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The Relationship between Mean Platelet Volume and Coronary Collateral Vessels in Patients with Acute Coronary Syndromes

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ABSTRACT

Background: Elevated mean platelet volume (MPV) has been proposed as a risk factor for coronary artery disease (CAD) and is associated with poor clinical outcome in acute coronary syndrome (ACS). However some studies have contradictory findings. Hence we aimed to evaluate the association of MPV with presence of coronary collateral vessel (CCV) in patients with ACS.

Objective: To find MPV value in ACS patients and to find predictive value of MPV in spectrum of CAD and to examine whether levels of MPV predict the presence of CCVs.

Methods: A total of 180 patients with first ACS were included in the study. Mean platelet volume (MPV) was measured. All patients underwent coronary angiography to know disease severity and coronary collateral vessels (CCVs). The CCVs are graded according to the Rentrop scoring system and According to coronary angiography results, patients were divided into two groups as Group 1 (poor CCV) and Group 2 (good CCV).

Results: The mean MPV was 10.74 ± 2 fl in poor collaterals group patients and 11.01 ±1.7 fl in good collaterals group (p value 0.421). Presence of CCV was not significantly associated with high levels of MPV. MPV value did not show any prediction of spectrum of coronary artery disease.

Conclusion: MPV on admission was not associated with development of CCV positively in patients with ACS. Also it is not associated with number of vessel involvements.

KEYWORDS: Acute coronary syndrome; coronary artery disease; mean platelet volume; Coronary collateral vessels; rentrop criteria.

INTRODUCTION

Acute coronary syndromes (ACS) are a set of signs and symptoms due to the rupture of a plaque and are a consequence of platelet-rich coronary thrombus formation. The thrombus leads to partial or complete coronary artery occlusion, which, in turn, leads to myocardial ischemia and various clinical manifestations ranging from unstable angina (UA) to acute myocardial infarction (AMI). Platelets play an important role in the pathophysiology of atherosclerosis and prothrombotic events leading to ACS.[1] Platelets are heterogeneous with respect to their size and reactivity. Large platelets are metabolically and enzymatically more active than small ones and have higher thrombotic potential. Generalized platelet activation occurs during the acute coronary event, where the increase rate of platelet consumption at the site of atherosclerotic plaque rupture leads to the release of large size platelets from the bone marrow. This activation process results in signaling pathways that induce platelets to change their shape (metamorphosis) and size and become more active in secreting thromboxane A2 and ADP into the circulation. Larger platelets are more adhesive and tend to aggregate more than smaller ones that contain more secretory granules and mitochondria and are known to be more active than smaller platelets. The release of thromboxane A2 and ADP also stimulates the neighboring platelets, causing them to become activated and in turn secrete additional thromboxane A2 and ADP. Activated large size platelets directly bind to the circulating coagulation protein fibrinogen, via the abundant platelet integrin, glycoprotein (GP) IIb/IIIa receptors. The platelet–fibrinogen–platelet connection initiates the process of platelet aggregation and thus, leads to coronary thrombus formation.[2] Mean platelet volume (MPV) is a useful biomarker of platelet activity.[1-3] Increase in MPV is associated with poor clinical outcome and impaired angiographic reperfusion in patients with myocardial infarction (MI).[4]Therefore; MPV is a marker of platelet reactivity. Unlike all other markers of platelet activation and reactivity, it is automatically calculated by most equipment for performing blood-cell count. Thus, platelet size determination through MPV is a simple, extremely inexpensive, and readily available measure in hospital and outpatient settings. Coronary collateral vessels (CCVs) circulation is a compensatory response to overcome injury in cases of severe ischemia secondary to tight stenosis or occluded vessels. Well developed coronary collaterals can provide a perfusion reserve in case of increased myocardial oxygen demand and preserve

ventricular function and viability, providing an alternative blood supply to an ischemic region in coronary artery disease. Prominent interindividual variability exists even among patients with similar degree of coronary artery disease.[5] however, it remains unclear which factors are responsible for these differences [6]. Several studies have shown that the development of CCs is impaired in the presence of many of the risk factors predisposing to atherosclerosis such as age, hypercholesterolemia, diabetes mellitus (DM) and smoking.[7-14] In addition, many serum biomarkers, such as high-sensitivity C-reactive protein (CRP), lipoprotein-associated phospholipase A2, paraoxonase activity and asymmetric dimethylarginine, have been reported to be associated with the development of CCs .[12-15]

