RESEARCH ARTICLE / *Araştırma Makalesi*

Mean Platelet Volume is Lower in Coronary Artery Ectasia!

Ortalama Trombosit Hacmi Koroner Arter Ektazisinde Düşüktür!

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Abstract

Objective	Coronary artery ectasia (CAE) are defined as the dilation of a segment of a coronary artery at least 1.5 times the adjacent segment. Several studies have shown the association between mean platelet volume (MPV) and cardiovascular diseases. But the results are different. For this reason, we aimed to investigate the association of MPV with CAE.
Materials and Methods	90 patients with normal coronary arteries and 70 patients with CAE were included. Routine blood and biochemical parameters were measured before the arteriography. Differences between groups for continuous variables were analyzed with t- test or Mann-Whitney U test. P values < 0.05 were considered significant.
Results	Baseline patient demographics, including age and clinical risk factors, were similar between the groups. Compared to the control group, MPV levels were significantly lower in the CAE group (8.84 ± 1.71fL vs. 10.43 ± 1.34, p < 0.001). MPV level of < 9,5 fL showed sensitivity , specificity value of 95%, 80%; area under the curve= 0.943, 95% CI, 0.906–0.980) for the prediction of CAE.
Conclusion	The present study suggests that MPV may decrease in patients with CAE.
Keywords	Angiography; Coronary Aneurysms; Coronary Artery Disesas; Mean Platelet Volume.

Öz

Amaç	*Koroner arter ektazi (KAE), bir koroner arterin bir segmentinin bitişiğindeki segmente göre en az 1.5 katı genişlemesi olarak tanımlanır. Birçok çalışma, ortalama trombosit hacmi (OTH) ile kardiyovasküler hastalıklar arasındaki ilişkiyi göstermiştir. Ancak çalışmaların sonuçları farklı olup kafa karıştırıcıdır. Bu nedenle OTH ile KAE ilişkisini araştırmayı amaçladık.*
Gereç ve Yöntemler	*Koroner arterleri normal 90 hasta ve KAE' li 70 hasta çalışmaya dahil edildi. Anjiyografiden önce rutin kan ve biyokimyasal parametreler çalışıldı. Sürekli değişkenler için gruplar arasındaki farklar t-testi veya Mann-Whitney U testi ile analiz edildi. P <0,05 değerleri anlamlı kabul edildi.*
Bulgular	*Hastaların başlıca yaş ve klinik risk faktörlerini içeren demografik verileri gruplar arasında benzerdi. Kontrol grubuyla karşılaştırıldığında, OTH düzeyleri KAE grubunda anlamlı olarak düşüktü (8.84 ± 1.71fL ve 10.43 ± 1.34, p <0.001). MPV seviyesi <9,5 fL iken KAE tahmini için duyarlılık ve özgüllük değerleri sırasıyla % 95,% 80; eğri altında kalan alan = 0,943, % 95 CI, 0.906–0.980) olarak bulundu.*
Sonuç	*Bu çalışma KAE' li hastalarda OTH' nin düşebileceğini düşündürmektedir.*
Anahtar Kelimeler	*Anjiyografi; Koroner anevrizma; Koroner arter hastalığı; Ortalama trombosit hacmi.*

INTRODUCTION

Coronary artery ectasia (CAE) is defined as the dilation of a segment of a coronary artery at least 1.5 times the adjacent segment.[1] CAE and aneurysms are encountered in 0.3-5.3% of coronary angiographies.[2,3] Ectasia affect most frequently the right coronary artery followed by circumflex artery and left anterior descending artery.[1,3-5] The etiologic cause is atherosclerosis in 50% of patients, congenital in 20-30% and inflammatory or connective tissue disorder in 10 to 20%.[5,6] Coronary artery ectasia is often accompanied by coronary artery disease (CAD) but can also be isolated. In patients with coronary ectasia, myocardial perfusion defects can be observed along the related artery region. Turbulent flow in the dilated segment, loss of axial flow leading to red blood cell aggregates and increased thrombogeneity in the same segment and the subsequent distal embolization of thrombi are significant contributors to microvascular perfusion defects. Several studies have shown the association between mean platelet volume (MPV) and cardiovascular diseases.

Platelets plays pivotal role in the formation of CAD and acute coronary syndrome owing to a variety of ways.[7] Their size, which is measured as MPV, can be determined easily by complete blood count test.

