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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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KEYWORDS

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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 fl10^{-4} μL^{-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.

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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 prothrombotic 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, $10^4/\mu L$	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, $fl10^{-4}\ \mu L^{-1}$	0.036 ± 0.010	0.030 ± 0.007	0.017

PC: platelet count; MPV: mean platelet volume.

(8.99 ± 1.54 FL) and the MPV values of the control group (7.67 ± 0.89 FL). Also, there was a significant difference ($p = 0.017$) between MPV/PC ratio between stroke patients and control. Among 50 stroke patients[16] were categorized as a poor stroke outcome (Rankin scores ⩾3) and others had the lowest score. There was no significant difference according to age, gender distribution and MPV/PC ratio ($p > 0.05$). But, those with higher Rankin scale had a significantly more occurrence of previous ischemic heart disease ($p < 0.001$). In terms of MPV levels and platelet count, there was a significant difference in comparison between groups with Rankin score ⩾3 and those with lower scores ($p = 0.011$ and $p = 0.022$) respectively (Table 2). For all patients ROC curve analysis, the area under the curve for MPV was 0.789 (95% confidence interval [CI], 0.675–0.877) ($p < 0.0001$) indicating the high discriminative value of MPV for predicting severe ischemic stroke based on Rankin score ⩾3 from a mild stroke event. When MPV level was taken as >8.1 femtoliter, a sensitivity of 68.0% and a specificity of 80.0% were found (Fig. 1). In concern of MPV/PC ratio, the area under the curve was 0.701 (95% confidence interval [CI], 0.579 to 0.804) ($p < 0.0025$). When MPV/PC ratio level was taken as >0.031 $fl10^{-4}\ \mu L^{-1}$, a sensitivity of 70.0% and a specificity of 75.0% were found (Fig. 2).

4. Discussion

MPV has been identified to be of clinical importance in thromboembolic diseases. Increment in the mean platelet volume (MPV) level has been observed in patients with stroke[18] and acute myocardial infarction[13] than in control subjects. In our study, we found that MPV and MPV/PC ratio was significantly higher in patients presenting with cerebrovascular stroke compared to a control group. Similarly, O'Malley et al.[5] found greater MPV values in patients with acute ischemic stroke than in controls. Conversely, Cho et al. did not find any significant difference between patients and controls in relation to MPV values,[19] but most of the studies proved that MPV levels were higher in stroke patients.[20,21] The current study evaluated the role of MPV for expecting severe and extensive acute ischemic brain stroke from its mild status, and it showed that measuring MPV within the first 24 h of brain stroke occurrence was strongly associated with the severity of disease, and could effectively distinguish a severe condition from a milder degree of the disorder. Also, we revealed that MPV increases early in the strokes characterized by more neurological impairment in comparison with those with less compromised categories according to modified Rankin score. This may indicate more release of reactive platelets in the circulation in reaction to mediators coming from the peripheral ischemic sites. Actually, the fact that MPV may be raised before the acute event has clearly been demonstrated by the PROGRESS study[14] which stated an 11% rise of the relative risk of stroke for every femtoliter of MPV increment in 3134 individuals with prior cerebrovascular disease, prospectively followed for a median period of 3.9 years. Thus, subjects with large platelets have an increased risk of ischemic stroke. Butterworth et al.[6] reported that there was a lower platelet count in the stroke group, whereas some studies showed that patients with acute ischemic stroke had higher

Table 2 Baseline characteristics and clinical data according to the severity of CVA.

Characteristics	CVA score 0–2 ($n = 34$)	CVA scores >3 ($n = 16$)	p-value
Age (years ±SD)	59.8 ± 13.3	64.8 ± 13.9	0.228
Sex			
Male	17(50)%	10(62.5%)	0.407
Female	17(50)%	6(37.5%)	
History of IHD, n (%)	3(8.8%)	4(25%)	<0.001
PC, $10^4/\mu L$	2.55 ± 81.71	2.91 ± 82.84	0.022
MPV, FL	8.62 ± 1.39	9.78 ± 1.57	0.011
MPV/PC ratio, FL $10^{-4}\ \mu L^{-1}$	.036 ± .010	.036 ± .011	0.984

CVA: cerebrovascular accident; IHD: ischemic heart disease; PC: platelet count; MPV: mean platelet volume.

