Original Article

Mean platelet volume levels in the presence of angiographically documented peripheral artery disease

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Abstract: Aim: Increased mean platelet volume (MPV) have been shown to be associated with peripheral artery disease (PAD). However in these studies, noninvasive methods for the diagnosis of PAD was used. In the literature, there is no studies examining the values of MPV in the angiographically documented PAD. We aimed to evaluate the relationship between angiographically documented PAD and MPV levels in the peripheral blood samples. Methods: In this study, retrospective analysis of 1386 patients was performed who underwent peripheral angiography at the cardiology service of the our hospital, between 2006 and 2012 for a suspected diagnosis of lower extremity peripheral arterial disease. Patients with a stenosis percent of 50% or above in the peripheral angiography were considered as having peripheral arterial disease. MPV values are affected by many factors. Only 84 patients who complied with the inclusion criteria were detected. The study patients were divided into 2 groups according to the results of peripheral angiography. 56 patients diagnosed with PAD based on the specified criteria were grouped into Group I (mean age 59 ± 10 years) while 28 patients without peripheral arterial disease were grouped into Group II (mean age 60 ± 11 years). Blood tests and angiographic images were analyzed from patients’ data. Results: Both groups were similar in terms of basic parameters of anemia including hemoglobin, hematocrit and red cell distribution width levels. There were no significant differences between MPV levels in both groups (8.08 ± 0.91 vs 8.28 ± 1.16, P > 0.05). Mean corpuscular volume and mean corpuscular hemoglobin levels, on the other hand, were significantly higher in Group I (P < 0.05). Conclusions: In our study, we did not found any significant changes in the MPV levels of angiographically documented PAD diseases. The use of MPV level as a risk factor for peripheral arterial disease is impractical due to the fact that MPV is affected by a lot of factors and there are several technical factors. Because of this, in the real life, we are not recommend to use MPV values as an indicator for peripheral artery disease.

Keywords: Peripheral arterial disease, mean platelet volume, peripheral angiography

Introduction

Peripheral artery disease (PAD) is defined as an atherosclerosis of the noncardiac vessels. The world wide prevalence of lower extremity PAD is between 3 to 12 percent [1-3]. It is a clinical process which is beginning with intermittent claudication and leads to limb amputation. The risk factors for PAD are similar to those for atherosclerosis such as smoking, diabetes and increased age [4, 5]. The diagnosis of PAD is quite difficult. A failure to diagnose PAD misses the opportunity of secondary prevention by instituting atherosclerosis risk factor modification [6].

It is known that platelets are essential in the pathogenesis of atherosclerosis and arterial thrombosis [7, 8]. Mean platelet volume (MPV) levels have been investigated in several situations such as diabetes mellitus, coronary artery disease, hypertension, cerebrovascular accident, PAD [9-18]. The association between PAD and MPV was evaluated previously, but in all these studies have been used noninvasive methods to diagnose PAD. Noninvasive methods have their own limitations for diagnosis of PAD. The aim of the present study was to investigate the relation between angiographically documented PAD and MPV levels, which plays an important role in the development of arterial
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Methods

In this study, retrospective analysis of 1386 patients was performed who underwent peripheral angiography at the cardiology service of our hospital between 2006 and 2012 for a suspected diagnosis of lower extremity peripheral arterial disease. 84 patients who complied with the inclusion criteria were included in this study. Age, gender, and past history of hypertension, diabetes, hyperlipidemia, and smoking were recorded. Patients with known coronary artery disease and peripheral arterial disease, cerebrovascular disease, chronic renal failure (creatinine > 2.0), liver failure, treated or untreated anemia, systemic inflammatory and infectious diseases, autoimmune disease, malignant disease, a reduced left ventricular ejection fraction (LVEF < 50%), and an acute coronary syndrome at presentation were excluded. Patients with a stenosis percent of 50% or above in the peripheral angiography were considered as having PAD. All the study patients were newly diagnosed.