In the literature, the results of the previous studies are confidential about the association between hematological parameters and CAE. For this reason, we aimed to investigate the association of MPV with CAE.

MATERIALS and METHODS

This study was designed as a case control study. Angiographic data of the patients who underwent coronary angiography (CAG) between 2016 January and 2019 April were retrospectively analyzed.A total of 160 patients were included: 90 with normal coronary arteries and 70 with CAE with no associated critical coronary artery stenosis. Coronary angiography was performed due to ischemic changes in electrocardiogram (ECG), positive exercise test or myocardial perfusion scintigraphy for ischemia.

Hypertension (HT) was defined as repeated blood pressure measurements >140/90 mmHg or usage of antihypertensive drugs. Diabetes mellitus (DM) was defined as fasting plasma glucose levels >126 mg/dL in multiple measurements or glucose level >200 mg/dL at any measurement or active use of antidiabetic medications. Current smoking was defined as smoking in the previous six months. Hypercholesterolemia was defined as a baseline cholesterol level of >200 mg/dL and/or a low-density lipoprotein (LDL) cholesterol level of >130 mg/dL or previously diagnosed and treated hypercholesterolemia. The exclusion criteria were patients with a history of coronary artery diseases, cardiomyopathy, congestive heart failure, moderate to severe renal failure, severe hepatic dysfunction, atrial fibrillation, severe valvular disease, history of blood transfusion in the last 3 months, leukemia or thrombocytopenia, active infection, history of collagen vascular disease, inflammatory disease, malignancy, hematologic disorders, received non-steroidal anti-inflammatory drugs.The study protocol was approved by the local ethics committee (Ethics committee approval was received from the Tokat Gaziosmanpasa University medical school with the project number 19-KAEK-260 dated 26.12.2019) and written informed consent was obtained from all patients.

Peripheral venous blood samples were drawn from patients who were admitted for angiography. Biochemical parameters were measured using an automated Beckman Coulter LH-750 Hematology Analyzer (Beckman Coulter, Inc., Fullerton, CA, U.S.A.). Serum glucose, creatinine, total cholesterol, high-density lipoprotein cholesterol, and low density lipoprotein cholesterol levels were measured. Blood samples were taken into standardized ethylene diamine tetra acetic acid (EDTA) containing tubes and in order to avoid the platelet swelling with time because of EDTA, measurements were done immediately after the blood sampling. Complete blood count and platelet volume were determined using simultaneous optical and

impedance measurements (Cell Dyn 3700; Abbott Diagnostics, Lake Forest, Illinois, USA). Platelet, lymphocyte, monocytes, white blood cell (WBC) and MPV values of each patient were recorded.

Coronary angiographies were performed through the radial or femoral artery. The coronary angiographies were evaluated by three interventional cardiologists who were blinded to the clinical and laboratory data of the patients. The ectasia location, flow slow, segmental backflow and stazis were evaluated.

Statistical analyses were carried out using the SPSS 18.0 Statistical Package Program for Windows (SPSS Inc., Chicago Illinois, USA). The distribution of the variables in the study groups was analyzed by the Kolmogorov-Smirnov test. Normally-distributed variables were compared by t-test and expressed as mean ± standard deviation. Variables without normal distribution were compared with the Mann Whitney U-test and expressed as median (interquartile range). Qualitative variables were expressed as numbers and percentages. The differences between independent groups were assessed by Student's t-test for normally-distributed quantitative variables and Mann-Whitney U-test for variables without normal distribution, whereas Chi-square test was used for qualitative variables. A receiver operating curve (ROC) analysis was performed to find MPVsensitivity and specificity, aiming to predict the presence of coronary ectasia. All results were considered statistically significant at the level of $p < 0.05$.

RESULTS

Baseline patient demographics, including age and clinical risk factors, were similar between the groups, except that the number of males was significantly lower in the ectasia group. Previous medications were also comparable between two groups (Table 1). Compared to the control group, serum blood glucose, creatinine and lipid levels were not significantly different (Table 2).

