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ORIGINAL

STUDY ON THE PREDICTIVE VALUE OF MHR COMBINED WITH THROMBOELASTOGRAPHY PARAMETERS FOR ACUTE CEREBRAL INFARCTION IN ATHLETE PLAYERS

Yi Jiang[1,2,a], Chaoping Wang[1,2,b], Jiali Shen[1,2,c,*]

[1]Department of Clinical Laboratory, Wujin Hospital Affiliated with Jiangsu University, Changzhou 213000, Jiangsu, China
[2]Department of Clinical Laboratory, the Wujin Clinical College of Xuzhou Medical University, Changzhou 213000, Jiangsu, China
[a]Email: jiangyi@njmu.edu.cn
[b]gauidaocp@sina.com
[*]Corresponding author
[c]Email: shenjiali8687@126.com

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ABSTRACT

Aims: To investigate the predictive value of peripheral blood monocyte count and high density lipoprotein cholesterol (HDL-C) ratio (monocyte/HDL-C, MHR) combined with thromboelastography (TEG) related parameters in acute Cerebral infarction (ACI). **Methods:**The study group included 201 patients with ACI, and the comparison group included 201 patients with non-ACI. Using dispersion analysis, changes in MHR and TEG were compared between the two groups. Using logistic regression analysis, valuable measures of model building were screened. Using receiver operating characteristic (ROC) curves, the predictive effect of a combination of single and multiple indices on ACI was evaluated. Based on NIHSS scores, the research team was also divided into a mild nerve injury group (152 cases) and a moderate to severe nerve injury group (49 cases). Compare the changes in the two groups of indicators. Correlations between NIHSS scores and each index were analyzed by pearson correlation. **Reasults:**Lymphocyte count, monocyte count, MHR, angle, MA, G and A30 were higher in the study group than in the control group. HDL-C, NLR, R and K values were lower in the study group than in the control group, and the differences were statistically significant (P<0.05). Among the indicators, MHR had the highest diagnostic concordance rate and area under the curve (AUC) (0.806 and 0.883, respectively), the highest sensitivity (0.891) for the count of

monocyte , and the highest R-value specificity (0.776). Logistic regression analysis showed that MHR>0.367, monocyte count >0.38×10^9/L, A30>63.1mm and R value<5.0min were independent risk factors for ACI. The 4-factor regression equation has been established: logit(P)=-2.19+1.541* monocyte count -1.731*R+1.466*A30+2.040*MHR. Using this model to predict ACI, the cut-off value was 0.409, the sensitivity was 84.1%, the specificity was 86.1%, the AUC was 0.912, and the diagnostic concordance rate was 85.1%. Specificity, diagnostic concordance, and AUC were higher than single index assays. The moderate-to-severe neurological deficit group had higher counts of neutrophil count, monocyte count, MHR, NLR, Angle, MA, G, and A30 than the mild neurological deficit group. Lymphocyte counts and HDL-C were lower in moderate-to-severe nerve injury groups than in mild nerve injury groups, and the difference was statistically significant (P<0.05). The NIHSS score was positively correlated with the counts of neutrophil count, monocyte count, MHR and NLR (P<0.001). Among them, the NIHSS score had the strongest correlation with MHR (r=0.674, P<0.001). **Conclusions:**MHR>0.367, monocyte count >0.38×10^9/L, A30>63.1mm, R value<5.0min were independent risk factors for ACI. Combining the four factors for detection is more effective in predicting ACI. The elevated MHR can be used as an index for judging the severity of ACI.

KEYWORDS: MHR, Thromboelastogram, Neurological Deficit, ACI

1. INTRODUCTION

Stroke is the second leading cause of death globally.CI, known as ischemic stroke, accounts for approximately 87 percent of all types of stroke and is the leading cause of disability in adults (Evans et al., 2018). Neurological dysfunction is the most common complication in ischemic stroke patients. The clinical prognosis of stroke patients depends on the degree of neurological damage in post-injury patients. An important criterion for evaluating the prognosis of ischemic stroke patients is the restoration of neurological function (Wan et al., 2014) . Neurological function score is an important indicator reflecting the severity of stroke patients. If CI can be detected and treated early, prognosis and quality of life can be improved. Therefore, it is very important to investigate the risk factors of CI and establish a predictive model for ACI.

