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Kararlı anjinası olan koroner arter hastalarında ortalama trombosit hacmi ve koroner aterosklerozun yaygınlığı

Mean platelet volume and the extent of coronary atherosclerosis in patients with stable coronary artery disease

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ÖZET

Amaç: Bu çalışmanın amacı, kararlı anjina nedeniyle koroner anjiyografi yapılmış hastalarda ortalama trombosit hacmi (OTH) ile koroner arter hastalığının (KAH) varlığı ve yaygınlığı arasındaki ilişkiyi değerlendirmektir.

Çalışma planı: Çalışmaya 540 ardışık hasta (350 erkek, 190 kadın, ortalama yaş: 59,6±11,4) alındı. Hastalar, KAH varlığı ve yaygınlığına göre dört gruba ayrıldı (Grup 1 önemli KAH olmayan, Grup 2 tek damar hastalığı, Grup 3 iki damar hastalığı, Grup 4 ise üç damar hastalığı olanlar). Ayrıca, her hastanın koroner anjiyografisinde Gensini skorları hesaplandı.

Bulgular: Grup 1'de 159, Grup 2'de 169, Grup 3'te 110, Grup 4'te ise 102 hasta vardı. Beklendiği gibi, gruplar arasında ortalama yaş, cinsiyet, hipertansiyon, diabetes mellitus, hiperlipidemi, sigara içimi ve aile öyküsünü içeren risk faktörleri açısından önemli farklılıklar olduğu görüldü. Diğer taraftan, trombosit sayısı ve OTH değerlerinde (Grup 1 için 8,5±0,1 fl, Grup 2 için 8,5±1,2 fl, Grup 3 için 8,6±0,9 fl, Grup 4 için 8,6±0,9 fl) gruplar arasında anlamlı bir farklılık bulunmadı. Gensini skorunun yaş, plazma ürik asit düzeyi, beyaz küre sayısı, hemoglobin, açlık kan şekeri, yüksek dansiteli lipoprotoein düzeyi ile önemli ölçüde korelasyon gösterdiği saptandı. Buna karşın, OTH ve Gensini skoru arasında bir ilişki gösterilemedi.

ABSTRACT

Objectives The aim of this study was to assess the relationship between mean platelet volume (MPV) and the presence and extent of coronary artery disease (CAD) in patients who underwent coronary angiography for stable chest pain.

Study design: A total of 540 consecutive patients (350 male, 190 female; mean age: 59.6±11.4 years) were included in the study. The patients were divided into four groups according to the presence and extent of their CAD as follows: Group 1 - patients with no significant CAD, Group 2 – one-vessel disease, Group 3 – two- vessel disease, and Group 4 – three- vessel disease. Also, Gensini score for angiographic severity of CAD was calculated for every patient.

Results: There were 159 patients in Group 1, 169 in Group 2, 110 in Group 3, and 102 in Group 4. As expected, we observed significant differences among the groups regarding mean age and other coronary risk factors including gender, hypertension, diabetes mellitus, hyperlipidemia, smoking, and family history of ischemic heart disease. However, there were no significant differences among the groups regarding platelet counts and MPV values (MPV values of Groups1,2,3, and 4 were 8.5±0.1 fl, 8.5±1.2 fl,

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Sonuç: Kararlı anjinası olan koroner arter hastalarında OTH ve koroner ateroskleroz arasındaki ilişkiyi değerlendiren geniş çaplı araştırmalardan biri olan bu çalışmada, OTH ile koroner atreosklerozun varlığı ve yaygınlığı arasında bir ilişkinin olmadığı saptandı.

8.6±0.9 fl and 8.6±0.9 fl respectively). Although the Gensini score was found to be significantly correlated with age, plasma uric acid level, white blood cell count, hemoglobin level, fasting blood glucose, and high density lipoprotein level, no significant association was detected between MPV and Gensini score values.

Conclusion: This study is one of the largest studies assessing the relationship between MPV and the extent of coronary atherosclerosis in patients with stable CAD to date. However, we found no association between MPV and the presence and extent of coronary atherosclerosis.

Abbreviations:

FBG Fasting blood glucose
DM Diabetes mellitus
HL Hyperlipidemia
HT Hypertension
CAD Coronary artery disease
MI Myocardial infarction
MPV Mean platelet volume
LVEF Left ventricular ejection fraction

Mean platelet volume (MPV) has been shown to be a potential marker for thrombocytic activation which will play an important role in the pathophysiology of atherosclerosis.[1] Increased MPV is thought to be a closely associated with cardiovascular diseases, mainly acute coronary syndromes, and also very well-known risk factors including hypertension (HT), diabetes mellitus (DM), and hyperlipidemia (HL).[2-5] However, limited number of studies studies have especially investigated the relationship between MPV, and extent of the coronary artery disease (CAD), and also available data remain to be contradictory.

