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The association between mean platelet volume and coronary collateral circulation

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Abstract. – BACKGROUND: Platelets are important in the pathogenesis of atherosclerotic complications. Higher mean platelet volume (MPV) levels are related to greater *in vitro* aggregation, and have been identified as an independent risk factor for myocardial infarction, and for death or recurrent vascular events.

AIM: To determine the relationship between MPV and the coronary collateral circulation.

METHODS: The sample consisted of 96 patients with coronary artery disease, and patients were separated into two groups according to their poorly developed or well-developed collateral circulation. Coronary collateral vessels were analyzed according to the Cohen and Rentrop grading system of 0-3.

RESULTS: All analyses were conducted using SPSS 11.5 (SPSS for Windows 11.5, Chicago, IL, USA). Continuous variables were expressed as mean ± SD, and categorical variables were expressed as percentages. Comparison of categorical and continuous variables between the group with well-developed coronary collateral vessels and the group with poorly developed vessels was performed using the chi-squared test and independent samples *t*-test, respectively. Platelet count and MPV values were similar between the two groups.

CONCLUSIONS: Our study found that MPV levels are not related to coronary collateral circulation.

Key Words:
Angina pectoris, Platelet activation, Coronary circulation.

Introduction

Platelets are important in the pathogenesis of atherosclerotic complications, as they initiate thrombus development after plaque rupture[1]. Mean platelet volume (MPV) is known as an indirect marker of platelet reactivity. Wide platelets include more dense granules and produce more thromboxane A2, both of which are associated with increased thrombocyte aggregation. Higher MPV levels are related to greater *in vitro* aggregation in response to adenosine diphosphate and collagen, and have been identified as an independent risk factor for myocardial infarction (MI) in patients with coronary heart disease, and for death or recurrent vascular events after MI[2-4].

Coronary collateral vessels are of clinical significance, as they potentially limit the severity of MI[5]. Important differences in the degree of collateral vessel development are known even with similar patterns of coronary disease[6], although chronic imbalances of myocardial oxygen supply and demand produced by coronary artery stenosis or occlusion have been shown to induce growth of the coronary collateral circulation[7]. In this context, studies have been conducted to explain the complex mechanism(s) of collateral circulation development. These investigations have illuminated the significant influence of various factors and disease states on collateral circulation development, including the influence of coronary stenosis severity[6]; diabetes mellitus[8]; MI history and clinical presentation with stable angina pectoris, and use of drugs[9,10]; and coronary vasomotor tone[11]. Several serum markers have also been reported as showing an association with the degree of collateral circulation developments. Some of these markers include high-sensitivity C-reactive protein[12], lipoprotein(a)[13], adhesion molecules such as vascular adhesion molecule-1[14], tumor necrosis factor-α[15], and total antioxidant capacity[16].

To our knowledge, no published data detail the relationship between MPV and coronary collateral flow. This study assesses whether a high level for MPV is associated with the extent of coronary collateral vessels visible during angiography performed in patients with coronary artery disease.

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Methods

Study Population

The local Ethics Committee approved the study, and all patients gave informed consent. Of the patients who presented to the outpatient clinic with stable angina pectoris or acute coronary syndrome and had undergone coronary angiography, those with at least one coronary stenosis (with ≥50% blockage) were enrolled in the study in a prospective manner. The degree of coronary artery stenosis was determined visually. Patients with chronic kidney disease (serum creatinine >1.4 mg/dl), chronic obstructive pulmonary disease (COPD), active malignancy, oxygen saturation of less than 92%, or who had undergone a previous coronary artery bypass graft operation were excluded from the study.

After exclusions, the study population consisted of 96 patients. Baseline characteristics including presence of hypertension, diabetes mellitus, and body mass index (BMI) were recorded. The presence of hypertension was defined as the active use of antihypertensive drugs or documentation of blood pressure greater than 140/90 mmHg. Diabetes mellitus was defined as fasting glucose level greater than 126 mg/dl or glucose level greater than 200 mg/dl at 2th h after 75 g oral glucose load, or as active use of antidiabetic drugs or insulin.

