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Mean platelet volume and mean platelet volume/platelet count ratio as a risk stratification tool in the assessment of severity of acute ischemic stroke

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Abstract The mean platelet volume (MPV) is a laboratory marker associated with platelet function and activity. Increased MPV in thromboembolic disease is reflected as an important risk factor. The aim of this study was to compare the MPV and mean platelet volume/platelet count (MPV/PC) ratio between ischemic cerebrovascular stroke and control subjects and furthermore, to find out their diagnostic value in an acute setting to help risk stratification in patients with ischemic stroke. *Methods:* The cross-sectional study was conducted in Kuwait city Medical Hospitals, the state of Kuwait from April 2015 to October 2015. It comprised 50 consecutive patients with acute ischemic stroke, and 20 healthy volunteers. Blood samples were taken to measure MPV and MPV/PC ratio. The Severity of ischemic stroke was assessed by the Modified Rankin scale. *Result:* The ischemic stroke patients had significantly higher MPV and MPV/PC ratio compared to the control group ($p = 0.001$ and $p = 0.017$) respectively. The MPV value was higher and more significant ($p = 0.011$) in patients group with high Rankin scale ($\geqslant 3$) in comparison with those with lower scores. Receiver operator characteristic analysis revealed that an MPV cutoff value of > 8.1 femtoliters provided 68.0% sensitivity and 80.0% specificity. An MPV/PC cutoff value of > 0.031 fl$10^{-4}\,\mu L^{-1}$ showed 70% sensitivity and 75% specificity. The area under the ROC curve for MPV and MPV/PC ratio was 0.789 and 0.701 respectively, which indicates the high discriminative value of MPV and MPV/PC ratio for predicting severe ischemic stroke based on Rankin score $\geqslant 3$ from a mild stroke. *Conclusion:* MPV and MPV/PC ratio could be considered meaningful laboratory markers for the risk of acute ischemic stroke.

1. Introduction

The mean platelet volume (MPV) is one of the most commonly used laboratory markers related platelet functions.[1,2] Because of their greater content in granules, large platelets are more reactive than ordinary size platelets,[3,4] produce more pro-thrombotic factors, and show greater aggregation to adenosine diphosphate (ADP), collagen or adrenaline and secrete more thromboxane A2 (TxA2).[5,6] Increased platelet size has been described in patients with vascular risk factors such as diabetes,[7] Hypercholesterolemia,[8] metabolic syndrome[9] and in patients with renal artery stenosis.[10] Higher mean platelet volume (MPV) values have been established in patients with stroke[6,11] and acute myocardial infarction[12,13] than in control subjects. Furthermore, MPV has been shown to be predictive of stroke, in patients with previous cerebrovascular events, even 3.9 years before the original event.[14] Additionally, a high ratio of MPV to platelet count (MPV/P) is considered a risk factor for various diseases and is associated with myocardial infarction, anemia, and hepatocellular carcinoma.[15,16] The connections between MPV with cerebrovascular accidents and their prognosis have already been questioned. Particular studies detected an increased MPV in different subtypes of brain stroke, both in the acute phase and long after disease.[17] Also, stroke patients with high mortality have been found to have a low platelet count.[11] These results lead to the hypothesis that the increase of MPV might have a critical role in the genesis or deterioration of brain stroke.

However, until now no studies have sufficiently assessed the role of MPV and MPV/PC ratio during acute ischemic events. The aim of this study was to compare the MPV and MPV/PC ratio between ischemic cerebrovascular stroke and control subjects and also to find out their diagnostic value in an acute setting to help risk stratification in patients with ischemic stroke.

2. Methods

2.1. Patients

The cross-sectional study conducted in the emergency department of Kuwait city Medical Hospitals in the state of Kuwait from April 2015 to October 2015 and comprised 50 patients with first acute ischemic stroke. The control group consisted of 20 age and sex matched healthy volunteers with no clinical evidence of any active vascular disease, previous cerebrovascular disease, malignancy or infarction and not taking medications known to affect platelet function. All data were collected, including demographics, medical history, especially previous history of ischemic heart disease or cerebrovascular accidents, biochemical parameters, medications, echocardiographic data, and neuroimaging studies. Exclusion criteria are for patients who had peripheral vascular disease, prior stroke, acute infection, positive C-reactive protein or inflammatory conditions, pregnancy, acute myocardial infarction, malignancies, cranial traumas, intracranial hemorrhage, hematomas, or with transient symptoms of cerebrovascular diseases. The diagnosis of ischemic stroke was made clinically with the evidence of acute infarction confirmed by brain CT or MRI within the first 24 h of presentation to the emergency department. Severity of ischemic stroke was judged by Modified Rankin scale that scores in patients on a scale of 0–6, with 0 being

asymptomatic and 6 being dead. Scores of 0–2 are considered "good" stroke consequences; in that these patients are able to lead fairly independent lives and are able to return to work in almost all cases. Scores of 3 or greater indicate that the patient will need considerable help with their daily activities.

2.2. Platelet measurements

Blood samples were drawn from a forearm vein, collected into tubes containing ethylenediaminetetraacetic acid (EDTA) and stored at room temperature until measurement, which was performed in all cases within 2 h after venipuncture. Platelet measurements were analyzed by flow cytometry in automated hematology analysis system (CELL-DYN Sapphire) that provided platelet count and MPV (in FL).

2.3. Statistical analysis

Statistical analysis was performed using SPSS 16.0 and Medcalc statistical software. Results were expressed as mean and Standard deviation. The comparison of groups with the different Rankin score, and also a comparison of the MPV and MPV/PC ratio among ischemic stroke patients and the control were done as follows: normally distributed continuous variables compared with 2-independent samples t-test, Mann Whitney test was used for non-normally distributed continuous variables and chi-Square test was used to compare qualitative data. Statistical significance was made at $p < 0.05$. There were no data about exact cutoff values for MPV or MPV/PC ratio in ischemic cerebrovascular diseases. Therefore, Receiver Operating Characteristic (ROC) curve analysis was done for the determination of sensitivity and specificity of the cutoff values of all patients. The area under the Receiver Operating Characteristic (ROC) curve was used to estimate the performance of MPV and MPV/pc ratio for discriminating severe ischemic stroke from a mild event.

3. Results

Our study selected 50 patients presented with cerebrovascular stroke besides 20 control subjects. Demographic characteristics and baseline factors of participants are shown in Table 1. The group of stroke patients composed of 23 females and 27 males, while the healthy controls comprised 12 females and 8 males ($p > 0.05$). The mean ages of the stroke patients were 61.4 ± 13.5 y and of the controls 53.6 ± 10.5 y ($p = 0.024$).

A statistically significant difference ($p = 0.001$) was observed between the MPV values of stroke patients

Table 1 Baseline characteristics of study population.

	Cases (n = 50)	Control (n = 20)	p value
Age (years ±SD)	61.4 ± 13.5 y	53.6 ± 10.5 y	0.024
Sex: Male/female	27/23	8/12	0.290
PC, 10⁴/μL	2.66 ± 82.96	2.66 ± 61.28	0.482
MPV, FL	8.99 ± 1.54	7.67 ± 0.89	0.001
MPV/PC ratio, fl10⁻⁴ μL⁻¹	0.036 ± 0.010	0.030 ± 0.007	0.017

PC: platelet count; MPV: mean platelet volume.