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ORIGINAL ARTICLE

The Value of Mean Platelet Volume for Prognosis of Patients with Acute Cerebral Infarction

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SUMMARY

Background: **The purpose of this study was to investigate the value of mean platelet volume (MPV) for prognosis of patients with acute cerebral infarction (ACI).**
Methods: **One hundred ACI patients and 80 healthy volunteers acting as healthy controls (HCs) were consecutively included in this study. Their baseline clinical and laboratory characteristics were extracted from an electronic-case system. ACI patients were followed for 90 days to collect the main study endpoints including poor prognosis, death due to cardiovascular causes, and the recurrence of stroke. ACI patients were evaluated after 7 days in the hospital using the National Institute of Health Stroke Scale (NIHSS) score to evaluate stroke severity on admission and using the modified Rankin Scale (mRS) to evaluate functional disorders. Receiver operating characteristic (ROC) curve analysis was used to estimate the predictive value of MPV on ACI. Kaplan-Meier survival analysis and Cox regression models were used to analyse the value of MPV as a predictor of ACI.**
Results: **This study suggested that MPV and rate of hypertension were higher in ACI patients than in the HC group. In the follow-up period, 32 ACI patients suffered study endpoints; they had higher average MPV, NIHSS scores, longer ACI onset times, and shorter event-free survival time compared to control patients. ROC curves showed that MPV was an index for prognosis of ACI patients with an AUC of MPV of 0.82 (95% confidence interval (CI): 0.74 - 0.90), and the best cutoff was 10.05 fL. MPV, NHISS scores, age, and TG were independent risk factors for endpoints of ACI patients. MPV with hazard ratio (HR) was 1.94 (95% CI, 1.37 - 2.72, p = 0.000), NIHSS score with HR was 1.22 (95% CI, 1.03 - 1.44, p = 0.021), age with HR was 1.06 (95% CI, 1.00 - 1.11, p = 0.038), and TG HR was 0.60 (95% CI, 0.36 - 1.00, p = 0.048) using Cox regression models. P < 0.05 for all groups was considered statistically significant.**
Conclusions: **Mean platelet volume was an independent risk factor and serves as a sensitive index for the prognosis of ACI patients.**
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KEY WORDS

mean platelet volume, acute cerebral infarction, prognosis, National Institute of Health Stroke Scale, modified Rankin Scale

INTRODUCTION

Acute cerebral infarctions (ACI) cause a significant proportion of the total number of deaths and disabilities in the elderly population worldwide [1]. Recent studies have suggested that platelets may play an important role in the pathophysiology of acute stroke, such as acute

myocardial infarction, ACI, and so on [1,2]. In recent years, platelet activity was disputed in the pathological process of ACI. Researchers note that platelets have a significantly higher reactivity in ACI patients, and drugs such as aspirin play an important role in preventing stroke recurrence by suppressing platelets, while other reports suggest lower platelet reactivity or no reactivity alterations in ACI [1,3-5]. Techniques to analyse platelet activity are costly and time-consuming [6]. In contrast to these specialized techniques, mean platelet volume (MPV) is a cheap, fast, and available index and could indicate the degree of platelet activation; higher MPV after acute ischaemic events such as in cerebrovascular and cardiovascular system is associated with worse outcomes [7,8]. However, the relationship between MPV and the pathology and prognosis of ACI remains unknown. Thus, the principle aim in this study was to investigate whether higher MPV has a correlation with ACI by analysing 100 ACI patients.

MATERIALS AND METHODS

Study population

A total of 100 ACI patients who were admitted to the Department of Emergency and Neurology of Wuxi Second People's Hospital less than 24 hours after the onset of stroke symptoms from January 2015 to February 2016 were recruited consecutively in this study as the ACI group (age, range from 41 to 85 years, mean ± SD 63.63 ± 7.52 years). Concurrently, 80 healthy individuals without any history of cerebrovascular diseases, who received a hospital physical examination, were recruited as the healthy control (HC) group (age, range from 38 to 79 years, mean ± SD 62.72 ± 8.08 years). All ACI subjects were confirmed by brain MRI within 24 hours after onset of symptoms using a 3.0-Tesla MR scanner (Siemens, Erlangen, Germany), and ACI patients received clinical follow-ups for 90 days post-ACI. The exclusion criteria were 1) patients requested discharge or transfer during treatment due to personal reasons; 2) patients did not receive blood cell and lipid analysis; 3) patients with malignancies; 4) patients with end-stage renal or liver disease. All clinical subjects are shown in Table 1.

