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Mean Platelet Volume is Elevated in Patients With Low High-Density Lipoprotein Cholesterol

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Abstract

A low high-density lipoprotein cholesterol (HDL-C) level is a predictor of increased cardiovascular risk. We assessed the mean platelet volume (MPV) in patients with low HDL-C. We studied 59 patients with low HDL-C (HDL-C $\leq$35 mg/dL) and 56 control participants (HDL-C levels >35 mg/dL) with similar cardiovascular risk factors. As expected, HDL-C was significantly lower among the patients with low HDL-C than that of the control group (32 $\pm$ 3 vs 51 $\pm$ 5 mg/dL, respectively; $P < .001$). Platelet count was significantly lower among the patients with low HDL-C than that of the control group (213 $\pm$ 60 vs 285 $\pm$ 75 $\times$ 10^9/L, respectively; $P < .001$). The MPV was significantly higher among the patients with low HDL-C than that of the control group (8.7 $\pm$ 0.6 vs 7.1 $\pm$ 0.5 fL, respectively; $P < .001$). We have shown that MPV was significantly elevated in patients with low HDL-C compared with control participants.

Keywords

mean platelet volume, high-density lipoprotein cholesterol, platelet activation

Introduction

Epidemiological studies have shown that high-density lipoprotein cholesterol (HDL-C) is a major independent risk factor for coronary heart disease.[1] A low level of HDL-C is a powerful predictor of increased cardiovascular risk, and this risk persists in people whose low-density lipoprotein cholesterol (LDL-C) is reduced to very low levels.[2] The HDL exerts its antiatherosclerotic effects in several ways. The HDL-C reverses cholesterol transport, reduces inflammation, promotes endothelial cell nitric oxide (NO) production, inhibits LDL-C oxidation, inhibits endothelial cell apoptosis, inhibits platelet activation, and inhibits expression of adhesion molecules.[3] Several studies showed that HDL-C has antiplatelet action.[4-8]

Mean platelet volume (MPV) is a surrogate marker of platelet activation.[9,10] Larger platelets have higher thrombotic potential.[9] In comparison with smaller ones, larger platelets have more granules, aggregate more rapidly with collagen, release more thromboxane A2, and express more glycoprotein Ib and IIb/IIIa receptors.[11-13]

Elevation in MPV values has been shown in atherosclerotic heart diseases, primarily acute coronary syndromes.[14,15] Previous studies have shown that MPV was elevated in patients with hypercholesterolemia.[16,17] However, to the best of our knowledge, there is no study investigating the relationship between HDL-C levels and MPV. Therefore, we assessed MPV in patients with low HDL-C and compared it with controls.

Materials and Methods

The study group consisted of 59 patients with low HDL-C (HDL-C $\leq$35 mg/dL; 17 females, 42 males, mean age 53.2 $\pm$ 7.9 years). Age-, gender-, and body mass index-matched patients with normal HDL-C with similar cardiovascular risk factors (HDL-C levels >35 mg/dL) comprised the control group (22 females, 34 males with a mean age 55.8 $\pm$ 9.1 years). We selected HDL-C $\leq$35 mg/dL level as a low HDL-C according to the literature.[8] The patients with low HDL-C and controls were selected in a consecutive manner from the catheterized patients during the same study period and who were found to have normal coronary angiograms. There were some patients with hypertension and some smokers in the low HDL-C group. Because of that controls were randomly selected, and we also included patients with hypertension and smokers to match the 2 groups and to eliminate the effect of hypertension and smoking on MPV. The blood samples were taken at admission before coronary angiography. All the

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patients with low HDL-C and controls were newly diagnosed and were not using any drugs at admission.

The indication for coronary angiography was either the presence of typical angina or the positive or equivocal results of noninvasive screening tests for myocardial ischemia in both the groups. Hypertension was considered to be present if the systolic blood pressure was >140 mm Hg and/or diastolic blood pressure was >90 mm Hg or if the individual was taking antihypertensive medications. Diabetes mellitus was defined as a fasting blood glucose level >126 mg/dL or current use of a diet or medication to lower blood glucose. Patients who were smoking before hospitalization were considered as smokers.