Studies have shown that some inflammatory factors, including IL-6, TNF-α (Vemuri, Gundamaraju, Shinde, & Eri, 2017), neutrophil-to-lymphocyte ratio (NLR) (Kocaturk, Besli, Gungoren, Kocaturk, & Tanriverdi, 2019), C-reactive protein (Kitagawa et al., 2019), etc., are involved in the pathogenesis of cerebral infarction. plays an important role. MHC is a new inflammatory index formed by combining monocytes with HDL-C, and studies have shown that it is also closely related to ischemic cardiovascular and cerebrovascular diseases. The blood of patients with CI is in a state of hypercoagulation due to thrombosis (FRICKE, 2017). Rombelastography (TEG) can Quickly and comprehensively reflect the onset of coagulation and changes in the entire coagulation process from fibrin formation to thrombolysis. Therefore, TEG plays a guiding role in the diagnosis, differential diagnosis and prognosis prediction of CI· However, in order to investigate Regarding the relationship with CI, there are almost no reports at home and abroad combining these two indicators to explore the relationship between them and cerebral infarction

(Boni & Molloy, 2021; Chiba et al., 1996). Currently, the diagnosis of CI mainly relies on imaging examinations. There are few reports on the predictive value of blood tests in patients with ACI (Zhang et al., 2021).

This study analyzed the relationship between the detection of peripheral blood MHR combined with TEG-related parameters and the occurrence and development of ACI, and preliminarily discussed its efficacy in predicting the occurrence of ACI and its application in evaluating the degree of neurological deficit in patients (M. Li et al., 2022).

2. MATERIALS AND METHODS

2.1. Study Population

A total of 201 patients with newly diagnosed acute cerebral infarction who were admitted to the Department of Neurology in our hospital from January 2019 to December 2020 were selected as the research group, including 118 males and 83 females (Han, Liu, & Gao, 2020), with an average age of 67.54±8.93 years; 201 non-acute cerebral infarction patients served as the control group, including 118 males and 83 females, with an average age of 66.58±8.51 years. Inclusion criteria: The clinical diagnosis of the research group met the diagnostic criteria in the "Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke in China 2018" (Zhong & Bo, 2019), (Petrone et al., 2019) and the diagnosis of acute ischemic stroke was excluded in the control group. Exclusion criteria: Any one of the following can be excluded: (1) Heart, liver, and renal insufficiency; (2) Complicated cerebrovascular accident; (3) Severe respiratory and circulatory system diseases; (4) Malignant tumors; (5)) history of drug abuse and drug intoxication (Ganjali et al., 2018). The families of the patients in the two groups voluntarily signed the informed consent. This study was approved by the Medical Ethics Committee of our hospital (Chik, Or, Luo, Yang, & Lau, 2013).

2.2. Collection of Clinical Data

After admission, the clinical data from all the patients were collected and archived, including general demographic data (gender, age), clinical features, and auxiliary examination results.

2.3. Collection and Test of the Blood Sample

Fasting cubital venous blood was collected on the day or the next day after admission. Blood routine test, blood lipids, and related indicators of thromboelastography were tested. The blood routine test was conducted by using Sysmex XN-9000 hematology analyzer and the accessory reagents. Neutrophil count (N), monocyte count (M), and lymphocyte count (L) were recorded, and neutrophil and lymph Cell ratio (NLR=N/L) was calculated. Blood lipids were detected by using Beckman automatic biochemical analyzer (AU5800/AU5400). The serum HDL-C level was recorded, and the ratio of monocyte count to high-density lipoprotein cholesterol (MHR=M/HDL-C) was calculated. The thromboelastogram test was conducted by using TEG5000 thromboelastometer (Haemoscope, USA) and the corresponding test kits. The