The Ethics Committee of Wuxi Second People's Hospital approved the research protocol and all subjects signed an informed consent form before the initiation of this study.

Clinical characteristics and clinical assessment

The data extracted from medical records included laboratory characteristics at diagnosis (platelet count, mean platelet volume, blood lipids), clinical characteristics (age, gender, smoking, time of stroke symptoms occurring, and chronic disease history such as hypertension, diabetes, hyperlipidaemia, and atrial fibrillation). Hematology was analysed using a Sysmex XE-2100. Blood lipids such as high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and total triglycerides (TG) were analysed using an Olympus 5421.

National Institute of Health Stroke Scale (NIHSS) score (range from 0 (normal) to 42 (death)) served as an index for evaluating stroke severity at 7 days, and the modified Rankin Scale (mRS) (range from 0 (normal) to 6 (death)) was used for evaluation of the prognosis of patients 90 days after onset of ACI. These scores determined which patients were divided into the good prognosis (mRS ≤ 2) and poor prognosis (mRS > 2) [9-11] groups.

Endpoints

Recurrence of ischaemic stroke, death, and poor prognosis from cardiovascular causes in the 90 days after ACI were defined as endpoints in this study. Stroke recurrence was an additional neurological deficit and corresponding positive lesions on diffusion-weighted imaging. All patients with the main study endpoints underwent brain MRI scans to exclude intracranial hemorrhage. A patient mRS score > 2 was deemed poor prognosis [10,12,13]. The event-free survival time, which was defined as the time from discharge to the occurrence of the endpoints, was recorded.

Statistical analysis

Quantitative data were expressed as the mean ± standard deviation (SD) or median and interquartile range (IQR), while qualitative data were presented as absolute values and percentages. For normally distributed data, independent sample *t*-tests were performed to determine the difference between two groups, and independent sample chi-square tests was used for comparison between percentages and constituent ratios of qualitative data. For multiple group comparisons, we used the Kruskal-Wallis H test and/or one-way analysis of variance (ANOVA). Receiver operating characteristic (ROC) curve analysis was applied to estimate whether MPV is predictive of the prognosis of ACI, and a COX regression model was used to determine whether MPV was an independent risk factor of in-hospital death. ACI patients were divided into a higher MPV group or a lower MPV group according to the median MPV. Kaplan-Meier survival analysis was used to find the association between levels of MPV and event-free survival time in ACI patients. Statistical analysis was performed using SPSS 17.0 (IBM Corporation, Armonk, NY, USA), and differences were considered statistically significant at a p-value of less than 0.05.

RESULTS

Clinical characteristics

As shown in Table 1, the clinical characteristics such as age, gender, the rate of diabetes, the level of blood lipids, etc. were not significantly different in the two groups, while the level of MPV and proportions of hy-

Table 1. Clinical and laboratory characteristics of all subjects.

Baseline characteristics	ACI group (n = 100)	HC group (n = 80)	p-value
Age (years)	63.39 ± 8.20	62.28 ± 9.96	0.411
Male (n/%)	62/62	44/55	0.343
Hypertension (n/%)	64/64	36/45	0.011
Diabetes (n/%)	26/26	24/30	0.552
History of smoking (n/%)	30/30	31/39	0.218
Time of ACI onset (hours)	8.08 ± 3.60	-	-
HDL-C (mmol/L)	1.10 ± 0.47	1.11 ± 0.31	0.816
LDL-C (mmol/L)	2.39 ± 1.07	2.46 ± 0.93	0.670
TG (mmol/L)	2.87 ± 1.04	3.11 ± 0.77	0.090
TC (mmol/L)	1.62 ± 0.71	1.74 ± 0.60	0.211
MPV (fL)	11.30 ± 1.69	10.62 ± 1.15	0.002
Platelet count (x 10^9/L)	188.24 ± 69.15	191.05 ± 71.70	0.790

HDL-C - high-density lipoprotein cholesterol, LDL-C - low-density lipoprotein cholesterol, TG - total triglycerides, TC - total cholesterol, MPV - mean platelet volume.

