Relationship between mean platelet volume and left ventricular systolic function in patients with metabolic syndrome and ST-elevation myocardial infarction

Abstract

Purpose: Mean platelet volume (MPV) is an indicator of platelet activation, which is a central process in the pathophysiology of coronary heart disease. Metabolic syndrome (MS) may lead to worsened left ventricular systolic function by causing recurrent thrombotic events and by aggravating systemic inflammation in the course of acute myocardial infarction. The present study was designed to investigate the relationship between MPV and left ventricular systolic function in patients with metabolic syndrome who had first ST-elevation myocardial infarction.

Methods: MPV was measured on admission in 33 patients who had preserved left ventricle systolic function (mean age, 56.9±10.2 years) and in 48 patients who had depressed left ventricle systolic function (mean age, 57.9±10.5 years) with metabolic syndrome and first ST elevation myocardial infarction. Depressed left ventricle systolic function was defined as ≤50% ejection fraction value. MPV levels were compared in the two groups.

Results: MPV was significantly higher in patients with depressed left ventricle systolic function in comparison with patients showing preserved left ventricle systolic function (p=0.02). Logistic regression analysis showed an independent relationship between MPV and deteriorated left ventricular systolic function, even after adjustment for potential confounders (1.08 (1.04-1.20), CI: 95%, p=0.02).

Conclusions: Increased MPV on admission can be associated with degree of left ventricle systolic depression in patients with metabolic syndrome with first ST-elevation myocardial infarction. MPV may prove to be useful as a prognostic marker in patients with metabolic syndrome and ST elevation MI.
Metabolic syndrome (MS) is characterized by clustering of closely associated interdependent atherosclerotic risk factors, including insulin resistance, high blood pressure, low level of high-density lipoprotein (HDL) cholesterol, high triglyceride level, high plasma glucose concentration and obesity. Its prevalence has gradually increased in the developed world [1]. An increased prevalence of metabolic syndrome has been shown in patients with acute myocardial infarction (AMI) [2]. MS causes an increased risk for coronary artery disease, cardiovascular morbidity and mortality [2,3]. Accelerated atherosclerosis, increased tendency to thrombosis and inflammation may have a role in increased cardiovascular disease-related morbidity and mortality in MS. This syndrome is also associated with a hypercoagulable state, characterized by increased levels of clotting factors as well as inhibition of the fibrinolytic pathway [4]. MS may lead to worsened left ventricular systolic function by causing recurrent thrombotic events and by aggravating systemic inflammation in the course of AMI.

Mean platelet volume (MPV) is an indicator of platelet activation [5], which has an important role in the pathophysiology of coronary artery disease related complications [6]. After erosion or rupture of atherosclerotic plaques in coronary arteries, platelet activation plays a critical role in the prothrombotic events leading to AMI. Elevated MPV levels have been identified as an independent risk factor for myocardial infarction in patients with coronary heart disease and for death or recurrent vascular events after MI [7,8].

Left ventricular ejection fraction (EF) is a widely-used parameter for evaluating left ventricular systolic function in daily practice and has been shown to be a powerful independent predictor of prognosis after AMI [9]. The goal of this study was to evaluate the relationship between MPV levels and left ventricular systolic function in patients with metabolic syndrome who had first ST-elevation AMI.

**Methods**

Between May 2005 and January 2007, 81 consecutive patients with MS, referred for the first ST-elevation AMI were prospectively included. The local ethic committee approval and informed consent from each patient was obtained. Inclusion criteria included continuous chest pain that lasted > 30 minutes within the preceding 12 hours, ST-segment elevation more than 1 mm in two contiguous leads on the 12 leads electrocardiograph and first ST elevation AMI who had MS. Exclusion criteria were renal dysfunction (creatinine > 2.5 mg/dl), previous myocardial infarction, Killip class ≥ 2, previous percutaneous coronary intervention or coronary artery bypass surgery, valvular heart disease, subacute period (accepted as admission > 12 h), inadequate echocardiographic image quality, hematological disorders, malignant disease and acute or chronic infection.

Reperfusion was determined by evaluating ST segment changes in the 12 lead electrocardiograph. Successfully reperfusion was described as ≥70% ST segment resolution 90 min after reperfusion therapy.

**Diagnostic criteria for metabolic syndrome**

The diagnosis of MS was based on the ATP III clinical definition of the metabolic syndrome [1]. This requires the presence of ≥3 of the following: 1) abdominal obesity (waist circumference > 102 cm in men and > 88 cm in women); 2) high triglyceride level (> 150 mg/dl); 3) low HDL-cholesterol level (≤ 40 mg/dl for men and < 50 mg/dl for women); 4) high blood pressure (systolic > 130 mmHg or diastolic > 85 mmHg, or on antihypertensive medication) and 5) a high fasting plasma glucose concentration (> 110 mg/dl).