Although the platelet, lymphocyte, monocytes and WBC counts were not significantly different between the two groups, MPV levels were significantly lower in the CAE group (8.78 ± 1.62 vs. 10.82 ± 1.28, $p < 0.001$) (Table 2). MPV level of < 9,5 fL showed sensitivity , specificity value of 95%, 80% (AUC = 0.943, 95% CI, 0.906–0.980) for the prediction of CAE (Figure 1).

Table 1. General characteristics of the study groups

Baseline characteristics	Ectasia (n = 70)	Control (n = 90)	P value
Age (mean ±SD) (years))	56 ± 14	54 ± 9	0.122
Male (%)	42 (60%)	39 (43%)	0.001
Smoking (%)	34 (48%)	45 (50%)	0.828
Family history (%)	16 (22%)	15 (16%)	0.114
Hypertension(%)	25 (35%)	20 (22%)	0.132
Diabetes mellitus (%)	16 (22%)	11 (12%)	0.111
Acetyl salicylic acid (%)	20 (28%)	23(30%)	0.219
Statin (%)	20 (35%)	28 (31%)	0.136
B-blocker (%)	22 (31%)	23 (25%)	0.16
ACE inhibitor (%)	3 (4%)	3 (4%)	0.974

ACE: angiotensin-converting enzyme; SD: Standard deviation

Table 2. Laboratory data of the study cohort

Variables (mean ± SD)	Ectasia	Control	P Value
Creatinine(mg/dL)	0.83 ± 0.32	0.81 ± 0.24	0.52
Glucose (mg/dL)	96 ±26	102 ± 19	0.98
LDL-cholesterol (mg/dL)	116 ± 38	111 ± 46	0.37
Triglycerides (mg/dL)	156 ± 104	168 ± 113	0.54
Total cholesterol (mg/dL)	191 ± 56	184 ± 54	0.58
Hemoglobin (gr/dL)	13.3 ± 1.5	13.5 ± 1.6	0.11
Hematocrit (N,%)	44 ± 8	42± 7	0.44
Platelet count (k/mm3)	268 ± 79.50	267 ± 73	0.68-
MPV(fL)	8.78 ± 1.62	10.82 ± 1.28	< 0.001
WBC (x103 µL)	8.4 ± 2.1	6.64 ± 1.21	0.17
Lymphocytes (x103 µL)	2.39 ±0.941	2.48 ± 1.22	0.50
Monocytes (x103 µL)	0.66 ±0.46)	0.65 ± 0.34	0.32

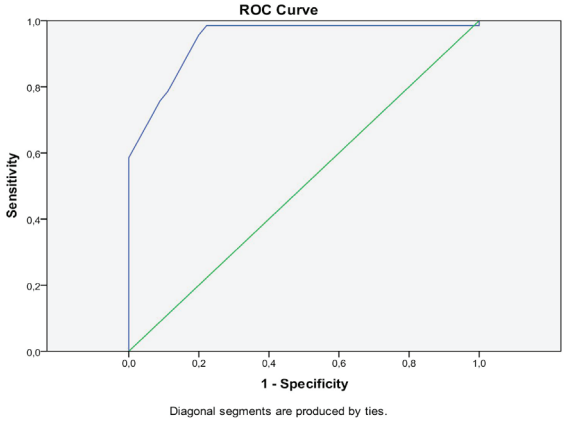
LDL: low-density lipoprotein cholesterol. MPV: mean platelet volume; WBC: White blood cells;
SD: Standard deviation

Echocardiographic measurements were similar (Table 3). The angiographic features of the ectasia group are summarized in Table 4 and Table 5.

Table 3. Echocardiographic findings of the study population			
Variables (mean ± SD)	**Ectasia**	**Control**	**P Value**
Left ventricle end-diastolic diameter (cm)	4.6 ± 0.45	4.5 ± 0.31	0.182
Left ventricle end-systolic diameter (cm)	3.5 ± 0.56	3.4 ± 0.52	0.123
Ejection Fraction (%)	60.4 ± 6.6	61.1 ± 1.56	0.102
Left atrium diameter (cm)	3.2 ± 0.46	3.3 ± 0.53	0.16
SD: Standard deviation			

Table 4. Angiographic findings of the ectasia		
Ectasia placement	N	%
Left main coronary artery	10	7
Left anterior descending artery	50	71
Circumflex coronary artery	54	77
Right coronary artery	58	82

Figure 1- : ROC curve analysis of the MPV data for predicting CAE



Tablo 5. According to segments of ectasic coronary arteries measured diameters	
Mean±SD (mm)	
Total	5.6±1.1
LMCA	6.3±0.7
LAD	
Proksimal	6.1±0.9
Mid	5.6±1.1
Distal	4.6±0.9
CX	
Proksimal	6.0±1.2
Mid	5.7±1.0
Distal	4.3±0.5
RCA	
Proksimal	5.9±1.0
Mid	5.5±1.0
Distal	4.1±0.7
LMCA: Left main coronary artery; LAD: Left anterior descending artery;RCA: right coronary arter;SD: Standard deviation.	