Table 2. Relationship between clinical characteristics and endpoints.

Baseline Characteristics	Endpoint group	Non-endpoint group	p-value
n	32	64	-
Age (years)	63.63 ± 7.52	62.72 ± 8.08	0.598
Male (n/%)	21/66	38/59	0.553
Hypertension (n/%)	19/59	42/66	0.549
Diabetes (n/%)	11/34	13/20	0.134
History of smoking (n/%)	10/31	17/27	0.630
The time onset of ACI (hours)	9.19 ± 4.19	7.30 ± 2.73	0.009
HDL-C (mmol/L)	1.13 ± 0.48	1.06 ± 0.43	0.470
LDL-C (mmol/L)	2.39 ± 1.00	2.37 ± 1.14	0.933
TG (mmol/L)	2.68 ± 0.91	2.97 ± 1.10	0.208
TC (mmol/L)	1.68 ± 0.66	1.57 ± 0.72	0.442
MPV (fL)	12.12 ± 1.32	10.42 ± 1.44	0.000
Platelet count (x 10^9/L)	202.69 ± 69.93	180.03 ± 66.27	0.124
NIHSS scores	9.53 ± 3.33	8.20 ± 1.95	0.016
Event-free survival time (days)	90 (IQR: 70.5, 90)	90 (IQR:90, 90)	0.028

HDL-C - high-density lipoprotein cholesterol, LDL-C - low-density lipoprotein cholesterol, TG - total triglycerides, TC - total cholesterol, MPV - mean platelet volume, NIHSS - National Institute of Health Stroke Scale, IQR - interquartile range.

pertension were higher in ACI patients than healthy controls ($p < 0.05$).

Clinical characteristics in patients with endpoints

Out of 100 ACI patients, 4 patients died because of the serious condition, and 96 patients were discharged from hospital and followed-up after 90 days. A total of 32 patients suffered endpoints: 2 died; 4 patients had recurrence of ischaemic stroke and others had poor outcomes in the follow-up period as part of the endpoint group; 74 patients were classified as the non-endpoint group which did not endpoint. MPV was significantly higher

Table 3. Cox regression models for endpoint in ACI patients.

	HR	95% CI	p-value
MPV (fL)	1.94	1.37 - 2.72	0.000
NIHSS score	1.22	1.03 - 1.44	0.021
Age (years)	1.06	1.00 - 1.11	0.038
Men	0.88	0.37 - 2.10	0.766
Hypertension	1.45	0.68 - 3.09	0.333
Diabetes	1.07	0.44 - 2.59	0.883
History of smoking	1.78	0.71 - 4.52	0.219
Onset time of ACI (hours)	0.96	0.84 - 1.08	0.461
HDL-C (mmol/L)	0.49	0.19 - 1.25	0.135
LDL-C (mmol/L)	0.99	0.67 - 1.47	0.967
TC (mmol/L)	0.98	0.51 - 1.89	0.952
TG (mmol/L)	0.60	0.36 - 1.00	0.048
Platelet count (x 10^9/L)	1.00	1.00 - 1.01	0.791

HDL-C - high-density lipoprotein cholesterol, LDL-C - low-density lipoprotein cholesterol, TG - total triglycerides, TC - total cholesterol, MPV - mean platelet volume, HR - hazard ratio, CI - confidence interval.