**Biochemical measurements**

Automated analyzers were used for the biochemical and hematological measurements. Blood samples for the biochemical measurements were drawn without stasis at 7–8 a.m. after 20 min of supine rest following a fasting period of 12 h. Glucose, creatinine and lipid profile were determined by standard methods. Blood samples for the MPV measurements were drawn within the first 1 hour after admission, were collected in tubes containing Na-citrate and were analyzed within 2 hours. An automatic blood counter (A Cell- Dyn 3500, Abbott, IL, USA) was used for whole blood analysis. The normal range for MPV in our laboratory is 7.0 to 11.0 fl.

**Echocardiography analysis**

The echocardiographic examination was done as soon as clinical stability of the patients was achieved after admission to coronary intensive care unit (mean 2.4 days). All patients were evaluated by two-dimensional echocardiography by using a Vivid 7 system (General Electric) with a 2.5-5 MHz transducer. Left ventricular systolic functions were assessed by EF determined using the modified Simpson method. End-systolic and end-diastolic LV cavity volumes were computed from the area measurement obtained from apical 2- and 4-chamber views at end-systole and end-diastole, respectively and averaged [10]. Patients were divided into two groups, according to LVEF, to evaluate the left ventricle systolic function: patients who had depressed left ventricle systolic function (group A = LVEF ≤50%), and patients who had preserved left ventricle
systolic function (group B = LVEF >50%). All of the echocardiographic examinations were done by one cardiologist who was blind to clinical information of the patients.

**Statistical analysis**

Continuous variables were given as mean ± SD; categorical variables were defined as percentages. To compare continuous variables, we used Student’s t-test or the Mann–Whitney U-test, where appropriate. Categorical variables were compared via the chi-square test. Logistic regression analysis were performed to determine if an independent relationship exits between MPV and deteriorated left ventricular systolic function. For all tests, a value of P<0.05 was considered to be statistically significant. The SPSS statistical software package (SPSS, version 16.0 for windows; SPSS Inc., Chicago, Illinois, USA) was used to perform all statistical calculations.

**Results**

Of 92 patients enrolled with first ST-elevation AMI and MS, 11 patients were excluded due to exclusion criteria. Of the remaining 81 patients (60 men, 21 women), the mean age was 57.5±10.3 years (range 33 to 80). The mean EF of the patients was 47.1±8.4%. There were no statistically significant differences between groups A and B according to age, gender, reperfusion treatment rate, time between reperfusion treatment and AMI, successfully reperfusion, family history for coronary artery disease, time between AMI and echocardiography, presence of hypertension or diabetes mellitus, and smoking habit (p >0.05).

The SPSS statistical software package (SPSS, version 16.0 for windows; SPSS Inc., Chicago, Illinois, USA) was used to perform all statistical calculations.

Logistic regression analysis showed an independent relationship between MPV and deteriorated left ventricular systolic function (group B = LVEF >50%). All of the echocardiographic examinations were done by one cardiologist who was blind to clinical information of the patients.

**TABLE 1. Clinical and laboratory parameters in study groups**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (EF ≤ 50%) (n=48)</th>
<th>Group B (EF &gt;50%) (n=33)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.9±10.5</td>
<td>56.9±10.2</td>
<td>0.68</td>
</tr>
<tr>
<td>Sex (men), No. (%)</td>
<td>36 (75%)</td>
<td>24 (72.7%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Hypertension, No. (%)</td>
<td>34 (70.7%)</td>
<td>18 (54.5%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Family history of CAD, No. (%)</td>
<td>17 (35.4%)</td>
<td>12 (36.3%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Current smoker, No. (%)</td>
<td>30 (62.4%)</td>
<td>25 (75.6%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Diabetes mellitus, No. (%)</td>
<td>10 (28.3%)</td>
<td>11 (33.3%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>102±10.1</td>
<td>100.1±10.7</td>
<td>0.47</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>192.4±39.4</td>
<td>195.7±41.8</td>
<td>0.7</td>
</tr>
<tr>
<td>LDL- cholesterol (mg/dl)</td>
<td>126±36</td>
<td>124±35</td>
<td>0.8</td>
</tr>
<tr>
<td>HDL- cholesterol (mg/dl)</td>
<td>39.3±7.8</td>
<td>38.5±9.9</td>
<td>0.68</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>128.6±53.6</td>
<td>146.9±55</td>
<td>0.17</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>148.9±38</td>
<td>151.8±69</td>
<td>0.83</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.12±0.4</td>
<td>1.23±1.1</td>
<td>0.55</td>
</tr>
<tr>
<td>Reperfusion therapy, No. (%)</td>
<td>39 (81.2%)</td>
<td>25 (75.7%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Reperfusion successfully (%)</td>
<td>30 (62.5%)</td>
<td>22 (66%)</td>
<td>0.8</td>
</tr>
<tr>
<td>AMI-Reperfusion therapy (min)</td>
<td>199±205</td>
<td>194±180</td>
<td>0.9</td>
</tr>
<tr>
<td>Anterior wall AMI, No. (%)</td>
<td>28 (58.3%)</td>
<td>10 (30.3%)</td>
<td>0.01</td>
</tr>
<tr>
<td>AMI–echocardiography (day)</td>
<td>2.7±1.7</td>
<td>2.8±1.6</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Abbreviations: CAD: Coronary artery disease, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, AMI: Acute myocardial infarction, CAD: Coronary artery disease

