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REGULAR ARTICLE

Relation between platelet microaggregates and ankle brachial index in patients with peripheral arterial disease

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KEYWORDS
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Abstract

Introduction: Peripheral arterial disease is one of the systemic atherosclerotic diseases, and patients with the disorder are classified in the high risk group of coronary artery disease. A lower ankle brachial index is a frequent finding in peripheral arterial disease. While platelet microaggregates are a significant predictor of adverse clinical outcome in coronary artery disease, the significance of platelet aggregability in peripheral arterial disease has not been elucidated.
Materials and methods: Small platelet aggregates measured using laser-light scattering and ankle brachial index were determined in 42 patients with both coronary artery disease and peripheral arterial disease (peripheral group), 56 patients with only coronary artery disease (coronary group) and 32 patients without both (control group).
Results: The level of small platelet aggregates was increased significantly in the peripheral group (4.3×10^4 [range 2.2×10^4 to 7.4×10^4]) compared with both the coronary (1.1×10^4 [range 0.3×10^4 to 5.0×10^4]) and control groups (0.5×10^4 [range 0.1×10^4 to 0.9×10^4]). There was a significant inverse correlation between log small platelet aggregates and ankle brachial index ($n=130$, $r=-0.422$,

Abbreviations: PAD, peripheral arterial disease; CAD, coronary artery disease; ABI, ankle brachial index; SPA, small platelet aggregates; AU, arbitrary units; ADP, adenosine diphosphate.

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$p<0.001$). Multivariate logistic regression analysis revealed that a lower ankle brachial index (<0.90) was an independent determinant of increased levels of small platelet aggregates.
Conclusions: Platelet aggregability was increased in patients with peripheral arterial disease with the degree of platelet aggregation being closely associated with ankle brachial index. It is possible that this change in platelet activity may be one mechanism to explain why a lower ankle brachial index is a predictor of poor prognosis in patients with peripheral arterial disease.

Peripheral arterial disease (PAD) is most commonly a manifestation of atherosclerosis in the lower limbs distal to the aortic bifurcation. Previous studies have shown that the presence of PAD is a strong indicator of systemic atherosclerosis [1], and there is evidence that patients with PAD have an increased risk of cardiovascular morbidity and mortality, particularly that of coronary artery disease (CAD), compared with patients without PAD [2—7]. It has been shown that the prevalence of CAD in patients with PAD is at least 40% [8—10].

Platelet aggregation is a useful biological marker for predicting coronary events and mortality in survivors of myocardial infarction [11]. However, platelet aggregation measured by conventional methods such as light transmission has the limitation of relatively low sensitivity for detecting the initial aggregation process, that is characterized by the formation of small platelet aggregates [12,13]. In contrast, a platelet aggregometer using laser-light scattering provide precise quantitative evaluation of both the size and number of platelet aggregates [14]. We reported recently that high levels of platelet microaggregates correlated with adverse clinical outcome in patients with CAD [15]. It is therefore likely that patients with CAD with increased numbers of small platelet aggregates (SPA) may represent a patient population with more advanced systemic atherosclerosis.

Several investigators have reported a relationship between blood coagulation and fibrinolytic parameters in patients with PAD [16—20] and there are also a few reports on platelet activation in PAD [21,22]. However, comparison of platelet aggregability in PAD with other atherosclerotic vascular diseases has not been studied extensively. Despite CAD and PAD both being classified clinically as atherosclerotic disorders, CAD patients do not always have PAD. This suggests that patients with CAD complicated with PAD have more advanced atherosclerotic characteristics compared with patients with CAD alone.

We hypothesized that platelet hyperaggregability was observed in patients with CAD complicated with PAD and platelet aggregability increased in parallel with severity of the disease. Therefore, the primarily, we compared platelet aggregability in patients with different severity of vascular disease, categorized as either the presence or absence of CAD and/or PAD. In addition, the relationship between ankle brachial index (ABI), an index of PAD severity, and platelet aggregability was also examined.

Patients in a clinical study and methods

Study population

Patients who complained of chest pain on admission to our institution were enrolled prospectively in the study. To determine the required number of patients, we performed power calculation based on our previous data. This study's target enrollment was approximately 120 patients. After written informed consent had been obtained all the patients (91 males and 39 females; mean age 71 ± 1 years, range 53—85) underwent diagnostic cardiac catheterization to confirm the diagnosis of CAD. CAD was defined as the presence of organic stenosis $>70\%$ in at least one major coronary artery. As shown in Fig. 1, the patients were divided into three groups with the first group containing patients with an ABI <0.90 in at least one leg regardless of the presence of CAD (PAD group), the second group containing patients with CAD whose ABI ≥ 0.90 (CAD group) and the third group containing the remaining patients who did not have either CAD or PAD (control group). Enrollment was continued prospectively until each group was matched for age and gender. At the end of enrollment the groups had the following characteristics: PAD group ($n=42$); CAD group ($n=56$); and control group ($n=32$). The entire PAD group and 51 (91%) of the CAD group were administered oral aspirin (100 mg/day). No patients were taking antiplatelet drugs other than aspirin. The protocol of the study was approved by the ethics committee of our institution.