Biochemical Measurements

Blood samples were drawn at admission in patients undergoing elective (following a fasting period of 12 hours) or urgent coronary angiography. Platelet count was determined by standard methods. We measured MPV in a blood sample collected in tripotassium ethylene diamine tetraacetic acid (EDTA) (7.2 mg) tubes. These blood samples were analyzed within 2 hours of venipuncture with an automatic blood counter a Sysmex XE-2100 (TOA Medical Electronics, Kobe, Japan) used for whole blood analysis. The expected values for MPV in our laboratory ranged from 7.0 to 11.0 fl. The analytic coefficient of variation for MPV ranged from 2.2 to 1.1%.

Evaluation of Coronary Angiography and Collateral Scoring

Coronary angiography was performed through the femoral artery using the Judkins technique. Two experienced cardiologists who were blinded to patient characteristics reviewed the angiograms and graded the extent of the coronary collateral vessels. Significant coronary narrowing was defined as stenosis >70% in at least one main branch of the coronary arteries. Coronary collateral vessels were analyzed according to the Cohen and Rentrop grading system of 0-3: 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[17]. The study population was divided into two groups according to the Rentrop collateral score: patients with poorly developed collateral circulation (Rentrop score 0-1), and patients with well-developed collateral circulation (Rentrop score 2-3).

Statistical Analysis

All analyses were conducted using SPSS 11.5 (SPSS for Windows 11.5, Chicago, IL, USA). Continuous variables were expressed as mean ± SD, and categorical variables were expressed as percentages. Comparison of categorical and continuous variables between the group with well-developed coronary collateral vessels and the group with poorly developed vessels was performed using the chi-squared test and independent samples *t*-test, respectively.

Results

We found no significant differences with respect to gender, age, presence of hypertension, diabetes mellitus, or BMI in the two groups. Additionally, no significant differences were found in the number of diseased vessels and in the presence of acute coronary syndrome. Platelet count and MPV values were similar between the two groups (Table I).

Discussion

Coronary collateral vessels are the remnants of the embryonic arterial system and develop under various conditions. In patients with normal or mild coronary artery disease, coronary collateral vessels cannot be visualized with coronary angiography; rather, coronary arteries must have a significant degree of stenosis for the collateral vessels to be visible[18]. The most important stimulating factor in the development of coronary collateral vessels is the pressure gradient between the normal and stenotic areas of the arteries[19]. This pressure gradient causes the opening of coronary collateral vessels by increasing the rate of blood flow in collateral circulation, the activation of endothelial cells, and the stimulation of growth factors[20-21].

Table I. General characteristics and MPV values of patients.

	Well-developed collateral group (n: 37)	Poorly developed collateral group (n: 59)	p
Age (years)	65 ± 13	61 ± 17	NS
Gender (M/F)	25/12	41/18	NS
BMI (kg/m^2)	24.5 ± 3.4	23.7 ± 3.8	NS
HT (n)	12	18	NS
DM (n)	7	10	NS
The number of diseased vessels	2.4 ±0.4	2.3 ± 0.6	NS
The presence of acute coronary syndrome (n)	12	19	NS
MPV (fl)	8.07 ± 1	8.06 ± 1.1	NS
Platelet count (10^6/ml)	266 ± 71	250 ± 59	NS

(M: Male, F: Female, BMI: Body mass index, HT: Hypertension, DM: Diabetes mellitus, MPV: Mean platelet volume).

Platelets play a crucial role in the pathogenesis of atherosclerotic complications, as they contribute to thrombus formation[1]. MPV is a marker of platelet function; that is, large platelets contain more dense granules and produce more thromboxane A2. Higher MPV levels have been identified not only as an independent risk factor for MI in patients with coronary heart disease, but also for death or recurrent vascular events after MI[4,22]. The aim of this study was to investigate whether there is an association between MPV and coronary collateral circulation. However, we found no significant differences in platelet count and MPV values between groups with well-developed and poorly developed collateral vessels.

In previous studies, increased platelet volume was shown to be associated with increases in DNA concentration in the nucleus of the megakaryocyte[23,24]. This increase results in the decrease in the number of platelets in the circulation and leads ultimately to the increased MPV in acute coronary syndrome. Platelets produced in the bone marrow quickly are of greater size; they are not consumed in the circulation as readily and, therefore, may increase MPV levels. Patients with thrombocytopenia (resulting from platelet loss or consumption) have higher MPV levels than do patients with marrow failure. The cause of increase is thought to be the consumption of platelets[25].