**TABLE 2. Hematological parameters in study groups**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (EF ≤ 50%) (n=48)</th>
<th>Group B (EF &gt;50%) (n=33)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (gr/dl)</td>
<td>13.9±1.9</td>
<td>14±1.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>41.7±5.1</td>
<td>41.4±4.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Platelet counts (x 10^3)</td>
<td>237.6±56</td>
<td>251.8±67</td>
<td>0.3</td>
</tr>
<tr>
<td>Mean platelet volume (fl)</td>
<td>9.94±1.09</td>
<td>9.14±1.05</td>
<td>0.02</td>
</tr>
</tbody>
</table>
tolic function, even after readjustment for potential confounders (age, gender, platelet counts, rate of anterior MI) (1.08 (1.04-1.20), CI: 95%, p=0.02).

Discussion
In the present study the relationship between MPV and left ventricle systolic function was investigated in patients with MS who had first ST-elevation AMI. In this selected population, patients with depressed left ventricle function had significantly higher MPV values than patients with preserved left ventricular function.

Platelets play an important role in the pathogenesis, morbidity, and mortality of acute coronary syndromes [11]. Previous studies have demonstrated that there is a close relationship between MPV and cardiovascular risk factors, such as metabolic syndrome, diabetes mellitus, hypertension and hypercholesterolemia [12-15].

Patients with MS are at increased risk for developing coronary heart disease as well as increased morbidity and mortality from cardiovascular disease [3,4]. Metabolic syndrome is thought to have a crucial role in the development of cardiovascular complications and a greater likelihood of thrombosis, complicating vessel injury such as atherosclerotic plaque rupture [16-18]. There are several mechanisms which are responsible for increased propensity to thrombosis. These mechanisms include increased activation of platelets [19], increased production and release of thromboxane A2 by platelets [20], increased platelet reactivity due to the direct effect of hyperglycemia [21] and vascular dysfunction due to decreased vascular endothelial production of prostacyclin and nitric oxide [22].

Increased platelet size reflects increased platelet activity. Mean platelet volume can reflect changes in the level of platelet stimulation and the rate of platelet production [23]. Heterostatically reactive platelets and larger platelets have more granules and adhesion receptors, which result in decreased bleeding time, an indication of increased activation [24]. On these grounds, MPV could be accepted as a parameter of platelet activity and has become a prognostic factor in coronary heart disease [25]. Previous studies have demonstrated a close relationship between MPV and AMI [8], unstable coronary syndromes [26], slow coronary flow [27] and coronary artery ectasia development [28]. High MPV values were found to be associated with unsuccessful reperfusion after both primary percutaneous coronary intervention and fibrinolytic therapy [29,30]. In addition, increased platelet activity may be associated with recurrent thrombotic events and no-reflow phenomenon, which are, in turn, associated with poorer left ventricular function. Martin et al. reported that elevated MPV were associated with both death and recurrent MI after first AMI [8]. In addition, Sezer et al. found that elevated MPV was associated with adverse microvascular outcomes in AMI [31]. In the light of these findings, it is possible to conclude that increased platelet activity may be more closely associated with worse left ventricular EF in patients with MS with their first AMI as a result of their procoagulable and proinflammatory states.

The rate of cardiovascular risk factors, e.g., hypertensions and diabetes, in the patients with metabolic syndrome is higher than in individuals without metabolic syndrome. In addition, the presence of metabolic syndrome is shown to be associated with elevated inflammation [1,4]. All these factors can trigger platelet activity by activating various pathways. Augmented platelet activity in an acute myocardial infarct (AMI) has been demonstrated to be associated with unsuccessful reperfusion, repeated myocardial infarcts and increased no-reflow phenomenon [8,29,31]. Particularly, impaired microvascular circulation due to thrombosis is expected during amplified thrombocyte activity [31]. All of these factors could be responsible, at least in part, for the left ventricular systolic dysfunctions at different extends.

The elevated MPV may be used as a marker for accelerated inflammatory and thrombogenic process and may be associated with poorer outcomes in patients with MS attending for AMI.

The main limitation of this study was relatively small sample size. Nevertheless, we think that the increased levels of MPV in the patients with left ventricular systolic dysfunctions are still clinically significant and not entirely incidental. Further studies with larger populations are needed to clarify potential association between MPV in the patients with left ventricular systolic dysfunctions. Second, unidentified confounders may have an influence on MPV levels. Third, the patients’ medications were not recorded but all patients included in the study were treated according to recent guidelines.

Conclusions
Elevated MPV on admission can be associated with degree of left ventricular systolic dysfunction in patients with metabolic syndrome who had first ST-elevation AMI and, thus, shows potential for use as a prognostic marker.

References