In this study, we aimed to assess the relationship between MPV, and severity, and extent of atherosclerosis in patients with stable angina, and also evaluate the place of MPV among conventional risk factors of atherosclerosis.

PATIENTS AND THE METHOD

With the intention to constitute our study population, 2050 patients who had undergone coronary angiography between March 2009, and August 2009 in our clinics with any indication were analyzed. A total of 540 consecutive patients with available detailed personal medical information who met the study criteria and had undergone coronary angiography with the indication of stable angina pectoris were included in our study.. Approval for the study was obtained from Educational Planning and Coordination Committee of our Institute. Patients with a history of coronary artery bypass, hematologic disease, oral anticoagulant use, and symptoms of severe valvular, peripheral artery, liver, kidney or heart failure, acute coronary syndrome and/or infection were excluded from the study. Diagnoses of. DM, HT, and HL were made according to the criteria stated in the guidelines of American Diabetes Association 2008, European Society of Cardiology 2007, and ATP III (Adult Treatment Panel III), respectively. [6-8] Positive family history was defined as the presence of angina pectoris, myocardial infarction (MI), CAD or history of coronary revascularization detected in the first-degree male (age, < 55 yrs), and female (age, < 65 yrs) relatives.

For hematologic measurements blood samples drawn from the patients after 12-hour fasting period were used. Biochemical parametres, and serum lipid levels were determined using standard methods. For the measurement of MPV, and some other hematologic parametres of the patients, blood samples were kept 2 hours in tubes containing tripotassium EDTA, and then analyzed using Advia 2120 Hemathology System (Siemens, Germany) analyzers.

Coronary angiography was routinely performed by the Judkins catheterization technique using 6-F left, and right coronary artery catheters. Angiograms were evaluated

by two experienced interventional cardiologists blinded to the clinical information of the patients. An atherom plaque which causes at least 50 % intraluminal stenosis in one of the three coronary arteries (left anterior descending artery, right coronary artery, and circumflex artery) was defined as the presence of an important angiographic vascular lesion.[2,9] Extent of coronary artery disease was evaluated using Gensini scoring system. [10]

Statistical analysis

In all analyses SPSS 10.0 (Chicago, IL.) program was used. Numerical variables were expressed as means ± standard deviation, and categorical variables as frequencies (%). For the comparison of numerical variables Bonferroni Post Hoc analysis, and analysis of variance, and for categorical variables *chi*-square test were used. For the evaluation of the correlation between numerical variables Pearson's correlation analysis was employed. $P<0.05$ was accepted as a criterion for statistical significance.

RESULTS

In the study a total of 540 consecutive patients who had undergone coronary angiographic examinations were analyzed. The control group consisted of patients without ≥ 50 % intraluminal stenosis of coronary arteries, and major coronary artery disease (Group 1). The cases with critical lesions were divided into 3 separate groups as single (Group 2), two-, (Group 3), and three-vessel (Group) diseases. As could be expected, severity of CAD was associated with risk factors as age, gender, family history of HT, DM, and CAD, smoking status, and lower HDL-cholesterol levels. The groups were comparable only with respect to total, and LDL cholesterol levels. Comparative characteristics of the groups are shown in Table 1.

Mean platelet volume of all patients was 8.5±1.0 fl, while it was 8.5±0.1 fl, 8.5±1.2 fl, 8.6±0.9 fl, and 8.6±0.9 fl in Groups 1,2,3, and 4, respectively. A statistically significant difference could not be demonstrated between the presence, and severity of CAD, and MPV.

Although similarities existed between Groups 3, and 4, apparently severity of CAD increased with age. Fasting blood glucose (FBG) levels demonstrated significant differences between groups, while the highest values were detected in three-vessel patients Serum creatinine, and uric acid levels also displayed significant intergroup differences, and their lowest levels were detected in Group 1. Total, and low-density lipoprotein cholesterol (LDL-C) levels in all groups were comparable, while relatively lower high-density lipoprotein cholesterol (HDL-C) levels were detected in Groups 3, and 4. Besides, hemoglobin values, and white blood cell counts (WBC) were significantly different among groups. The highest WBC counts were encountered in Groups 3, and 4. On the contrary, hemoglobin values were relatively lower in these two groups. We have concluded that left ventricular ejection fraction (LVEF) decreases in parallel with the severity of CAD. As can be expected, Gensini scores differed significantly among all groups ($p<0.001$).

Mean Gensini score related to all patients was calculated as 24.9±27.3. Evaluation of the relationship between these Gensini scores, and other parametres based on Pearson correlation analysis is shown in Table 2.

Accordingly, any significant correlation was not seen between MPV, and Gensini scores ($p=0.12$, $r=0.07$). Besides, a linear correlation was found between Gensini scores, and age, uric acid levels, white blood cell counts, serum creatinine, and FBG values, while an inverse correlation was detected between this scores, and LVEF, blood hemoglobin, and HDL-C measurements.