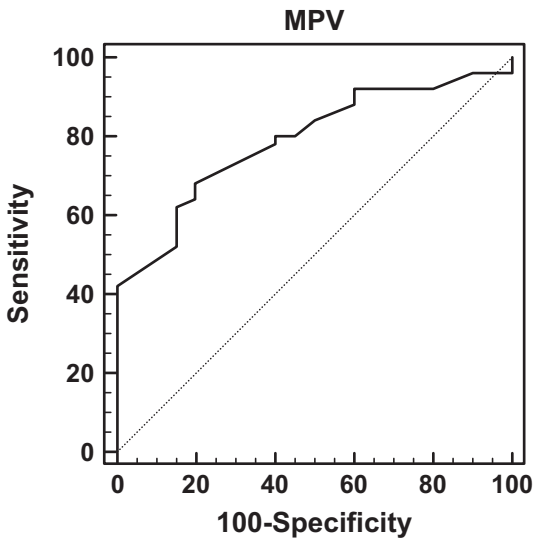

Figure 1 Specificity and sensitivity of mean platelet volume in predicting ischemic stroke severity. Area under the curve: 0.789, standard error: 0.0545.

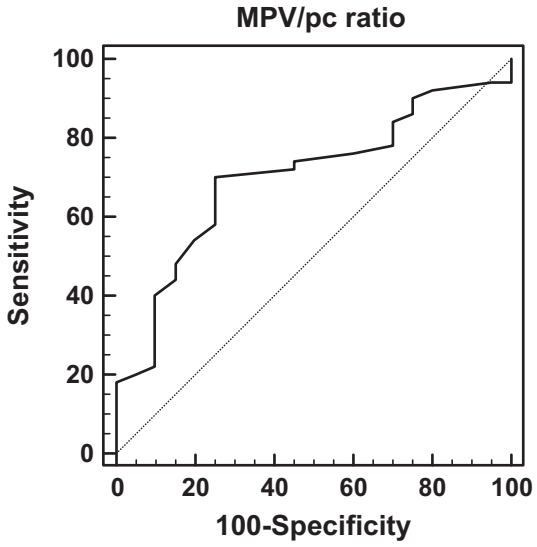

Figure 2 Specificity and sensitivity of mean platelet volume in predicting ischemic stroke severity. Area under the curve: 0.701, standard error: 0.0664.

platelet counts than the control groups which came in compatible with our result.[11,22] Cho et al.[19] showed that MPV levels were higher in female patients than in male. In contrast, We did not find significant difference in MPV or MPV/PC ratio according to gender. Hypertension, DM, coronary heart disease, smoking and hyperlipidemia have an impact on MPV.[13] But in some studies, no influence of vascular risk factors on MPV was found.[23,24] In our study, there was no clear association of MPV with IHD; this came in accordance with study done by Fu¨ sun et al.[17] who did not report an association of MPV with coronary events. Our ROC analysis verified that MPV (cutoff value of >8.1 FL) and MPV/PC ratio (cutoff value of >0.031 FL 10^{-4} μL^{-1})) could be used as surrogate laboratory markers for detecting cerebrovascular stroke with 68% and 70% sensitivity and 80% and 75% specificity, respectively. In comparison Nurettin et al.[25] reported that an MPV cutoff value of 9.95 femtoliter had 46.2% sensitivity and 80.0% specificity.

5. Conclusion

Increased MPV and MPV/PC ratio is related to cerebrovascular stroke. Also the MPV and MPV/PC ratio tests considered a simple, cost-effective and meaningful laboratory markers test for early detection and risk stratification of cerebrovascular stroke.

6. Recommendation

According to our results, we recommended further studies to investigate the role of MPV and MPV/PC ratio as a prognostic factor in the severity of ischemic stroke and its outcome.

7. Limitation of the study

Our study had some limitations: We measured MPV only in the Emergency Department (ED) and did not perform further serial measurements during the following days. Serial measurements might be useful in studying the prognosis of the patients.

Conflict of interest

The authors declared that there is no conflict of interest.

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