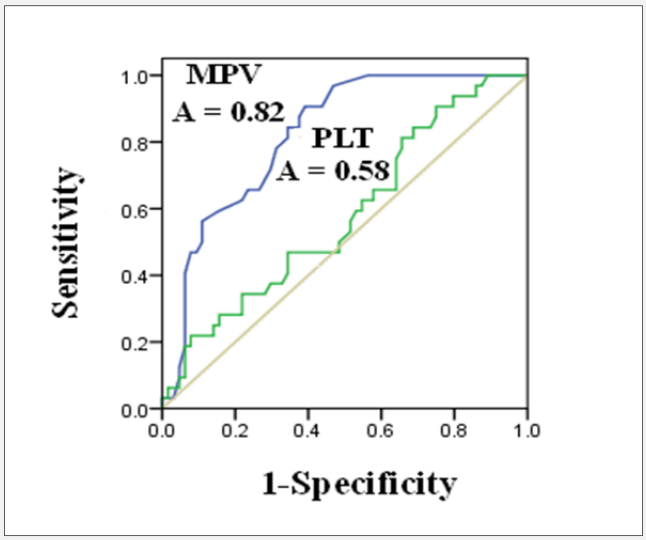

Figure 1. The value of MPV and platelet count in predicting prognosis for endpoints (A: AUC; PLT: platelet counts).

in the endpoint sub-group patients than those without endpoints. Meanwhile, the time onset of ACI and NIHSS score had a positive correlation with the proportion of endpoints. Event-free survival time was longer in non-endpoint patients than in endpoint patients. The results of these analyses are shown in Table 2.

Value of MPV in predicting in prognosis of ACI

ROC curves were used to predict the value of MPV and platelet counts in prognosis for endpoints. The area under the curve (AUC) for MPV was 0.82 (95% confidence interval (CI): 0.74 - 0.90, $p < 0.05$) and the best cutoff was 10.05 fL, and the AUC for platelets count was 0.58 (95% CI: 0.46 - 0.70).

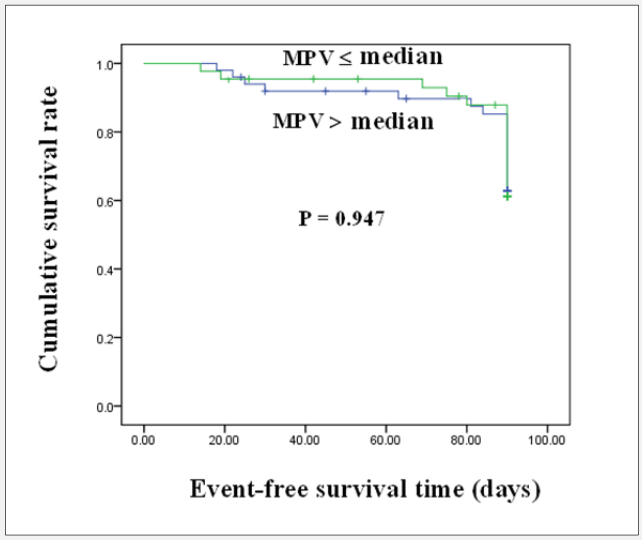

Figure 2. Kaplan-Meier survival analysis for time to endpoints in ACI patients according to the median of MPV (P = 0.947).

Relationship between risk factors and endpoint

ACI patients were divided into higher MPV group and lower MPV group according to the median MPV (MPV = 10.9 fL). We failed to find an association between MPV level and event-free survival time in ACI patients (p = 0.947) by using Kaplan-Meier survival analysis, as shown in Figure 2. In Table 3, we found that MPV, NHISS score, age, and TG were independent risk factors for the endpoint of ACI patients. MPV with hazard ratio (HR) was 1.94 (95% CI, 1.37 - 2.72, p = 0.000), NIHSS score with HR was 1.22 (95% CI, 1.03 - 1.44, p = 0.021), age with HR was 1.06 (95% CI, 1.00 - 1.11, p = 0.038), and TG HR was 0.60 (95% CI, 0.36 - 1.00, p = 0.048) using Cox regression models.