The presence of CCV is correlated with well clinical outcomes in patients with ACS.[16]Although many studies have reported the role of mean platelet volume (MPV) in various cardiovascular diseases[17] some studies suggested that increased MPV predicted the risk of coronary artery disease (CAD) and cardiac mortality.[18] So our interest is whether increased MPV predict the presence of collaterals, which is also a major predictor of mortality in ACS. Association of higher MPV values with collaterals in ACS has been mostly studied among western patients.[19] A few reports have revealed larger MPV values in Indian patients with ACS[20-21]but no association of MPV with coronary collaterals is studied till now in Indian patients. In the present study, Our aim was to find MPV value in ACS patients and to find predictive value of MPV in spectrum of CAD and to examine whether levels of MPV predict the presence of CCVs, one of the major predictors of mortality in patients with ACS.

METHODS

Study Population

A total of 180 consecutive patients who were admitted to hospital with first episode of ACS were prospectively included in the study. Patients who underwent coronary angiography at the Department of Cardiology, SMS Hospital, Jaipur) between January 2015 and June 2015 were evaluated. Demographic and clinical data were obtained from the patients' medical records and detailed history. DM was defined as a history of DM, the use of antidiabetic

drugs or fasting plasma glucose levels of ≥7 mmol/L. Hypertension (HTN) was defined as a history of HTN or use of antihypertensive drugs, or a blood pressure ≥140/90 mmHg. Smoking status was defined as current smoking. The study protocol was approved by the local ethics committee. Patients with hepatic or renal dysfunction (serum creatinine level >2mg/dl), previous ACS patients, previous revascularization (coronary artery bypass graft operation or percutaneous coronary intervention) history, severe valvular disease, myocardial or pericardial disease, and technically inadequate coronary angiography were excluded from the study. Patients who were diagnosed with hematological disease, cancer, systemic inflammatory or autoimmune disease, thrombocytopenia and the use of anticoagulant agents were also excluded from the present study. Sample size was calculated to allow detection of a 30% difference in MPV between different groups and with α of .05 and power of 80 %. Total 180 subjects were recruited and studied in two groups. According to coronary angiography results, patients were divided into two groups as Group 1 (poor CCV) and Group 2 (good CCV).Informed consent was obtained from all patients. The study was approved by our local ethics committee.

Laboratory Analysis

In all cases, venous blood samples were drawn at admission before starting any medication. Serum glucose, blood urea, serum creatinine, were measured by standard methods. Tripotassium ethylenediaminetetraacetic acid (EDTA) based anticoagulated blood samples were drawn and assessed using the Beckman Coulter LH 750 and Hmx systems (Beckman Coulter, USA) using original reagents. Hemoglobin, platelet count, white blood cell (WBC) count and mean platelet volume were analyzed using a blood counter (Sysmex 4000 Roche, Mannheim, Germany) that measures platelet size using aperture-impedance technology. All patient samples were processed within 2 hours after venipuncture as recommended in the literature[17] to avoid bias due to excessive platelet swelling .The expected values for MPV in our laboratory ranged from 7.0 to 10.5 fl. A high MPV was defined as a value ≥10.5 fl.