Studies have shown that platelet volume returned to normal within days following the increase in platelet volume after acute ischemic events. Deniz et al[26] concluded that a high MPV in patients with ischemic stroke returns to a normal level after a certain period of time; persistent MPV elevation in these patients is associated with a poor prognosis. Similarly, increased MPV gradually declines to a normal level after MI, and persistent high MPV levels are associated with myocardial infarction-related complications[27].

In a study that compared MPV values for two groups of patients in whom coronary angiography had been performed, these values were not significantly different between patients without coronary artery disease and patients with one or two stenotic coronary arteries[28]. Another report found no significant difference in MPV values between patients with and without risk factors for coronary artery[29-30]. Additionally, Luca et al[31] conducted a large prospective study that showed no association between MPV and either the extent of coronary artery disease or median thickness of the carotid intima. These researchers note that these data are supported by the absence of any relationship between platelet aggregations, resistance to aspirin, and MPV.

Potential limitations of the present study include the relatively small sample size and the cross-sectional study design. Collateral vessels shown on angiograms are only part of the total collateral circulation. Finally, as collateral vessels less than 200 mm in diameter cannot be evaluated[32]. Future studies should be performed at the microvessel level.

In conclusion MPV levels are not related to coronary collateral circulation.

References

1) Ross R. Atherosclerosis an inflammatory disease. N Engl J Med 1999; 340: 115-126.
2) Smith NM, Pathansali R, Bath PM. Platelets and stroke. Vasc Med 1999; 4: 165-172.
3) Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C, Jordanova N,

Christ G, Thalhammer R, Huber K, Sunder-Plassmann R. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. Br J Haematol 2002; 117: 399-404.

4) Martin JF, Bath PM, Burr ML. Influence of platelet size on outcome after myocardial infarction. Lancet 1991; 338(8780): 1409-1411.

5) Cohen M, Rentrop KP. Limitation of myocardial ischemia by collateral circulation during sudden controlled coronary artery occlusion in human subjects: a prospective study. Circulation 1986; 74: 469-476.

6) Pohl T, Seiler C, Billinger M, Herren E, Wustmann K, Mehta H, Windecker S, Eberli FR, Meier B. Frequency distribution of collateral flow and factors influencing collateral channel development. Functional collateral channel measurement in 450 patients with coronary artery disease. J Am Coll Cardiol 2001; 38: 1872-1878.

7) Buschmann I, Schaper W. The pathophysiology of the collateral circulation (arteriogenesis). J Pathol 2000; 190: 338-342.

8) Abaci A, O uzhan A, Kahraman S, Eryol NK, Unal S, Arinç H, Ergin A. Effect of diabetes mellitus on formation of coronary collateral vessels. Circulation 1999; 99: 2239-2242.

9) Kilian JG, Keech A, Adams MR, Celermajer DS. Coronary collateralization: determinants of adequate distal vessel filling after arterial occlusion. Coronary Artery Dis 2002; 13: 155-159.

10) Pourati I, Kimmelstiel C, Rand W, Karas RH. Statin use is associated with enhanced collateralization of severely diseased coronary arteries. Am Heart J 2003; 146: 876-881.

11) Boodhwani M, Sodha NR, Mieno S, Xu SH, Feng J, Ramlawi B, Clements RT, Sellke FW. Functional, cellular, and molecular characterization of the angiogenic response to chronic myocardial ischemia in diabetes. Circulation 2007; 116(11 Suppl): I31-37.

12) Gulec S, Ozdemir AO, Maradit-Kremers H, Dincer I, Atmaca Y, Erol C. Elevated levels of C-reactive protein are associated with impaired coronary collateral development. Eur J Clin Invest 2006; 36: 369-375.

13) Aras D, Geyik B, Topaloglu S, Ergun K, Ayaz S, Maden O, Yildiz A, Balci M, Ozeke O, Korkmaz S. Serum level of lipoprotein (a) is inversely associated with the development of coronary collateral circulation. Coronary Artery Dis 2006; 17: 159-163.

14) Guray U, Erbay AR, Guray Y, Yilmaz MB, Boyaci AA, Sasmaz H, Korkmaz S, Kutuk E. Poor coronary collateral circulation is associated with higher concentrations of soluble adhesion molecules in patients with single-vessel disease. Coron Artery Dis 2004; 15: 413-417.

