The evaluation of mean platelet volume levels in patients with idiopathic and ischemic cardiomyopathy: an observational study

İdiyopatik ve iskemik kardiyomiyopatili hastalarda ortalama trombosit hacmi düzeylerinin değerlendirilmesi: Gözlemsel bir çalışma

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ABSTRACT

Objective: Cardiomyopathy (CMP) is a disorder associated with an increased risk of thromboembolism due to blood stasis, platelet activation and altered coagulation status. In this study, we aimed to investigate mean platelet volume (MPV) in patients with idiopathic CMP and ischemic CMP and to compare with those of the controls, and aimed to determine whether there is a relationship between MVP and echocardiographic parameters in patients with CMP.

Methods: This study was designed as an observational cross-sectional study. A total of 100 subjects with idiopathic CMP (n=35), ischemic CMP (n=35) and controls (n=30) were included in the study. The MPV values were measured in all participants. All subjects underwent transthoracic echocardiography and angiographic evaluation. We used Chi-square test, one-way ANOVA and Pearson correlation tests for statistical analysis.

Results: The MPV values were significantly higher in patients with idiopathic CMP and ischemic CMP than those of the controls (9.03±1.3 and 8.77±0.9 vs. 7.95±1.0 fl, respectively, p<0.001). The MPV values were although not statistically significant also tend to be higher in patients with idiopathic CMP than in patients with ischemic CMP (p=0.328). The MPV values were found to be positively correlated with left ventricular end-diastolic and end-systolic diameters (r=0.369, p<0.0001; r=0.325, p=0.001, respectively), and left atrial diameter (r=0.403, p<0.0001), but inversely correlated with left ventricular ejection fraction (r=-0.392, p<0.0001).

Conclusion: Patients with idiopathic or ischemic CMP have higher MPV values indicating tendency to platelet aggregation regardless of the etiology, when compared to controls and an enlarged dysfunctional left ventricle may also be associated with higher MPV values.

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Key words: Mean platelet volume, thrombosis, cardiomyopathy, echocardiography

ÖZET

Amaç: Kardiyomiyopati (KMP) kan stazı, trombosit aktivasyonu ve değişen koagülasyon durumu nedeniyle, artmış tromboemboli ile ilişkili bir hastalıktır. Biz, bu çalışmada iskemik ve idiyopatik KMP'li hastalarda ortalama trombosit hacmini (OTH) belirlemeyi ve onları kontrol grubuyla kıyaslamakla birlikte, KMP'li hastalarda OTH ile ekokardiyografik parametreler arasında bir ilişki olup olmadığını da belirlemeyi amaçladık.

Yöntemler: Bu çalışma gözlemsel enine-kesitli çalışma olarak dizayn edildi. Çalışmaya idiyopatik KMP'li 35 hasta, iskemik KMP'li 35 hasta ve kontrol grubu 30 kişi olmak üzere toplam 100 birey dahil edildi. Çalışmaya katılan tüm bireylerin OTH değerleri ölçüldü ve tüm katılanlara transtorasik ekokardiyografi ve anjiyografik değerlendirme yapıldı. İstatistiksel analizler için Ki-kare testi, tek yönlü ANOVA ve Pearson korelasyon testleri kullanıldı.

Bulgular: Çalışmamızda OTH değeri idiyopatik ve iskemik KMP'li hastalarda kontrol grubuna göre anlamlı olarak daha yüksek bulundu (9.03±1.3'e karşın 8.77±0.9 ve 7.95±1.0 fl, sırasıyla, p<0.001). Ayrıca OTH değeri idiyopatik KMP'li hastalarda iskemik KMP'li hastalara göre daha yüksekti, ancak bu yükseklik istatistiksel olarak anlamlı değildi (p=0.328). Çalışmamızda OTH değeri ile sol ventrikül diyastol sonu ve sistol sonu çap (r=0.369, p<0.0001; r=0.325, p=0.001, sırasıyla) ve sol atriyal çap (r=0.403, p<0.0001) değerleri arasında pozitif ilişki sol ventrikül ejeksiyon fraksiyonu arasında negatif ilişki bulundu (r=-0.392, p<0.0001).