Exclusion criteria were coronary artery disease, valvular heart disease, heart failure, peripheral arterial disease, diabetes mellitus, renal and hepatic dysfunction, hematological disorders, history of malignancy, acute or chronic infection, stroke, and any drug use affecting MPV and HDL-C. The study was approved by the institutional ethics committee, and informed consent was obtained from all patients.

Blood Sampling

Blood was drawn from the antecubital vein by careful vein puncture with a 21G needle without stasis at 08.00 to 10.00 AM after a fasting period of 12 hours. Glucose, creatinine, and lipid profiles were determined by standard methods. The MPV was measured in a blood sample collected in dipotassium EDTA tubes. An automatic blood counter (Beckman-Coulter Co, Miami, Florida, USA) was used for whole blood counts. The MPV was measured within 30 minutes after sampling.

Statistical Analysis

Data were analyzed with the SPSS software version 10.0 for Windows. Continuous variables from the study groups were reported as mean ± standard deviation and categorical variables as percentage. To compare continuous variables, the Student *t* test or Mann-Whitney *U* test were used as appropriate. Categorical variables were compared with the chi-square test. Statistical significance was defined as a 2-tailed $P < .05$.

Results

Clinical and laboratory characteristics of the patients with low HDL-C and control group are presented in Table 1. There were no statistically significant differences between the 2 groups with respect to age, gender, body mass index, incidence of hypertension and smoking, levels of glucose, creatinine, total cholesterol, triglyceride, LDL-C, hemoglobin, white blood cell count, and platelet distribution width. As expected, HDL-C was significantly lower among the patients with low HDL-C than that of the control group (32 ± 3 vs 51 ± 5 mg/dL, respectively; $P < .001$). Platelet count was significantly lower among the patients with low HDL-C than that of the control group (213 ± 60 vs 285 ± 75 × 10^9/L, respectively; $P < .001$). The MPV was significantly higher among the patients with low HDL-C than that of the control group (8.7 ± 0.6 vs 7.1 ± 0.5 fL, respectively; $P < .001$).

Table 1. Comparison of the Clinical and Laboratory Characteristics of the Study and the Control Groups.[a]

	HDL-C ≤ 35 mg/dL (n = 59)	HDL-C > 35 mg/dL (n = 56)	*P*
Age, years	53.2 ± 7.9	55.8 ± 9.1	.09
Sex, M/F	42/17	34/22	.23
BMI, kg/m^2	25.8 ± 2.9	25.7 ± 2.7	.94
Smoking, n (%)	13 (22%)	10 (18%)	.57
HT, n (%)	18 (30%)	16 (28%)	.82
Glucose, mg/dL	96 ± 8	99 ± 10	.07
Creatinine, mg/dL	1.0 ± 0.2	0.9 ± 0.2	.09
Total cholesterol, mg/dL	172 ± 39	185 ± 35	.06
Triglycerides, mg/dL	167 ± 83	144 ± 62	.09
LDL-cholesterol, mg/dL	102 ± 38	108 ± 33	.33
HDL-cholesterol, mg/dL	32 ± 3	51 ± 5	<.001
Hemoglobin, g/dL	14.1 ± 1.8	14.5 ± 1.7	.22
WBC, ×10^9/L	7.1 ± 1.8	6.5 ± 1.5	.07
Platelet count, ×10^9/L	213 ± 60	285 ± 75	<.001
MPV, fL	8.7 ± 0.6	7.1 ± 0.5	<.001
PDW, %	16.4 ± 0.6	16.2 ± 0.5	.33

Abbreviations: M/F, male to female; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; WBC, white blood cells; MPV, mean platelet volume; PDW, platelet distribution width; HT, hypertension.
[a] *P* value is for comparison between control and study population.

Discussion

In the present study, we investigated the MPV in patients with low HDL-C levels. We found that MPV, an indicator of platelet activation, is significantly elevated in patients with low HDL-C when compared with control patients with normal HDL-C.

