Is Mean Platelet Volume a Reliable Marker to Predict Ischemic Stroke in the Follow-Up of Patients with Carotid Stenosis?

Ibrahim Ilker Oz, MD,* Murat Yucel, MD,† Muammer Bilici, MD,‡ İsmail Şerifoğlu, MD,* Raşit Sayın, MD,§ Sevil Uygun Ilikhan, MD,‡ and Mustafa Acıkgoz, MD‖

Background: The objective of the study is to evaluate the reliability of mean platelet volume (MPV) for predicting ischemic stroke (cerebrovascular event [CVE]) among patients with different degrees of carotid stenosis. *Methods:* Fifty-two patients with CVEs, 136 patients with carotid artery disease (CAD), and 40 healthy volunteers were enrolled in this study. All participants were divided into the following groups according to CAD: absence of stenosis, less than 50% stenosis, 50%-69% stenosis, and 70% or more to total occlusion of the internal carotid artery. For each participant, the parameters of CAD were assessed using ultrasonography. To obtain the values of CRP and MPV and the leukocyte and platelet counts, all samples were processed within 30 minutes after blood collection. Univariate and multivariate analyses were used to evaluate the association between the values of serum C-reactive protein (CRP) and MPV and carotid stenosis. *Results:* In terms of age and gender, there was no statistically significant difference between the groups ($P = .094$ and $P = .428$, respectively). However, CRP values in patients with CAD and CVEs were significantly higher than those in the controls ($P < .001$). There was no statistically significant difference between the CRP values in patients with CAD and CVEs ($P = .249$). Moreover, the MPV values did not show any significant difference between the groups ($P = .053$) and among the patients with CAD ($P = .64$). There was no positive correlation between serum CRP and MPV values in patients with CAD regarding the degree of carotid stenosis ($r = .061$, $P = .477$). *Conclusion:* The findings of this study claim that MPV has no predictive value during follow-up of the patients with CAD for CVEs. **Key Words:** Mean platelet volume—C-reactive protein—carotid stenosis—stroke.

Introduction

Stroke remains a major public health problem worldwide and is the third greatest cause of death and the main cause of invalidity. It is known that 80%-90% of all strokes are due to ischemic cerebral infarction. In addition, extracranial internal carotid artery (ICA) stenosis is one of the main risk factors for ischemic cerebrovascular events (CVEs) and causes approximately 20%-30% of all strokes.[1-5] The prevalence of carotid atherosclerosis increases with age and the presence of cardiovascular risk factors.[6] The degree of carotid stenosis is the strongest determinant of stroke risk and most emboli result from the activation of platelets on the atherosclerotic plaque surface.[5,6] However, most people with carotid stenosis have no symptoms until the artery becomes severely narrowed or a clot forms.[7,8]

From the *Department of Radiology, School of Medicine, Bülent Ecevit University, Zonguldak, Turkey; †Department of Cardiovascular Surgery, Ahi Evren Training and Research Hospital, Trabzon, Turkey; ‡Department of Internal Medicine, School of Medicine, Bülent Ecevit University, Zonguldak, Turkey; §Department of Cardiology, School of Medicine, Bülent Ecevit University, Zonguldak, Turkey; and ‖Department of Neurology, School of Medicine, Bülent Ecevit University, Zonguldak, Turkey.

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Address correspondence to Ibrahim Ilker Oz, MD, Department of Radiology, School of Medicine, Bülent Ecevit University, Esenköy, Kozlu, Zonguldak, 67600, Turkey. E-mail: ilkeroz@yahoo.com; oz@beun.edu.tr.

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Atherosclerosis is not merely the passive accumulation of lipids within artery walls. It is also a chronic progressive inflammatory disease.[9] The markers of inflammation, such as C-reactive protein (CRP), serum amyloid A, and interleukin-6, have been investigated as being useful in predicting an increased risk of atherosclerosis-related diseases including coronary heart disease and CVEs.[9,10] Furthermore, carotid atherosclerosis is not only a marker for stroke but is also a part of systemic atherosclerosis.[7]

