22
Monocyte (%)	4.8±3	5.9±3	6.1±2	0.28
Eosinophil (%)	0.3±0.1	0.3±0.1	0.4±0.1	0.44
Basophil (%)	2.5±1.6	2.7±0.1	2.5±8.7	0.36
Red blood cell (10^{12}/L)	4.4±0.9	4.2±0.9	4.4±0.5	0.63
Hemoglobin (gr/dl)	14.1±2	12.6±2	13.6±1	0.28
Hematocrit (%)	42±6.8	37.1±7.7	40.4±4	0.22
Mean corpuscular volume (fl)	89.2±7	87.1±6	91.7±5	0.07
Platelet count (10^9/L)	350.1±102.8	256.5±78	221.2±69.8	0.21
Mean platelet volume (fl)	8.1±0.7	7.9±0.7	8.7±1	<0.01

*: p value demonstrates the comparison between the NSTEMI and STEMI groups

Discussion

Circulating platelets are heterogeneous in size, density, and reactivity (19,20). Changes in these variables may be causal in acute coronary syndromes (13). Initial plaque rupture in the coronary artery and subsequent exposure of thrombogenic components of the vessel wall to platelets might be the precipitating event in thrombus formation. However, independent of the prothrombotic changes in the plaque, the presence of larger, more reactive platelets is also likely to contribute to thrombosis (21-23). Platelet size has been shown to reflect platelet activity. MPV can reflect changes in the level of platelet stimulation (physiology) and the rate of platelet production (biology) (24).

Changes in the platelet size and count, on the other hand, was relatively well documented in patients with acute coronary syndromes. P selectin and MPV, two markers associated with platelet reactivity, were shown to be elevated in acute coronary syndromes (27).

Our study showed higher MPV values in STEMI as compared to NSTEMI patients. Also, when these results were compared with healthy controls, only STEMI patients' MPV results were significantly higher.

In our study, platelet counts were similar in both NSTEMI and STEMI patients, not reaching statistical difference, but comparison of platelet counts between healthy and NSTEMI as well as healthy and STEMI patients demonstrated significantly lower platelet counts, consistent with the literature (2,9,26). No significant difference in MPV was reported in chronic stable patients with ischemic disease waiting for cardiac surgery compared with healthy volunteers (28). One might argue that only the transition from the stable to the unstable form of coronary artery disease is accompanied by activation of thrombopoiesis and may produce larger platelets with lower platelet numbers, which is also consistent with our findings comparing the healthy normal individuals with acute myocardial infarction patients (28).

Further evidence implying that an increased MPV contributes to the prothrombotic state in acute coronary syndromes has been reported in a recent study by Pizzulli et al performed on 981 patients (9). They have found a significant increase in MPV in patients with unstable angina as compared to stable angina and noncardiac chest pain. This increase in platelet size has been accompanied by a decrease in platelet count, which is also consistent with our findings (9).

There was no statistical difference in platelet counts between STEMI and NSTEMI patients. To the best of our knowledge, this has not been reported in the literature previously. When we compared MPV for both STEMI and NSTEMI groups, we found higher MPV values for STEMI compared to healthy controls, which was consistent with larger and reactive platelets causing a higher prothrombotic state leading to consumption of larger and reactive platelets (29,30). Although not reaching statistical significance, smaller MPV values were found in NSTEMI compared to healthy controls. Therefore, one may conclude why STEMI is a more emergent and mortal state in the early period of acute myocardial infarction comparing to NSTEMI rather than the late period and deserves more aggressive approach in terms of emergent revascularization (10).

Another important finding of our study was that, when MPV values in STEMI and NSTEMI groups were compared with healthy individuals, larger MPV were found in STEMI, possibly leading to increased consumption of larger and reactive platelets causing a higher prothrombotic state in STEMI rather than the NSTEMI (10). It has also been reported that a combination of higher MPV and lower platelet count is a major risk factor for myocardial infarction, which is again consistent with our findings in terms of increased early mortality only in STEMI but not in NSTEMI (31,32).

Early PCI (with or without abciximab) should be the default mechanical reperfusion therapy in STEMI. Although overall long-term survival is in general excellent in non-shock patients with STEMI and NSTEMI undergoing mechanical reperfusion therapy, close follow-up of patients with both STEMI and NSTEMI is warranted because of their increased rates of ischemic events one month to one year after primary PCI because of increased prothrombotic state in both conditions.

In conclusion MPV but not platelet count differs between STEMI and NSTEMI patients, which deserve further clinical research in terms of understanding the pathophysiological basis of these clinical circumstances and developing new therapeutic strategies for this particular acute coronary syndrome.

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