Sonuç: Hem idiyopatik hem iskemik KMP'li hastalarda kontrollerle kıyaslandığında daha yüksek olan OTH değerleri, KMP'li hastaların etiyolojisi ne olursa olsun, trombosit agregasyonuna eğilimini gösterir. Ayrıca, bu hastalarda genişlemiş ve bozulmuş sol ventrikül ile artmış OTH değerleri arasında bir ilişki olabilir. *(Anadolu Kardiyol Derg 2011; 11: 595-9)*

Anahtar kelimeler: Ortalama trombosit hacmi, tromboz, kardiyomiyopati, ekokardiyografi

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Introduction

Cardiomyopathies (CMP) are a group of disorders characterized by dilatation and impaired contraction of left ventricle (LV) and, thromboembolic event is a serious complication in these patients. At least 11% of patients with dilated CMP have one or more embolic event during the course of this illness, and mural thrombus is more frequently observed in the LV than in the left atrium (1, 2).

It has been reported that mean platelet volume (MPV) - index of platelet size reflects platelet function and activity (3-5). Changes in the platelet behavior, such as increased platelet aggregability, have been proven as the independent risk factors for cardiovascular events (3, 4). Platelet production and stimulation indirectly elevate values, which can result in cardiovascular disease, as larger platelets are more reactive than normal-sized ones (5, 6). Accordingly, previous reports have suggested that platelet thrombin and fibrinolytic activities are increased in patients with CMP (7, 8).

However, to date, head-to-head comparison of MPV values in patients with idiopathic and ischemic CMP has not been performed yet. Additionally, the relationship between MVP and echocardiographic parameters in patients with CMP has not been shown in previous studies.

The purpose of this study was to measure and compare MPV, a simple marker of platelet activation, in patients with idiopathic or ischemic CMP and in the controls. Another purpose of this study was to evaluate whether there is a relationship between MVP and echocardiography parameters in patients with CMP.

Methods

Study design and patients

This study was designed as an observational cross-sectional study.

We enrolled 100 consecutive subjects with sinus rhythm, who were evaluated at our center. The patients were divided into three groups; patients with idiopathic CMP (n=35), ischemic CMP (n=35) and controls (n=30). The CMP was defined as global left ventricular (LV) ejection fraction ≤ 30 % and/or LV end-diastolic diameter ≥ 56 mm. Ischemic etiology of CMP was defined as the presence of significant epicardial coronary artery disease confirmed by coronary angiography. Control subjects were selected among those with angiographically confirmed normal coronary artery and having normal echocardiography.

Exclusion criteria were the presence of atrial fibrillation, decompensated heart failure, acute coronary syndrome within the last two months, LV thrombosis, moderate-to-severe valvular heart disease, hematological disorder, active infectious disease, malignancy, immunological disease, prosthetic valves, renal and hepatic failure. None of the subjects were using anti-platelet or anticoagulant drugs except aspirin. However, aspirin had been stopped at least 7 days before blood sampling.

The study protocol was approved by the institutional ethics committee and all individuals gave their informed consent.

Blood sampling

Blood samples were drawn from the antecubital vein at 08.00-10.00 a.m. after an overnight fasting period. Blood samples were collected in dipotassium ethylenediaminetetraacetic acid containing tubes. All measurements were performed immediately after venipuncture to prevent in vitro platelet activation. The MPV was measured by using Beckman Coulter LH 780 Hematology Analyzer (USA). The expected values for MPV in our hematology laboratory ranged from 6.8 to 10.8 fl. The other biochemical analyses were determined by standard methods.