The study patients were divided into two groups according to the results of peripheral angiography. 56 patients diagnosed with PAD based on the specified criteria were grouped into Group I (mean age 59 ± 10 years) while 28 patients without peripheral arterial disease were grouped into Group II (mean age 60 ± 11 years). Blood tests and angiographic images were analyzed from patient data. Blood tests measured on the day of peripheral angiography were evaluated. Peripheral venous blood samples were drawn into EDTA-containing biochemistry tubes. Whole blood cell count and volume analyses were performed using Beckmann Coulter LH 780 Hematology Analyzer device. Images of peripheral angiographies were reviewed by two cardiologists who were unaware of the clinics of the patients.

Patients who had fasting blood glucose above 126 mg/dl and using oral antidiabetic drugs or insulin were accepted as having diabetes mellitus. Patients using antihypertensive drugs or having a blood pressure greater than 140/90 mmHg on presentation were accepted as hypertensive. ATPIII criteria were used for defining hyperlipidemia [19]. The ethics committee of our institute approved the study protocol.

Statistical analysis

SPSS (Statistical Package for the Social Sciences ver. 13.0, SPSS Inc, Chicago, Illinois, USA) was used for statistical analysis. The continuous variables were expressed as mean ± standard deviation while the categorical variables were expressed as number and percentage (%). Normally distributed variables were compared across groups by means of student t test. The non-parametric variables were compared using the Mann-Whitney U test. Logistic regression analyses were performed to rule out the confounding effect of imbalance clinical features between two groups. Categorical variables were compared via Chi-square test. A P-value < 0.05 was considered to be statistically significant.

Results

There were no significant differences between Group I and Group II with respect to age, gender, and the number of diabetic or hyperlipidemic patients. Group I had a significantly higher

| Table 1. Characteristics of groups with presence or absence of peripheral artery disease |
|---------------------------------|-----------------|-------------|
|                                | Group I (n = 56) | Group II (n = 28) |
| Age (Years)                    | 59 ± 10         | 60 ± 11      | 0.57    |
| Sex M/F                        | 53/3            | 26/2         | 0.74    |
| Diabetes Mellitus (n, %)       | 12 (21.4%)      | 5 (17.9%)    | 0.38    |
| Hypertension (n, %)            | 19 (34%)        | 6 (21%)      | 0.09    |
| Dyslipidemia (n, %)            | 42 (75%)        | 19 (67.9%)   | 0.48    |
| Smoking (n, %)                 | 39 (69.9%)      | 7 (25%)      | 0.001   |
| LVEF (%)                       | 58% ± 4         | 56% ± 8      | 0.58    |
| Glucose (mg/dl)                | 124 ± 62        | 120 ± 50     | 0.90    |
| Total cholesterol (mg/dl)      | 215 ± 46        | 200 ± 42     | 0.17    |
| LDLcholesterol (mg/dl)         | 139 ± 36        | 129 ± 35     | 0.20    |
| HDLcholesterol (mg/dl)         | 37 ± 11         | 41 ± 9       | 0.13    |
| Triglyceride (mg/dl)           | 177 ± 100       | 170 ± 90     | 0.65    |
| Urea (mg/dl)                   | 32 ± 10         | 33 ± 12      | 0.72    |

LVEF: Left ventricular ejection fraction; LDL: Low density lipoprotein; HDL: High density lipoprotein.
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Table 2. Hemogram parameters in subjects with and without peripheral artery disease