15) Seiler C, Pohl T, Billinger M, Meier B. Tumour necrosis factor alpha concentration and collateral flow in patients with coronary artery disease and normal systolic left ventricular function. Heart 2003; 89: 96-97.

16) Demirbag R, Gur M, Yilmaz R, Kunt AS, Erel O, Andac MH. Influence of oxidative stress on the development of collateral circulation in total coronary occlusions. Int J Cardiol 2007; 116: 14-19.

17) Rentrop KP, Cohen M, Blanke H, Phillips RA. Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. J Am Coll Cardiol 1985; 5: 587-592.

18) Elayda MA, Mathur VS, Hall RJ, Massumi GA, Garcia E, de Castro CM. Collateral circulation in coronary artery disease. Am J Cardiol 1985; 55: 58-60.

19) Chilian WM, Mass HJ, Williams SE, Layne SM, Smith EE, Scheel KW. Microvascular occlusions promote coronary collateral growth. Am J Physiol 1990; 258(4 Pt 2): H1103-1111.

20) Glasser SP, Selwyn AP, Ganz P. Atherosclerosis: risk factors and the vascular endothelium. Am Heart J 1996; 131: 379-384.

21) Schaper W, Sharma HS, Quinkler W, Markert T, Wünsch M, Schaper J. Molecular biologic concepts of coronary anastomoses. J Am Coll Cardiol 1990; 15: 513-518.

22) Huczek Z, Kochman J, Filipiak KJ, Horszczaruk GJ, Grabowski M, Piatkowski R, Wilczynska J, Zielinski A, Meier B, Opolski G. Mean platelet volume on admission predicts impaired reperfusion and long-term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention. J Am Coll Cardiol 2005; 46: 284-290.

23) Cameron HA, Phillips R, Ibbotson RM, Carson PH. Platelet size in myocardial infarction. Br Med J 1983; 287(6390): 449-451.

24) Martin JF, Plumb J, Kilbey RS, Kishk YT. Changes in volume and density of platelets in myocardial infarction. Br Med J 1983; 287(6390): 456-459.

25) Nelson RB 3rd, Kehl D. Electronically determined platelet indices in thrombocytopenic patients. Cancer 1981; 48: 954-956.

26) Deniz O, Çelikbas M, Degirmenci S, Kaya H, Yazman Y. Iskemik stroklu hastalarda trombosit sayısı, trombosit volümü ile bunların serebral infarkt çapı ve prognozla ilişkisi. Atatürk Üni Tıp Bül 1997; 29: 429-432.

27) Açikel M, Erol K, Bozkurt E, Alp N, Senocak H. Akut miyokard infarktüsünde ortalama trombosit hacmi ile erken dönem komplikasyonlar arasındaki ilişki. Türk Kardiyol Dern Arş 2001; 29: 229-232.

28) Sahin M, Elçik M, Köşüş A, Balci B, Yesildağ O, Sağkan O. Koroner arter hastalığının klinik ve anjiyografik görünümü ile trombosit sayısı ve volümünün ilişkisi. Ondokuz Mayıs Üniv. Tıp Dergisi 2000; 17: 98-102.

29) Funiak S, Kv tenský J, Hudecek J, Belicová M, Stasko J, Markuljak I, Kubisz P. Large blood platelets–risk factors in myocardial infarction. Vnitr Lek 1994; 40: 167-169.

30) Halbmayer WM, Haushofer A, Radek J, Schon R, Deutsch M, Fischer M. Platelet size, fibrinogen and lipoprotein(a) in coronary heart disease. Coron Artery Dis 1995; 6: 397-402.

31) De Luca G, Santagostino M, Secco GG, Cassetti E, Giuliani L, Franchi E, Coppo L, Iorio S, Venegoni L, Rondano E, Dell'Era G, Rizzo C, Pergolini P, Monaco F, Bellomo G, Marino P. Mean platelet volume and the extent of coronary artery disease: results from a large prospective study. Atherosclerosis 2009; 206: 292-297.

32) White FC, Carroll SM, Magnet A, Bloor CM. Coronary collateral development in swine after coronary artery occlusion. Circ Res 1992; 71: 1490-1500.