Echocardiographic measurements

All participants underwent 2-D and Doppler echocardiographic evaluation by using commercially available echocardiography equipped with 2.5-and 3.5-MHz transducer (ATL HDI-5000 Bothell, Washington, USA). Two-dimensional and pulsed wave Doppler echocardiographic studies were performed in the left lateral decubitus position with the conventional views (parasternal long- and short- axis, apical four-chamber views). Left atrial diameter, LV end-diastolic diameter and LV end-systolic diameter were measured by M-mode echocardiography. LV ejection fraction was determined from apical two and four-chamber views, using Simpson's biplane method.

The assessment of LV thrombosis was made according to the presence of a distinct echodense mass from the LV wall, identified in at least two different echocardiographic views and, associated with regional or global wall-motion abnormality (9).

Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 11.0 software (Chicago, Illinois, USA). All continuous variables are expressed as mean±SD, and categorical variables are expressed as numbers. Normality of distribution for continued variables in groups was determined by the Shapiro-Wilk test. The variables showed normal distribution ($p>0.05$). Continuous variables were compared by using one-way ANOVA, followed by Schaffer post-hoc test. Categorical variables were compared using Chi-square test. Correlations between MPV and other variables were evaluated by the Pearson and Spearman rank correlation tests where appropriate. Statistical significance was accepted as p value less than 0.05.

Results

Baseline demographic, clinical and laboratory parameters are given in Table 1. Distribution of sex, age, diabetes mellitus, hypertension and smoking were similar in each group. Echocardiographic parameters are also given in Table 1. Left atrial and ventricular dimensions were significantly higher, while LV ejection fraction was markedly lower in patients groups as compared to controls ($p<0.001$ for all).

Table 1. The comparison of clinical characteristics, laboratory and echocardiographic findings of the study population

Variables	Idiopathic CMP (n=35)	Ischemic CMP (n =35)	Controls (n =30)	F*	p**
Age, years	58.3±15.4	60.1±9.4	57.2±7.7	0.5	NS
Males/females, n	19/16	18/17	16/14		NS
DM, n	5	7	5		NS
HT, n	15	17	13		NS
Smoking, n	11	10	8		NS
WBC, $\times 10^9$/L	6.3±1.4	6.0±1.2	5.9±1.4	0.6	NS
Hemoglobin, gr/dL	13.4±1.8	13.2±2.0	13.5±1.7	0.2	NS
MPV, fl	9.03±1.3#	8.77±0.9##	7.95±1.0	8.5	0.001
Total platelet count, $\times 10^9$/L	256.3±78.4	244.8±79.1	265.3±64.6	0.6	NS
LA diameter, mm	45.9±5.5†	43.5±5.1††	33.1±4.1	58.1	<0.001
LVEDD, mm	62.5±5.2∞	58.9±4.9∞∞	46.4±3.8	103.1	<0.001
LVESD, mm	50.2±5.3ϕ	46.0±5.6ϕϕ	31.2±4.5	116.1	<0.001
LV EF, %	26.8±3.2¶	26.3±3.8¶¶	61.8±5.5	739.5	<0.001

Data are presented as mean±SD values and numbers
*F values for one-way ANOVA test
**p values Chi-square test and one-way ANOVA test
Schaffer post-hoc test:
#p=0.001 vs Controls; ##p=0.001 vs Controls
†p<0.001 vs Controls; ††p<0.001 vs Controls
∞p<0.001 vs Controls; ∞∞p<0.001 vs Controls
ϕp<0.001 vs Controls; ϕϕp<0.001 vs Controls
¶p<0.001 vs Controls; ¶¶p<0.001 vs Controls
CMP - cardiomyopathy, DM - diabetes mellitus, HT - hypertension, MPV - mean platelet volume, LA - left atrial, LVEDD - left ventricular end-diastolic diameter, LVESD - left ventricular end-systolic diameter, LVEF - left ventricular ejection fraction, NS - statistically not significant, WBC -white blood cell

