Usefulness of mean platelet volume for predicting stroke risk in atrial fibrillation patients

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Early detection of atrial fibrillation patients at high risk for stroke is important. There are some studies which indicate that mean platelet volume (MPV) determines the prognosis and risk in patients with a stroke. In this study, our aim was to investigate the association between the MPV measured in stroke patients with atrial fibrillation. Consecutive patients referred to our center between January 2010 and April 2012 were included in this study. The patients with atrial fibrillation were classified into two groups according to presence or absence of a history of stroke by combining data from the medical histories after a thorough review of the medical records. MPV determination was made within 24 h following the onset of stroke. We studied 63 consecutive stroke patients with atrial fibrillation and 77 atrial fibrillation patients without stroke history. In receiver-operating characteristic (ROC) curve analysis, the value for MPV levels to detect stroke with a sensitivity of 63.5% and specificity of 64.4% was 9.4 fl. High MPV (>9.4 fl) was significantly associated with the occurrence of stroke [odds ratio (OR) 4.021, 95% confidence interval (CI) 1709–9464, $P<0.001$]. Our study supports the hypothesis that a high MPV is associated with an increased risk of stroke in atrial fibrillation patients. *Blood Coagul Fibrinolysis* 24:55–58 © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

Atrial fibrillation is the most common clinically significant cardiac arrhythmia, and its prevalence is anticipated to increase [1]. Patients with atrial fibrillation are more likely to have a severe stroke and increased mortality [2]. Despite all the advances in the treatment of atrial fibrillation, the risk of stroke is still a major threat. Thus, early detection of patients at high risk for stroke is important. There are many reasons for the development of thromboembolism in patients with atrial fibrillation and activation of platelets is one of the most important. Activated platelets are larger and they have a large number of vasoactive and prothrombotic factors. Therefore, mean platelet volume (MPV) can be used as a marker for the reactivity of platelets [3]. MPV has been found to be elevated in many diseases, such as hypertension, diabetes mellitus, and stroke [4–7]. Some data about the relationship between atrial fibrillation and MPV exist [8,9]. Similarly, there are some studies that indicate that MPV determines the prognosis and risk in patients with a stroke [10–12]. In this study, our aim was to investigate the association between the MPV measured in stroke patients with atrial fibrillation.

Methods

Patients

Consecutive patients referred to our center between January 2010 and April 2012 were included in this study. The patients with atrial fibrillation were classified into two groups according to presence or absence of a history of stroke by combining data from the medical histories after a thorough review of the medical records. Healthy individuals without any disease and complaints were recruited into the control group. Patients were excluded if they had a history of prior myocardial infarction, systolic heart failure and valvular heart disease, hemorrhagic stroke, intracerebral hemorrhage, elevated liver enzymes, untreated hypothyroidism, familial hypercholesterolemia, renal failure, or known cancer. At the time of blood sampling, a complete clinical history, including the presence or absence of cardiovascular risk factors, was obtained from all the patients. The study was approved by our institutional ethics board. Either written or oral informed consent was obtained from all the patients.

Biochemical measurements

Blood samples were drawn following a fasting period of 12 h. Venipuncture was performed within 24 h of

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symptom onset and before the commencement of medical therapy, and in all cases, glucose, creatinine, and lipid profiles were determined by standard methods. MPV was measured in a blood sample collected in tripotassium ethylenediaminetetraacetic acid (EDTA) (7.2 mg) tubes. Blood samples were analyzed within 2 h of venipuncture using an automatic blood counter. MPV determination was made within 24 h following the onset of stroke.

Echocardiography analysis

Echocardiographic examination was done as soon as clinical stability of the patients was achieved after admission to our ICU. All patients were evaluated by two-dimensional echocardiography by using a Vivid 5 system (General Electric) with a 2.5–5 MHz transducer. Left-ventricular systolic functions were assessed by ejection faction determined using the modified Simpson's rule. End-systolic and end-diastolic left-ventricular cavity volumes were computed from the area measurement obtained from apical two and four-chamber views at end systole and end diastole, respectively, and were averaged.

Left-atrial size was measured by two-dimensional guided M-mode echocardiography in the parasternal long-axis view. Left-atrial volume (LAV) was calculated using the Cube method, through the following formula: $LAV = 4/3\pi \times [\text{anteroposterior dimension}/2]^3$.

Statistical analysis

All analyses were performed using SPSS V 16.0 for Windows (SPSS, Chicago, Illinois). Quantitative variables were expressed as mean value + standard deviation (SD) for parametric variables. Categorical variables were compared using the chi-square test. Statistical differences among groups were tested by one-way analysis of variance (ANOVA) and Kruskal–Wallis tests for parametric and nonparametric variables, respectively. When a significant difference between three groups was observed by using one-way ANOVA test and Kruskal–Wallis tests, independent-samples *t*-test and Mann–Whitney *U*-test were used to determine the differences between the two groups. Backward linear and logistic regression analyses were performed to assess the independent effects of several variables on stroke, respectively.