On the other hand, in conclusion, MPV demonstrated a negative correlation between platelet counts among the abovementioned variables ($p<0.001$), while it did not correlate significantly with other parametres.

Table 1. Comparison of clinical, and laboratory data of all patients, and groups

	All patients (n=450) n (%)	Coronary artery disease Group 1(n=159) Control n (%)	Group 2 (n=169) Single vessel n (%)	Group 3 (n=110) Two-vessel n (%)	Group 4 (n=102) Three- vessel n (%)	*p*
Gender						
Male	350 (64.8)	72 (45.3)	121 (71.6)	82 (74.5)	75 (73.5)	**<0.001**
Female	190 (35.2)	87 (54.7)	48 (28.4)	28 (25.5)	27 (26.5)	
Hypertension	332 (61.5)	85 (53.5)	88 (52.1)	76 (69.1)	83 (81.4)	**<0.001**
DM	149 (27.6)	20 (12.6)	47 (27.8)	36 (32.7)	46 (45.1)	**<0.001**
Hyperlipidemia	295 (54.6)	57 (35.8)	87 (51.5)	67 (60.9)	84 (82.4)	**<0.001**
Family history	184 (34.1)	13 (8.2)	54 (32)	57 (51.8)	60 (58.8)	**<0.001**
Smoking	202 (37.4)	22 (13.8)	72 (42.6)	53 (48.2)	55 (53.9)	**<0.001**
Previous MI	98 (18.1)	0	26 (15.4)	32 (29.1)	40 (39.2)	**<0.001**
Mean ± SD	Ort.±SS	Ort.±SS	Ort.±SS	Ort.±SS	Ort.±SS	
Age	59.6±11.4	55.2±11.2	59.4±10.7	63.6±10.2	62.6±11.6	**<0.001**
LVEF (%)	57.2±7.7	61.7±4.8	58.0±7.2	54.4±8.2	52.0±7.2	**<0.001**
FBG (mg/dl)	117.7±44.5	107.4±36.2	118.3±43.8	117.5±47.3	133.3±5	**<0.001**
Serum creatinine (mg/dl)	0.9±0.3	0.8±0.2	0.9±0.3	0.1±0.3	1.0±0.4	**<0.001**
T. cholesterol (mg/dl)	180.4±25.4	182.3±41.2	177.2±41.4	180.5±39.6	182.6±47.1	0.659
LDL-C (mg/dl)	108.3±34.9	107.2±32.9	105.5±35.0	110.2±33.7	112.5±38.7	0.392
HDL-C (mg/dl)	41.3±12.5	44.7±13.2	41.7±12.3	39.9±10.9	37.1±11.9	**<0.001**
Triglyceride (mg/dl)	154.9±81.9	147.8±78.8	151.3±76.1	158.2±81.2	168.6±95.1	0.209
Uric acid (mg/dl)	5.6±1.4	4.9±1.2	5.7±1.4	6.1±1.5	5.9±1.2	**<0.001**
Hemoglobin (g/dl)	13.5±1.8	13.7±1.5	13.7±1.7	13.5±2.2	12.9±1.9	**0.003**
Hematocrit (%)	41.2±5.6	41.8±5.8	41.6±5.3	41.3±5.6	39.3±5.5	**0.003**
WBC (x $10^3/\mu l$)	8.2±2.4	7.7±2.3	8.2±2.6	8.5±2.6	8.6±2.1	0.008
MPV (fl)	8.5±1.0	8.5±0.1	8.5±1.2	8.6±0.9	8.6±0.9	0.862
Platelet (x $10^3/\mu l$)	288.2±78.6	287.0±71.3	283.0±77.0	286.2±74.2	300.6±94.9	0.338
Mean Gensini score	24.9±27.3	2.2±2.4	15.5±10.1	34.0±17.7	66.2±25.9	**<0.001**

DM: Diabetes mellitus; MI: myocardial infarction; LVEF: Left ventricular ejection fraction; FBG: Fasting blood glucose; T. cholesterol: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; MPV: Mean platelet volume

Table 2. Correlation of Gensini score with other parametres as assessed by Pearson correlation analysis

		Age	UA	MPV	Pct	Plt	WBC	MCV	Hgb	Crtn	FBG	T.chls	LDL-C	HDL-C	TG	LVEF
Gensini score	r	0.20	0.22	0.07	0.06	0.04	0.13	0.03	-0.11	0.22	0.21	0.01	0.07	-0.18	0.07	-0.49
	p	**<0.001**	**<0.001**	0.12	0.20	0.38	**0.003**	0.48	0.009	**<0.001**	**0.004**	0.78	0.12	**<0.001**	0.12	**<0.001**

UA: uric acid; MPV: Mean platelet volume; Pct: Platecrit; Plt: Platelet; WBC: white blood cell; MCV: Mean corpuscular volume; Hemoglobin: Hemoglobin; Crtn: Creatinine; FBG: Fasting blood glucose; T.chls: Total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglyceride; LVEF: Left ventricular ejection fraction

DISCUSSION

In our study which included 540 patients who had undergone coronary angiography, we concluded that MPV measurements did not differ significantly between patient, and control groups or among patient groups with one-, two-, and three-vessel disease.