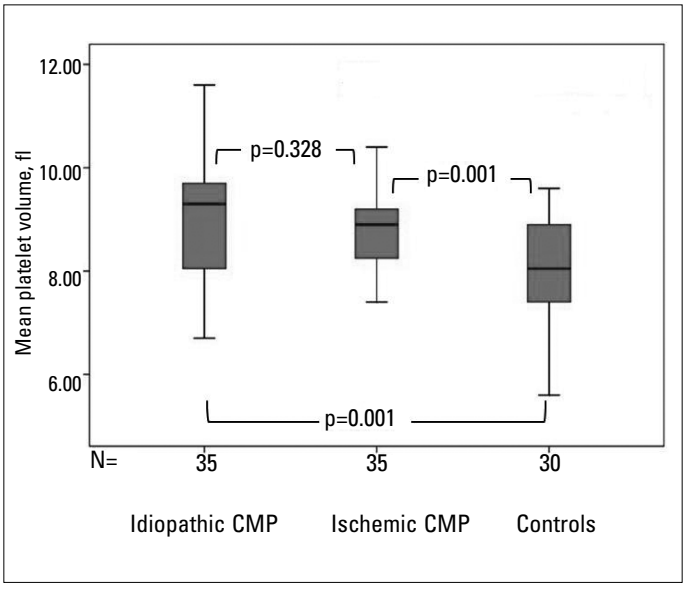

Figure 1. The comparison of mean platelet volume values in patients with idiopathic and ischemic CMP and controls
CMP - cardiomyopathy

The MPV values were significantly higher in patients with idiopathic or ischemic CMP than in the controls (9.03±1.3 vs. 8.77±0.9 vs. 7.95±1.0 fl, respectively, p=0.001, Table 1). The MPV values were although not statistically significant also tend to be higher in patients with idiopathic CMP than in patients with ischemic CMP (p=0.328) (Fig. 1).

The MPV values were found to be correlated with echocardiographic parameters including LV end-diastolic diameter, (r=0.369, p<0.0001), LV end-systolic diameter (r=0.325, p=0.001) and left atrial diameter (r=0.403, p<0.0001). The MPV values were also found to be inversely correlated with LV ejection fraction (r=-0.392, p<0.0001).

Discussion

In the present study, we found that MPV was significantly higher either in patients with idiopathic or ischemic CMP, when compared with those of the controls. MPV was also associated with LV end-diastolic and end-systolic diameters and ejection fraction. In addition, MPV values were higher in patients with idiopathic CMP than in patients with ischemic CMP, although it was not statistically significant.

Cardiomyopathies are a group of disorders associated with an increased risk of thromboembolism due to low output state, blood stasis by a dilated chamber and poorly contracting ventricle, platelet activation and altered coagulation status (10-12). Previously, some studies have evaluated the coagulation system in patients with idiopathic CMP using these hemostatic molecular markers. Asakura et al. (13) reported that the plasma levels of thrombin-antithrombin III complex and prothrombin fragment 1+2 were moderately increased in patients with CMP and atrial fibrillation. However, in our study, patients with atrial fibrillation were excluded. LV thrombus is frequently observed in patients with dilated CMP using echocardiography. Falk et al. (14) reported that it was significantly more common in patients with dilated CMP with fractional shortening <10% than in those with fractional shortening of 11% to 25%. Ischemic etiology, lower LV ejection fraction and increased LV end-diastolic diameter (>60 mm) are other well-known factors contributing to the formation of LV thrombus (15, 16). Accordingly, in our study, elevated MPV was associated with increased LV diameter and low LV ejection fraction. Yılmaz et al. (17) showed that MPV was increased in patients with dilated CMP and sinus rhythm having LV thrombosis, when compared with those without LV thrombosis. However, in that study, the patients with dilated CMP were not classified as those with and without ischemic etiology. In addition, in our study, those with LV thrombosis were excluded. Erbay et al. (18) investigated plasma levels of molecular markers for platelet activity, thrombin activation and fibrinolytic status in patients with dilated CMP with and without LV thrombosis and in controls. They found that platelet activity, thrombin activation and fibrinolytic activity were increased in patients with dilated CMP compared to controls but found no difference in terms of these

markers between those with and without LV thrombus. However, the study population was heterogeneous. Weildinger et al. (19) have demonstrated that platelet survival is shortened and cardiac platelet uptake diffusely enhanced in patients with dilated CMP of either idiopathic or ischemic origin. Accordingly, we showed that MPV values were higher in patients with ischemic and idiopathic CMP when compared to controls.