Results

We studied 63 consecutive stroke patients with atrial fibrillation and 77 atrial fibrillation patients without stroke history. The control group consisted of 87 people without any disease. The baseline characteristics of the overall population and MPV levels are summarized in Tables 1 and 2. Patients with stroke were significantly older, had diabetes mellitus more often, and showed a higher MPV and LAV than patients with atrial fibrillation and normal individuals.

In receiver-operating characteristic (ROC) curve analysis, the value for MPV levels to detect stroke with a sensitivity of 63.5% and specificity of 64.4% was 9.4 fl. The area under the curve was 0.703 (Fig. 1).

Admission low-density lipoprotein (LDL), creatinine, platelet counts, and LAV were measured and the study population was classified on the basis of their quintiles. We also performed univariate logistic regression including high LDL cholesterol, creatinine, LAV, platelet count, MPV, and other risk factors for stroke (Table 3).

In the multivariate regression model, four parameters significantly influenced the model of stroke prediction (Table 4). High MPV (>9.4 fl) was significantly associated with the occurrence of stroke [odds ratio (OR) 4.021, 95% confidence interval (CI) 1709–9464, $P < 0.001$].

Discussion

Our study supports the hypothesis that a high MPV is associated with an increased risk of stroke in patients with atrial fibrillation. In addition, we found an increase in LAV values, which may also be predictive for stroke.

Table 1 Baseline characteristics of participants

	Normal	AF	CVA	*P*
N	58	77	63	
Age	56 ± 10	63 ± 9	69 ± 8	<0.001β
Male (%)	51.7	57.4	52.4	>0.05
Hypertension (%)	–	66.2	54	>0.05
DM (%)	–	31.2	49.2	0.02
Smoking	55.2	55.8	46	>0.05
Acetyl salicylic acid treatment (%)	–	54.5	49,2	>0.05
Clopidogrel treatment (%)	–	13	19	>0.05
Anticoagulant treatment (%)	–	44.3	41.3	>0.05
Hemoglobin (mg/dl)	12.7 ± 1.2	12.8 ± 1.1	13 ± 1.4	>0.05
Platelet count ($\times 10^3$/l)	213 ± 72	264 ± 94	245 ± 73	<0.001Ω
Serum creatinine (mg/dl)	0.92 ± 0.3	0.94 ± 0.3	1 ± 0.3	>0.05
Total LDL (mg/dl)	113 ± 30	113 ± 35	125 ± 30	>0.05
Left-ventricular ejection fraction (%)	61 ± 4	60 ± 3	60 ± 4	>0.05
Left atrium volume (ml)	23.6 ± 14.6	45.6 ± 25.5	55.8 ± 30.2	<0.001β

β: CVA AF > normal group, Ω: AF = CVA normal group, AF, atrial fibrillation; CVA, cerebrovascular accident; DM, diabetes mellitus; LDL, low-density lipoprotein.

Table 2 Mean difference of mean platelet volume between groups

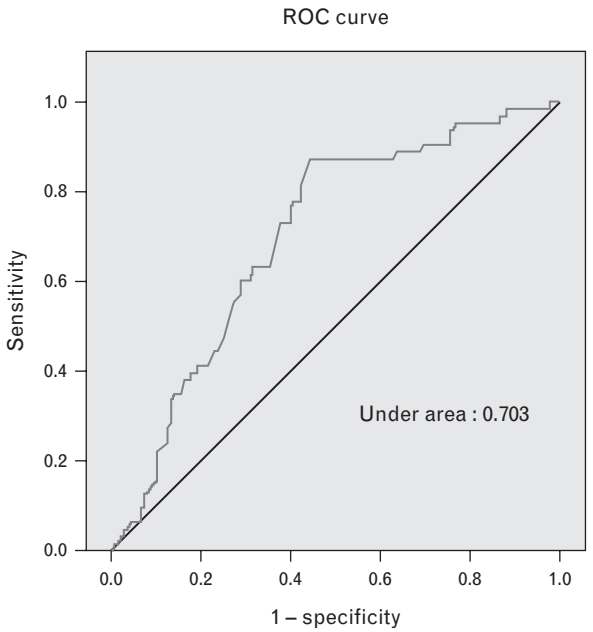
	Normal	AF	CVA	
MPV (fl)	8.6 ± 1.3	9.1 ± 1	9.7 ± 0.9	$P < 0.001\beta$

β: CVA AF > normal group.