Previous studies have revealed that platelets have an important role in the pathophysiology of ischemic CVEs.[11-14] Platelets are anucleate cytoplasts that are shed from the cytoplasm of megakaryocytes and circulate in the bloodstream for 7-10 days.[15] Their main function is to contribute to hemostasis. Furthermore, platelets play a key role in modulating inflammatory processes by secreting cytokines, chemokines, and other inflammatory mediators after deploying to sites of injury.[16-19] Platelet size is regulated by various intrinsic and extrinsic factors and is consistent with the function and reactivity of platelets.[20] Larger platelets, indicating an increased mean platelet volume (MPV), contain denser granules and are functionally, metabolically, and enzymatically more active than smaller ones, as well as larger platelets having higher thrombotic potential.[15,17,21] Increased MPV has been shown among patients with chronic inflammatory disorders such as inflammatory bowel disease, rheumatoid arthritis, and ankylosing spondyloarthritis, and in patients with vascular risk factors such as diabetes mellitus, hypercholesterolemia, myocardial infarction, ischemic stroke, smoking, and metabolic syndrome.[13,22]

Increased MPV, as an index of activated platelets, has been reported in the literature in patients with ischemic CVEs.[12-14,21,23] It is known that platelet size is regulated by various intrinsic and extrinsic factors at the level of the progenitor cell.[13,15,20,24,25] In the present study, we aimed to consider the predictive value of MPV compared with CRP among patients with different degrees of carotid stenosis, which is a major risk factor for ischemic CVEs.

Materials and Methods

From January 2013 to December 2014, a total of 136 patients with carotid atherosclerosis, 52 patients with ischemic CVEs, and 40 healthy volunteers were enrolled in the study. The patients with carotid artery disease (CAD) had no history of CVEs. All patients were determined using carotid Doppler ultrasound from among patients with coronary artery disease.[24] Magnetic resonance imaging of the brain was performed for all patients with CVEs within 24 hours of the event. For each participant, the parameters of carotid stenosis were assessed using ultrasonography, which was performed by 2 radiologists using a Logiq 9 (GE Healthcare, Waukesha, WI) machine in accordance with the criteria published by the Society of Radiologists in Ultrasound.[26] Carotid Doppler ultrasound measurements of the ICA were grouped into 4 categories for statistical analysis: absence of stenosis, less than 50% stenosis, 50%-69% stenosis, and 70% or more to total occlusion. In the patients with CAD and CVEs, the stenosis of external carotid arteries and sonographically visible plaques in common carotid arteries was accepted as absence of ICA stenosis. All patients underwent a baseline evaluation including a detailed medical history, typical physical examination, and blood tests. Exclusion criteria were disorders that cause chronic inflammation including diabetes mellitus, myocardial infarction, smoking, metabolic syndrome, inflammatory bowel disease, rheumatoid arthritis, ankylosing spondyloarthritis, multiple sclerosis, psoriasis, connective tissue disease, nephrotic and nephritic syndromes, and end-stage renal disease.

In total, a sample of 8-10 cc of blood was withdrawn from all the participants in the morning after 8 hours of fasting. The values of the following were collected for the study: serum low-density lipoprotein cholesterol and fasting plasma glucose, CRP, leukocyte count, hemoglobin, platelet count, MPV, and platelet distribution. The blood was collected in EDTA tubes and all samples were processed within 30 minutes of blood collection. The CRP and MPV values as well as the leukocyte and platelet counts were compared between the groups.

The study protocol conformed to the ethical guidelines of the World Medical Association's Helsinki Declaration as reflected in a priori approval by our institution's human research committee. Informed consent was obtained from all individuals.

Statistical analysis

SPSS 19.0 for Windows (SPSS Inc., Chicago, IL) was used for statistical analysis. Continuous variables are given with mean, standard deviation, median, minimum and maximum values; categorical variables are given with frequencies and percentages. The Shapiro–Wilk test was used for normality tests. The Kruskal–Wallis test was used for comparisons of 3 or more groups, and the Bonferonni-corrected Mann–Whitney *U*-test was used for subgroup comparisons. Receiver operating characteristic (ROC) curve analysis was performed to determine the predictive value of CRP and MPV regarding carotid stenosis. For all statistical analyses, a *P* value less than .05 indicated statistical significance.

Results

The main characteristics of 136 patients with CAD, 52 patients with CVEs, and 40 healthy volunteers are shown in Table 1. There was no statistically significant difference in terms of age and gender ($P = .094$ and $P = .428$, respectively) between the groups. The participants were divided into 4 groups according to carotid Doppler ultrasound measurements.