DISCUSSION

Mean platelet volume (MPV) is a marker that reflects platelet activity and plays an important role in atherothrombosis, such as cerebrovascular diseases and cardiovascular diseases. Liu et al. explored the relationship between MPV and acute myocardial infarction and showed a positive correlation between MPV and in-hospital mortality [14,15]. However, few studies have investigated whether MPV affects ACI. A total of 180 participants were enrolled in this study, including 100 ACI patients and 80 healthy volunteers. We investigated the relationship between MPV and prognosis of ACI. The results of this study are listed in the following paragraph.

The most significant findings in this study were: 1) compared with the HC group, ACI patients had higher MPV and rates of hypertension; 2) patients with endpoints had a higher level of MPV, NIHSS scores, longer ACI onset times, and shorter event-free survival times compared to patients without endpoints; 3) MPV was an index and independent risk factor for the prognosis of ACI patients; the AUC of MPV was 0.82 (95% CI: 0.74 - 0.90) and the best cutoff was 10.05 fL. MPV with HR was 1.87 (95% CI, 1.36 - 2.58), as shown by receiver ROC curves and Cox regression, 4) No relationship between MPV and event-free survival time of endpoints by Kaplan-Meier survival analysis was observed.

To our knowledge, few studies have investigated the predictive value of MPV for endpoints in ACI patients whose onset times of ACI are less than 24 hours. We found that MPV was associated with death, recurrence of stroke, and poor prognosis after ACI, higher MPV up-regulated the rate of endpoints, and a negative relationship between MPV and outcomes of ACI patients was revealed. Recent studies show that increased MPV is an independent predictor of poor outcomes in patients with acute anterior circulation stroke undergoing mechanical thrombectomy and a predictor of up-regulation risk of cardioembolic stroke in patent foramen ovale patients [16,17]. Additionally, a study based on 388 large artery atherosclerosis (LAA) stroke patients showed that MPV was a good predictor for outcome in LAA stroke [18]. We speculate that the larger MPV results in faster thrombosis formation at the rupture site, and the larger thrombus volume results in poorer ACI prognosis. De Luca et al. stated that MPV altered by medications such as clopidogrel and acetylsalicylic acid improves progno-

sis in patients with acute coronary syndrome [19]. For ACI patients with high MPV, more aggressive treatment may be needed to improve the outcome of ACI. The rate of hypertension is higher in the ACI group than in the HC group in this study, possibly due to the relationship between hypertensive subclinical organ damage and stroke, as observed in a previous study [20]. To decrease the risk of acute stroke and hypertensive subclinical organ damage in patients with hypertension, blood pressure levels need to be reduced. These measures are also conducive to the prognosis of acute cerebral infarction. In Table 2, we show that the time of ACI onset and NIHSS scores were higher in patients with endpoints than those without, and NIHSS score was a risk index for ACI. The shorter the time to begin successful therapy, the better the prognosis for ACI. Higher initial NIHSS scores are suggested to be related to larger ischaemic brain volumes, so NIHSS score has a negative correlation with prognosis of ACI. Thus, we found that NIHSS score was a risk factor for endpoints in ACI patients, which was similar to previous studies [11,21]. In addition, age and level of TG also serve as risk factors for endpoints. Other studies confirm that higher blood lipids are associated with recurrent stroke risk, and greater age is an independent predictor of long-term mortality after stroke [22,23].

Some limitations in this study must be noted. The major limitation is that this is a single centre study with a small sample size, thus patient selection bias could not be completely avoided. Second, ACI patients in this study were followed for only 90 days, which was too short. The third point is that our analysis used only NIHSS scores on day 7 after admission as an indicator, rather than describe related information such as location of cerebral infarction and stroke size. It was not indicated that these factors are correlated with MPV. Finally, we ignored MPV changes several days after discharge, despite finding some studies that showed that platelet aggregation was increased several days after the stroke but was constant during the acute period [24]. Further studies with a larger number of enrolled patients are needed to rigorously evaluate the predictive value of MPV for prognosis of ACI.

CONCLUSION

This study suggested that MPV is significantly higher in ACI patients than in healthy subjects. MPV of ACI patients on admission is a good marker in prediction of endpoints, and MPV severity is an independent risk factor for prognosis in ACI patients.

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Declaration of Interest:
The authors declare no conflict of interest.

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