Atrial fibrillation is common and increases the risk of stroke five-fold when present [13]. Moreover, despite the production of new drugs and devices, this risk has not disappeared completely. Therefore, early detection of patients with risk is very important. It is not easy to find an appropriate test to determine the risk due to the frequency of the disease and economic reasons. MPV may be useful for predicting high-risk patients. MPV is a marker, requiring simple, cheap, and common technology.

Platelets play a key role in the pathogenesis, morbidity, and mortality in stroke. Platelets with high MPV are metabolically and enzymatically more active and secrete more mediators. These mediators can contribute to inflammation and atherogenesis [3]. Therefore, many studies have investigated the relationship between MPV and thrombotic disorders such as coronary artery disease, risk of stent restenosis, peripheral artery disease, diabetes mellitus, and metabolic syndrome [14]. For example, Ozkan *et al.* [15] found that MPV was one of the independent predictors of acute myocardial infarction in young patients. Similar studies have been reported in patients with atrial fibrillation and also stroke patients.

Fig. 1



ROC curve for MPV values. MPV, mean platelet volume; ROC, receiver-operating characteristic.

Table 3 Univariate analysis for stroke's risk factors

	β	*P*
Age > 75	6.350	<0.001
Male sex	1.103	0.749
Hypertension	1.931	0.030
DM	4.480	0.001
Smoking	0.682	0.212
Left atrium volume >49.8 ml	4.080	<0.001
Serum creatinine	0.980	0.952
LDL levels >132 mg/dl	2.175	0.030
Platelet counts $>256 \times 10^3$/l	1.146	0.952
MPV >9.4 fl	3.152	<0.001

AF, atrial fibrillation; DM, diabetes mellitus; LDL, low-density lipoprotein.

In this study, we found a higher value of MPV in patients with atrial fibrillation than the control group. This result is similar to other studies. Colkesen *et al.* [8] found that MPV was higher in patients with paroxysmal atrial fibrillation than the normal group, and this might be an expression of increased platelet activity. In another study, Choudhury *et al.* [16] demonstrated that patients with permanent atrial fibrillation had higher levels of MPV compared with those who had paroxysmal atrial fibrillation.

There are many studies related to MPV in stroke patients. According to some of these studies, high MPV values are associated with the prognosis in patients with stroke [10,17,18]. Butterworth and Bath [19] found that platelet volume is increased in patients with acute ischemic stroke. O'Malley *et al.* [20] noticed high values of MPV in all subtypes of ischemic stroke. The PROGRESS study showed that MPV could predict the risk of a second stroke [12]. Greisenegger *et al.* [17] indicated that an elevated MPV is associated with a worse outcome for acute ischemic cerebrovascular events independent of other clinical parameters. Similar results were found in our study; MPV values were higher in stroke patients than the normal group and patients without a history of stroke. In patients with high MPV values (>9.4 fl), risk of stroke is increased up to four-fold. The risk of stroke is also increased in patients with high MPV value, especially in the elderly and patients with diabetes mellitus. Therefore, the MPV value may be an additional marker for the decision to use anticoagulant therapy in patients with atrial fibrillation.

Similar results were observed in another recently published study [21]. However, our study also has some differences. Ha *et al.* [21] recruited only atrial fibrillation

Table 4 Multivariate regression analysis

	β	Sig.	95% CI
Age >75	4.186	0.013	1.357–12.912
DM	2.570	0.045	1.022–6.460
Left atrium volume >49.8 ml	3.186	0.013	1.320–7.690
MPV >9.4 fl	4.021	0.001	1.709–9.464

CI, confidence interval; DM, diabetes mellitus; MPV, mean platelet volume.

patients in their study and patients were followed up for stroke occurrence. In the present study, a control group with healthy individuals was recruited. Patients' number of stroke was higher than the other study. We have recruited stroke patients after event. Additionally, we have showed a significant correlation between LAV and stroke.

Current treatment guidelines suggest the different algorithms to identify high-risk patients. However, LAV has not been evaluated as a risk factor. The relationship between left-atrial size and stroke has been shown in many studies [22,23]. Benjamin *et al.* [24] demonstrated that left-atrial size was significantly related to the risk of stroke in men. In this study, we found high LAV values (>49.8 ml) may determine the risk of stroke and may be a marker of decision for anticoagulant therapy as MPV.

The use of antiplatelet and anticoagulant drugs reduces the risk of stroke. In addition, these drugs may decrease MPV, but in our study, there was no difference in the frequency of anticoagulant and antiplatelet medication use between groups.

Limitations

The study was constituted from a relatively small population. Also, the method used in the volume of the left atrium was not according to the body index. Finally, we did not evaluate other risk factors for stroke patients such as fibrinogen and CD40 ligand.

In conclusion, high MPV values may be a predictor of stroke in atrial fibrillation patients. This is a simple, easily accessible, and cheap method to identify high-risk patients. MPV and LAV may be used to inform the selection of patients that receive anticoagulant therapy.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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