Platelets play a crucial role in the pathogenesis of atherosclerotic complications, contributing to thrombus formation or apposition after plaque rupture. The MPV is a marker of platelet function and large platelets contain more dense granules and produce more thromboxane A2 (5, 6, 20-22). Increased MPV has been associated with greater in vitro aggregation in response to ADP and collagen (20-21). Further, elevated MPV levels have been identified as an independent risk factor for myocardial infarction in patients with coronary artery disease, and for death or recurrent vascular events after MI (4). On the other hand, increased platelet size has been reported in patients with vascular risk factors such as diabetes, hypercholesterolemia, smoking, and acute ischemic stroke (3, 23-25). Therefore, increased MPV could be regarded as a marker for thromboembolic complications in cardiovascular disorders.

In our study, we found that MPV levels in patients with idiopathic CMP were similar to the levels in ischemic CMP patients and, elevated MPV was associated with increased LV diameter and low LV ejection fraction. There was no study comparing MPV levels in patients with idiopathic and ischemic CMP. The blood stasis caused by a dilated chamber and poorly contracting ventricle might be a facilitating or triggering factor on platelet behavior, leading to the stimulation of the platelets and finally an increase in MPV (7, 26-28). The course of CMP, regardless of the etiology, is the result of the dilated chamber and low LV ejection fraction. Hence, we speculate that elevated MPV in patients with CMP is more closely related to the changes in the course of the disease than the etiology of CMP.

The current available guidelines for the treatment of patients with CMP restrict the administration of anticoagulant and antiplatelet agents only to patients who have some specific comorbidities, including coronary artery disease, atrial fibrillation, a history of thromboembolic event and LV mural thrombosis (29). The rationality for extending the application of anti-platelet and anticoagulant therapy beyond these specific patient subgroups relies on the occurrence of thromboembolic complication and, on the other hand, on the pathophysiology of the disease itself. Therefore, there is still conflicting data for the use of anti-platelet and anticoagulant agents in CMP. While some studies recommend the use of anti-platelet and anticoagulant agents in CMP, some studies do not recommend (30-35). Moreover, use of antiplatelet agents has been associated with increased hospitalization rate due to their interactions with angiotensin-converting enzyme inhibitors (33, 34).

From the clinical point of view, only depending on increased MPV values, it is difficult to claim that anti-platelet and anticoagulant agents should be given to all CMP patients. However, at least, it should be kept in mind that increased MPV values together with the other markers of platelet, thrombin and fibrinolytic activity may be one of the parameters facilitating thromboembolic complications in these patients.

Study limitations

Our study has several limitations. A limited number of patients were included in the study and, the other markers of platelet activation and aggregation were not studied. Actually, if the other markers of platelet activation had been studied, it would be more supportive to our findings. In addition, none of the patients underwent transesophageal echocardiography, although apparent thrombosis and spontaneous echo contrast were not observed by transthoracic echocardiography. Finally, in our study also consisted of healthy control subjects as well as the patients with ischemic and dilated CMP so the treatment, that may be a potential confounding factor, was very difficult to be similar to each other in all groups. As a result, the important limitation of our study is that the treatment has not been standardized in all groups.

Conclusion

We concluded that either patient with ischemic or idiopathic CMP have higher MPV values indicating tendency to platelet aggregation regardless of the etiology, when compared to controls and, an enlarged and dysfunctional LV may be associated with higher MPV values. However, further large-scale studies are required to clarify whether the patients with CMP having high MPV values are at greater risk of thromboembolism and may benefit from the anti platelet therapy.

Conflict of interest: None declared.

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