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 56)</th>
<th>Group II (n = 28)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>14.4 ± 1.2</td>
<td>14.3 ± 1.3</td>
<td>0.57</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>42.6 ± 3.5</td>
<td>42.4 ± 3.5</td>
<td>0.79</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>90.5 ± 4.5</td>
<td>88.5 ± 4.3</td>
<td>0.03</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>30.6 ± 1.8</td>
<td>29.8 ± 1.7</td>
<td>0.03</td>
</tr>
<tr>
<td>MCHC (g/dl)</td>
<td>33.8 ± 1.0</td>
<td>33.7 ± 0.8</td>
<td>0.80</td>
</tr>
<tr>
<td>Neutrophils (× 10³/mm³)</td>
<td>5.145 ± 1.676</td>
<td>5.664 ± 1.931</td>
<td>0.35</td>
</tr>
<tr>
<td>Eosinophils (× 10³/mm³)</td>
<td>0.213 ± 0.149</td>
<td>0.229 ± 0.165</td>
<td>0.76</td>
</tr>
<tr>
<td>Monocytes (× 10³/mm³)</td>
<td>0.671 ± 0.240</td>
<td>0.739 ± 0.329</td>
<td>0.47</td>
</tr>
<tr>
<td>Neutrophil/Lymphocyte Ratio</td>
<td>2.6 ± 1.2</td>
<td>2.3 ± 1.3</td>
<td>0.16</td>
</tr>
<tr>
<td>Platelet count (× 10³/mm³)</td>
<td>262.16 ± 74.488</td>
<td>251.96 ± 80.536</td>
<td>0.83</td>
</tr>
<tr>
<td>MPV (fl)</td>
<td>8.08 ± 0.91</td>
<td>8.28 ± 1.16</td>
<td>0.37</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>13.92 ± 0.78</td>
<td>14.26 ± 1.0</td>
<td>0.09</td>
</tr>
</tbody>
</table>

MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; MPV: Mean platelet volume; RDW: Red cell distribution width.

rate of smoking habit (P < 0.05). Both groups were similar in terms of left ventricular ejection fraction (P > 0.05). Basic demographic features of all study patients with or without peripheral arterial disease are summarized in Table 1.

No significant differences were found between both groups with regard to fasting blood glucose, total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride, and blood urea (P > 0.05). Both groups were also similar in terms of basic parameters of anemia including hemoglobin (Hgb), hematocrit (HTC) and red cell distribution width (RDW) levels. There were no significant differences between MPV levels of both groups (P > 0.05). Mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) levels, on the other hand, were significantly higher in Group I (P < 0.05). Neutrophil, eosinophil, and monocyte counts as well as neutrophil-lymphocyte ratio were statistically similar in both groups (Table 2).

Discussion

Our study had two major conclusions. First, we did not found any significant changes in the MPV levels of angiographically documented PAD diseases. Second, PAD patients had a significantly increased MCV and MCH levels.

Atherosclerosis is a systemic disease of large and medium-sized arteries. When non-cardiac arteries involve, is called peripheral arterial disease. PAD is an important public health problem due to a high rate of morbidity and prevalence. Studies aiming at readily measured, easy-to-use and economical biochemical parameters to predict PAD have been on the rise in recent years. In this regard, one of the most disputed parameters is MPV level derived from complete blood count. MPV is an indicator of thrombocyte function and activation. Large and big thrombocytes are more active and have a tendency to aggregate. This type of thrombocytes contains denser granules, secretes more serotonin and β-thromboglobulin and produces more thromboxane A2 compared to small thrombocytes [20, 21]. Thrombocyte size does not depend on the age of thrombocyte. Thrombocyte size is determined at the production from the megakaryocyte [22]. Some studies have suggested that MPV levels increase as a result of peripheral arterial disease [9, 10]. In these studies, however, peripheral arterial disease is diagnosed by means of noninvasive methods such as clinical history, physical examination, or ankle brachial index (ABI). All these modalities have their own limitations for diagnosis of peripheral arterial disease. The diagnostic value of ABI is limited in diseases that cause stiffened arteries and non-compressibility (e.g. as a result of diabetes, end stage renal insufficiency and advanced age) [23]. A similar diagnostic challenge exists in patients with borderline ABI level and atrial fibrillation [24]. For these reasons, ABI measurement method is not hundred percent reliable method because of the some technical problems of the measurements of ABI and the value is affected by some of the patient’s parameters. However in our study, peripheral arterial disease was diagnosed by peripheral angiography, which is still the gold standard for diagnosis. In this context, our study is the first study in the literature assessing the relationship between MPV and angiographically documented PAD.
In our study, unlike previous studies, MPV levels were not different in the groups with angiographically documented PAD and the control group. This may have resulted from two factors: first, the number of patients in the study was small. There are so many parameters that affect the level of MPV. Therefore, many patients from the study were had to exclude. From the group of 1384 patients, only 84 patients were included into the study. But at this point our study showed that it is quite difficult to find the patient who does not have the other influence factors on the MPV level. Second, time from drawing blood into EDTA-containing tubes to studying in the laboratory may have differed. In the previous studies indicated that large variations in thrombocyte volumes when they use EDTA as the anticoagulant [25-27]. Subsequent studies have demonstrated that platelets swell until 120 minutes in EDTA and different brand’s tubes can represent a clinically relevant source of variations on MPV [28, 29]. In our center, blood samples stored in EDTA-containing tubes and complete blood count measurements were performed in accordance with previously defined standards so that the results are minimally affected. Nevertheless, since our study was a retrospective one, we were not able to standardize exact study times of blood samples.