Angiographic Evaluation and CC Grading

Coronary angiography was performed using standard techniques (Siemens Axiom Artis zee, Siemens Healthcare, Erlangen, Germany). Coronary angiography was performed through the femoral artery or radial artery for all patients using the Judkin technique. Each angiogram was interpreted by two experienced cardiologists who were blinded to the clinical details and results of the other investigations of each patient. Coronary collaterals vessels were graded according to the Rentrop grading system of 0 to 3: 0 = no filling of any collateral vessel; 1 = filling of the side branches of the artery to be perfused by collateral vessels without visualization of the epicardial segment; 2 = partial filling of the distal epicardial segment by collateral vessels; and 3 = complete filling of the distal epicardial segment by collateral vessels [22]. The vessel that had the highest Rentrop grade with collaterals was used for analysis when more than one occluded vessel was present. In cases for which more than one collateral vessel to the same occluded vessel was present, the highest Rentrop grade was used. Rentrop grade 0 accepted as no development of CCV and Rentrop Grade ≥1 was accepted as presence of CCV .The study population was divided into two groups according to the Rentrop collateral score. Patients with grade 0 to 1 collateral development were classified as the poor collateral group; and patients with Rentrop grade 2 to 3 collateral development were classified as the good collateral group.

Statistical Analysis

All analyses were performed using SPSS V 16.0 for windows (version 16.0, SPSS, Chicago, IL, USA). Quantitative variables were expressed as mean value ± SD. Comparison of quantitative variables between two groups was performed by means samples t test. Categorical variables were compared by the chi-square test. P-value < 0.05 was considered statistically significant of independent.

RESULTS

1. Table 1 shows baseline clinical characteristics of the patients.
2. Tables 2 and 3 show the relation between the presence of CCV and baseline clinical and laboratory characteristics of the patients. The mean platelet count was 218.6 ± 98.4($\times 10^3$) in poor collateral group patients and 206.3 ±76.53 (10^3) in good collaterals group patients.(p value 0.447).there was also no correlation of platelet counts with mean platelet volume. The mean MPV was 10.74 ± 2 fl in poor collaterals group patients and 11.01 ±1.7 fl in good collaterals group (p value 0.421) . Presence of CCV was not significantly associated with high levels of MPV (p = 0.421).
3. Table 3 also MPV value did not show any prediction of spectrum of coronary artery disease .Mean platelet volume was not significantly different in number of vessel involvement (single vessel disease v/s double vessel disease v/s triple vessel disease). Mean age was 58.34± 11.04 years in poor collaterals group and 57.36±8.5 in good collaterals group. Rentrop 0, 1, 2, and 3 were determined in (table 4 and figure1), 102 (56.66 %), 34 (18.88 %), 30 (16.66%), and 14 (7.77 %) patients respectively. Rentrop 0-1 (poor collaterals group) were determined in 136 (75.5 %) patients. There was no significant difference in MPV value in rentrop score. Mean MPV value was 11.33 ±1.23 in normal coronaries patients while in coronary artery disease patients Mean MPV value was 10.77±1.96 (p value 0.325). Mean MPV value was not different in diabetic patients from non diabetic patients.

DISCUSSION

Previous studies showed Effect of platelet volume on coronary adverse outcomes. [1–4]Well-developed CCs are important compensatory mechanisms in the protection of myocardium in the ischemic region during coronary occlusion. The factors involved in the development of CCs have been investigated in numerous studies. Several demographic, clinical and biochemical factors have been reported to be associated with the degree of CC development.[7-15]However, there are insufficient data regarding the relation between MPV