DISCUSSION

In this study, we showed that MPV levels were significantly reduced in the CAE group when compared to that with normal coronary arteries.Stable angina is the most common presentation in patients with CAE.[8] Patients with CAE without stenosis had positive results during myocardial perfusion scintigraphic evaluation and treadmill exercise tests.[9,10] ST-elevation myocardial infarction (MI), non-ST elevation MIcan occur from altered blood flowby distal embolization or occlusion of ectatic segment with thrombus.[11-14]

Coronary ectasia is most common in right coronary artery RCA, at least in left main coronary artery LMCA.[15] In a study based on registration data the most common involvement was seen in RCA in 20 087 patients.[16] Yip et al. reported that ectasia was most commonly observed in RCA, followed by left anterior descending LAD and circumflex Cx involvement, respectively.[17] Similarly, in our patient group, ectasia was seen most frequently in RCA, then in LAD, Cx and LMCA, respectively.

Platelet activation is an important component of the thrombotic and inflammatory processes.[18,19] Chemokines, cytokines, and other inflammatory mediators are secreted by activated platelets.[19] MPV is a routine complete blood count parameter which reflects the platelet size and it may be used as an indicator of platelet activation and the severity of inflammation.[20] Elevated MPV levels are associated with adverse cardiovascular events.[7,18,19] A number of diseases, such as metabolic syndrome, myocardial infarction, acute ischemic stroke and diabetes mellitus have been associated with increased MPV.[19,21] Conversely, lower MPV has been reported in subjects with rheumatoid arthritis, Nasal Polyps and ankylosing spondylitis.[22,23] It has been proposed that lower and higher MPV values in different conditions are related with high and low-grade inflammation states. Gasparyan et al. reported that diseases characterized by marked inflammation (e.g. rheumatoid arthritis) are associated with lower MPV values, while low-grade inflammation (e.g. nasal polyps, Behcet's disease) are associated with increased MPV levels.[24]

MPV was found to be higher in most cardiovascular diseases.[19,21] Ozbek at al was showed that increased MPV is associated with the severity of CAE. MPV values >10.85 fL may indicate the presence of CAE.[25] However, interestingly, MPV in CAE patients was found to be lower than in the control groups. Inflammation plays a major role in the initiation and progression of atherosclerosis and triggers cardiovascular disease events.[26,27] We speculate that, unlike acute coronary syndromes, CAE may be associated with a low but continuous inflammatory burden. The intensity of systemic inflammation has varying impact to platelet size; in particular, a higher grade of inflammation was associated with smaller circulating platelets, whereas inflammation of less degree was associated with larger platelets.[24] Another possible explanation for the results of our study was the effect of age on the maintenance of platelet functions. Young platelets are relatively large and more active, which can lead to more platelet adhesion and aggregation. A lower MPV might be related to a less active platelet function, and it might reflect declining of marrow or total physical function. Some authors speculate that overproduction of pro-inflammatory cytokines and acute phase reactants can suppress the dimensions of platelets by interfering with the process of megakaryopoiesis in the bone marrow.[19] Unfortunately, this is the first study in the literature that evaluated MPV in CAE.

Limitations in the Study

The retrospective cross-sectional design and single-center nature are two important limitations of the present report. Another limitation could be the relatively small study cohort. As far as we know, there are no data about the association of inflammation and CAE. The lack of analysis of inflammatory markers is another important limitation.

CONCLUSION

The present study suggests that lower MPV may be associated with CAE. Therefore, we suggest the use of MPV to determine CAE in patients, considering it is a cost-effective and simple test.

Authors; declares that the manuscript has not been sent to another journal simultaneously and has not been previously published in another journal.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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