Similarly, in coronary artery disease (CAD) which is one of the significant atherosclerotic disease, assessment of the MPV level is a still controversial issue. In the literature, some studies showed that MPV levels were increased in stable CAD [14, 15]. On the other hand some authors suggest that there were not any relationship between MPV level and stable CAD [16, 29-31]. In the literature, the number of studies with CAD patients is much greater than the number of PAD studies. In this regard, our study is the first study which is the patients were diagnosed by peripheral angiography and we found no significant change on MPV level in PAD patients.

In this context, our study suggests that MPV analysis falls short of guiding physicians in real life due to the fact that it is affected by many factor and there are some technical problems in its measurement. These results suggest that MPV may be a useless criterion in the assessment of peripheral arterial disease.

Our results indicated that MCV levels were significantly higher in patients with peripheral arterial disease compared to controls. Mueller et al. also reported higher MCV levels in patients with angiographically documented critical peripheral arterial disease [32]. Similarly, Halmayer et al. suggested that MCV levels were related to the severity of peripheral arterial disease [33]. Also in our study, consistent with the literature in patients with peripheral arterial disease were found to have high level of MCV. It is not clear by which mechanism MCV takes part in the occurrence and severity of peripheral arterial disease. There is a need for further studies on this subject.

Smoking rate was also significantly higher among patients with peripheral arterial disease compared to controls, similar to the literature [5].

There are some limitations of our study. First, we used the EDTA containing tube for blood samples. EDTA can change the platelet volume. However widely in all the world, for the measurement of platelet volume EDTA-containing tubes are used. In our hospital, we also use these tubes. Second, this is a retrospective study. Furthermore, the number of subjects in our study was small. Thus, MPV levels in angiographically documented PAD patients may be studied in prospective study in a large population with standardize study time of blood samples.

Conclusions

In conclusion, this study indicated that MPV levels were not differ in patients with angiographically documented peripheral arterial disease. Nowadays there is a trend to use the level of MPV for predicting to PAD, coronary artery disease, congenital heart disease, coronary intervention, ischemic stroke and such diseases. We found no association between MPV and the presence peripheral artery disease. Our findings suggest that, using a routine laboratory procedure mean platelet volume cannot be used as a predictive marker for peripheral arterial disease in clinical practice.

Disclosure of conflict of interest

None.
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Abbreviations

PAD, Peripheral artery disease; MPV, Mean platelet volume; Hb, Hemoglobin; HTC, Hematocrit; RDW, Red cell distribution width; MCV, Mean corpuscular volume; MCH, Mean corpuscular hemoglobin; LVEF, Left ventricular ejection fraction; LDL, Low density lipoprotein; HDL, High density lipoprotein; ABI, Ankle brachial index; CAD, Coronary artery disease.

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