Epidemiological studies consistently demonstrated that a low plasma level of HDL-C is associated with increased cardiovascular risk.[1,2] In relation to this, several studies showed that HDL-C has antiplatelet action.[4-8] Naqvi et al demonstrated that platelet aggregation is inversely correlated with HDL-C levels, suggesting that HDL has antiplatelet actions.[18]

Reconstituted HDL administration to humans or the infusion of apoA-I Milano into rats inhibits platelet aggregation, further supporting the concept that HDL inhibits platelet activation in vivo.[19,20] The HDL-C might reduce platelet activation directly, but it may also act indirectly on platelet activation via effects on endothelial cells.[5,21] The HDL-C might regulate platelet function by downregulating the release of platelet-activating factor or by upregulating nitric oxide (NO) synthesis and release from endothelial cells.[22] It has also been shown that HDL-C downregulates the biosynthesis of thromboxane A2, and it upregulates prostacyclin production, which in turn can decrease platelet aggregation.[5,23]

Recently, Shah et al investigated the relationship between diabetes mellitus, metabolic syndrome, metabolic syndrome components, and platelet activity as measured by MPV in

retrospective analysis of 13 021 participants in the National Health and Nutrition Examination Survey.[24] They found that MPV was significantly higher in patients with low HDL-C and abdominal obesity.

The MPV is universally available with routine blood counts by automated hemograms and a simple and easy method of assessing platelet function. Platelets are heterogeneous in size, density, and reactivity. Larger platelets have a greater mass and are both metabolically and enzymatically more active than smaller platelets.[9] Previous studies demonstrated that platelet activation is present in patients with low HDL-C; however, there is no study about MPV levels in patients with low HDL-C. We speculated that MPV, an indicator of platelet activation, can increase in patients with low HDL-C. We found that MPV was significantly elevated in patients with low HDL-C compared with controls. It is evident that diabetes mellitus, smoking, overweight, high triglyceride levels, and lack of physical activity cause low HDL-C. Furthermore, low HDL-C is also a component of the metabolic syndrome. These cardiovascular risk factors and cardiovascular diseases including atherosclerotic heart diseases, valvular heart diseases, and heart failure can also cause elevated MPV.[25-27] In our study, we excluded cardiovascular diseases. Also, there was no difference in patients with low HDL-C and controls with normal HDL-C with respect to hypertension and smoking. In this context, we demonstrated that MPV is increased in patients with low HDL-C, independent of other factors. So other mechanisms may play a role in this result, and elevated MPV might be due to other confounding factors, such as oxidative stress and inflammation in patients with low HDL-C.

The HDL-C has anti-inflammatory and antioxidant activities that protect from cardiovascular diseases.[22,23] Patients with low HDL-C have elevated oxidative stress and inflammation. On the other hand, low-grade inflammation can cause an increase in MPV.[28] So low-grade inflammation existing in low HDL-C conditions can be a possible cause of increased MPV. The HDL-C might also regulate platelet function by upregulating NO synthesis and release from endothelial cells. The NO and cytokines in turn influence megakaryocytopoiesis.[29] The HDL can also be dysfunctional in acute and chronic inflammation, yielding a proinflammatory and prooxidative phenotype.[30] In our study, we excluded acute or chronic infection. Diet, weight loss, exercise, and statin treatment increase HDL-C.[2,4] Recently, a meta-analysis showed that statin therapy does not alter the association between low levels of HDL-C and increased cardiovascular risk.[31] As a result, other treatment modalities can also be advised for patients with low HDL-C.

Our study has some limitations. First, the number of patients with low HDL-C was small. Our patients with low HDL-C were newly investigated patients free of cardiovascular diseases, and they were not using any drug-affecting MPV and HDL-C. Because of that our sample size was small. Second, our analysis was based on a baseline determination at a single time point that may not reflect patient status over long periods. Third, the National Cholesterol Education Panel Adult Treatment Panel III guidelines raised the cut point for low HDL-C levels from 35 to 40 mg/dL. We selected 35 mg/dL as a cut point for low HDL-C as in the literature.[8] Our patients with low HDL-C and controls did not include patients with metabolic syndrome.

In this study, we found that MPV was significantly elevated in patients with low HDL-C compared with the controls. The increased MPV might indicate altered platelet reactivity in patients with low HDL-C. Antiplatelet treatment might be reasonable in these patients with low HDL-C. We do not know whether increasing low HDL-C decreases MPV values. Further prospective studies are mandatory to establish the pathophysiological and clinical significance of increased MPV in patients with low HDL-C.

Declaration of Conflicting Interests

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