and CCV. Well developed CCVs can limit myocardial ischemia, may minimize the infarct size, and can protect the viable myocardium in patients with ACS.[5–8]The absence of CCV is correlated with bad clinical outcomes in patients with ACS.[23] Resting distal coronary pressure consistently falls as stenosis severity exceeds 70%.[23] Although the underlying mechanism remains uncharacterized, myocardial ischemia, growth factors [such as fibroblast growth factor (FGF) and vascular endothelial growth factor], various cells such as endothelial, monocytes, smooth muscle, cytokines, and shear stress are likely factors that contribute to initiating and remodeling for collateral development during tissue hypoxia.[24-27]Endothelial dysfunction is associated with poorer collateral growth[28] Also duration of angina pectoris and the extent of CAD are well-established determinants of CCVs[29] Platelets play a key role in the pathogenesis, morbidity, and mortality of ACS[30]Increase in platelet activation is associated with CAD, carotid artery disease, and transplant vasculopathy[31-34]Elevated MPV has been recognized as an independent risk factor for MI[35] Large platelets are metabolically and enzymatically more active than smaller ones and secrete and express more mediators such as adhesive proteins (fibrinogen, thrombospondin, and fibronectin), growth factors [platelet-derived growth factor (PDGF), transforming growth factor-β, basic FGF], chemotactic and mitogenic factors [platelet factor 4 (PF4), coagulation factors (factor V, factor XI), and cytokine-like factors (interleukin-1, CD40 ligand)][36-38]Chemokines that are secreted from active platelets also stimulate smooth muscle cells and contribute to inflammation and atherogenesis[37]Inflammatory markers may also contribute to absence of CCV via endothelial dysfunction[39]However some studies showed High MPV on admission was associated with presence of CCV in patients with ACS.[40,41]Howecer some other studies suggest opposite effect.[42,43]Recently,Egeetal. reported that MPV levels were significantly higher and Gensini score was significantly lower in the patients who had inadequate CCV in patients with CAD [43]In another study, high MPV levels were associated with severe coronary artery disease but not associated with development of coronary collaterals.[44] In our study, we found that high levels of MPV were not associated with the presence of CCV in patients with ACS.

Between MPV and known ischemic heart disease risk factors .We did not find any association between development of CCV and age, hypertension, smoking, or gender. In our study there were not a sufficient Previous reports showed that there is a close relationship between MPV and other prognostic factors, such as smoking, diabetes and hypertension[45,46] But our study showed no clear association number of patients of risk factors to assess the impact of these factors on the presence of collaterals. Thus, it is not possible to determine the effects of prognostic factors on the presence of collaterals according to the results of this study. Although the mechanism is still unclear, the increased megakaryocyte ploidy is positively and number of megakaryocytes is negatively correlated with platelet volume.[4] Our study showed no association between elevated MPV and the total platelet count. Our study group includes only patients with ACS. We know that collaterals take time to develop but some studies showed early angiographic evidence of collateral circulation in patients with acute MI and non-ST elevation MI In our study means platelet volume was not significantly different in unstable angina from Non ST elevation myocardial infarction or ST elevation myocardial infarction. We did not find any correlation between coronary collaterals and acute coronary syndrome presentation. Patients with ACS and a well-developed collateral circulation may have profited from a gradually developing stenosis via slow growth of mural thrombi. Finally, different methods can be used to analyze platelet activation. All tests have some limitations. Thus MPV may provide an important, simple, effortless, and cost-effective marker which can be useful for evaluation of platelet activation but it is not predictive of development of Coronary collaterals. Nonetheless, conflicting results of other studies make this issue controversial, which warrants performing of more comprehensive studies in future.

CONCLUSION

MPV on admission was not associated with development of CCV positively in patients with ACS. Also it is not associated with number of vessel involvements.

LIMITATIONS

The present study had some limitations. First, the study population was relatively small. Second, inflammatory markers such as CRP and interleukin-6 were not analyzed. We did not quantify and compare CCs with invasive parameters other than the Rentrop scoring system. Patients with non-cardiac chest pain (atypical symptoms) might have unstable angina in the absence of electrocardiography changes and cardiac troponin positivity, have resulted in selection bias. Also there are no data about physical activity of the patients, which encourages the development of CCVs. Angiographic techniques do not demonstrate vessels of which the luminal diameter is 1.0 mm or less. Finally Individuals were enrolled from a single interventional cardiology center.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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