Larger platelets containing higher number of granules conceivably possess increased biochemical, functional, and metabolic activities.[5,11-14] Morphological, and physiological characteristics of the platelets are determined during fragmentation of their precursor cells, i.e. megakaryocytes. Increased megakaryocytic ploidy was revealed to be correlated with an increase in the volume of megakartocytes, and platelets.[3,11,15] On the other hand, depletion of smaller platelets during episodes of acute ischemia can lead to an increase in MPV secondary to compensatory production of platelets. [2,16] Starting from this corollary, MPV has been proposed as an indicator of thrombocytic activity.[17-19] Due to their important role in the repair process of damaged blood vessels, age of the platelets or marker of their increased production gains importance in many clinical disorders where vascular damage plays a critical role. Various studies performed so far, have demonstrated increased MPV measurements in acute MI, [5,12,20,21] unstable angina pectoris, [2,12] and congestive heart failure. [20]

Halbmayer et al .[22] suggested that MPV could not be a predictive marker of MPV in ischemic heart disease or acute MI. We didn't observe a significant correlation between MPV, and presence, and extent of CAD. This increase in MPV can be explained by increases in the number of larger circulatory platelets originating from bone marrow. In compliance with outcomes obtained from other previous investigations, negative correlation we have found between number of platelets, and MPV also supports this finding.[23] Therefore, whether or not MPV is an indicator of thrombocytic activity seems to be also debatable. For example, van der Planken et al.[24] reported against a relationship between platelet prothrombinase activity and MPV. Instead, if we think of larger platelets as precursors, this condition might conceivably result in decreased aggregation. Endler et al [5] revealed that MPV is an independent risk factor for acute MI, but similar to our outcomes the authors also suggested that MPV is not a risk factor in patients with stable angina pectoris. However Pizzuli et al[2] compared patients with stable, and unstable angina pectoris to non-cardiac chest pain, and arrived at a similar conclusion. Intracoronary thrombus induces the development of acute ischemic syndromes as unstable angina, acute MI, and sudden cardiac death. At this stage, activation of platelets plays a very important role.. Therefore, higher levels of MPV can be expected in cases with acute ischemic events. However as a concluding remark at the end of their study after investigating all basic risk factors, McGill et al [25] advocated that MPV estimates are higher in stable ischemic heart disease when compared with the control group, and also asserted that in this group of patients, platelets agregate more rapidly as a response to adrenalin. On the other hand, in their large scale prospective study, De Luca et al [26] demonstrated lack of any correlation between MPV, and platelet aggregation, carotid intima-media thickness, and extent of CAD.

Limitations of the study

Even though more than five hundred participants included in the study, contributed greatly to the statistical power of the study, the most important limitation of the study might be thought to be related to its non-prospective design. One might question if the prognostic value of MPV can be ascertained in a non-prospective study. In fact, some small scale studies have indicated that MPV might be helpful in risk stratification, and prediction of complications especially in acute coronary syndromes.[18,27,28] Patients with acute coronary syndrome were not included in our study. As an another important issue, it has been suggested that MPV is a measurement technique which requires use of blood samples treated with EDTA left in situ for a while. In many studies, blood samples treated with EDTA were left in situ at least for one hour (range. 2-4 hrs) so as to avoid the interference of rapid turnover. [2,4,5,15,20,21,27] Also, ın our study blood samples were placed in EDTA containing tubes, and evaluated 2 hours later. Though methodologic variations do not allow the establishment of standardized normal limits

for mean platelet volume measurements, every laboratory can determine normal MPV limits using their specific method of measurement. In addition to MPV which is accepted as a rough measure for thrombocytic function, measurement of more costly, and more infrequently used sophisticated parametres of thrombocytic function might provide further information about pathogenesis, and risk factors of CAD.

Conclusion

According to our results, MPV does not correlate with the presence, and extent of CAD in patients who had undergone coronary angiographic examinations with the initial diagnosis of stable angina pectoris. Even though this study is devoid of a follow-up period, it is one of the largest scale population screening investigation. Progressive studies assessing especially MPV which is thought to be an indicator of risk for coronary artery disease will shed light on this issue.

Conflict of interest: None declared

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Key words: Angina pectoris; atherosclerosis; coronary disease/ blood; myocardial infarction; platelet; platelet activation;
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