test items were recorded, including reaction time (R value, the time from the initiation of coagulation to the formation of the first fibrin clot, reflecting the effects of all coagulation factors), K value (the time required from the end of the R time to the time when the amplitude of the clot intensity reaches 20mm,reflecting the function of fibrinogen), Angle (the converging rate of blood clot, reflecting the function of fibrinogen), MA value (the maximum amplitude on the thromboelastogram, reflecting the maximum strength of the blood clot and the stability of the blood clot; this value is greatly affected by platelets), G value (the maximum shear stress intensity of the blood clot, reflecting the hardness of the blood clot), A30 (the amplitude on the gram at 30 minutes, reflecting the quality and quantity of the platelets) (Su et al., 2018).

2.4. Evaluation of Neurological Impairment

The study subjects were scored according to the National Institutes of Health Stroke Scale (NIHSS) on admission. Based on the score, the patients were assigned into group of mild neurological deficit (NIHSS score ≤ 5 points) (n=152) and group of moderate-to-severe neurological function deficit (NIHSS score> 5 points) (n=49).

2.5. Statistical Analysis

Univariate regression analysis was used to screen clinical variables related to ACI, followed by multivariate regression analysis to identify independent risk factors for ACI. Using logistic regression analysis, a regression equation for MHR combined with TEG detection was established. Plot the ROC curve of the equation and calculate the area under the curve (AUC). These were compared with tests that used a single indicator to assess diagnostic value. Using pearson correlation analysis, correlations between NIHSS scores and each index were analyzed. P<0.05 was considered statistically significant.

3. RESULTS

3.1. Comparison of Clinical Data between Two Groups of Patients

The laboratory data includes a total of 12 items. The results in Table 1 show that the lymphocyte count, monocyte count, MHR, Angle, MA, G, and A30 in the study group were higher than those in the control group. The high-density lipoprotein cholesterol, NLR, R value and K value in the study group were lower than those in the control group. The difference was statistically significant (P<0.05).

Table 1. Comparison of clinical data between two groups of patients

Items	CI group	Control group	t	P
Neutrophil count (10^9/L)	4.94±2.12	4.71±2.17	1.059	0.290
Lymphocyte count (10^9/L)	1.88±0.71	1.31±0.53	9.904	0.000
Monocyte count (10^9/L)	0.57±0.20	0.36±0.13	12.191	0.000
HDL-C (mmol/L)	0.99±0.20	1.21±0.33	-8.054	0.000
MHR	0.60±0.28	0.31±0.13	13.112	0.000
NLR	3.28±3.85	5.20±6.97	-3.418	0.001
R value (min)	4.73±0.66	5.68±0.92	-11.864	0.000
K (min)	1.39±0.33	1.84±0.63	-9.034	0.000
Angle (deg)	69.41±4.83	63.96±6.78	9.298	0.000
MA (mm)	66.61±4.87	59.76±6.41	12.062	0.000
G (d/sc)	10218.48±2390.62	7691.03±1783.36	12.014	0.000

A30 (mm)	66.37±4.95	59.52±6.61	11.759	0.000

3.2. The Diagnostic Value of Individual Index for ACI

Eleven indicators were screened. There was statistical significance in predicting ACI by using each indicator alone. The ROC curve was drawn to determine the diagnostic value of individual indicator for ACI. As shown in Table 2, the AUC of MHR, monocyte count, R value, MA, G, and A30 was relatively high, which indicated better diagnostic efficiency. The sensitivity of monocyte count and HDL-C was high, but the specificity is low. The specificity of NLR and K value was high, but the sensitivity was low. The specificity and sensitivity of MHR were relatively high.

Table 2. The effectiveness of individual indicator in predicting CI

Items	AUC	0.95CI of AUC	P	cut point (Diagnostic critical value)	Sensitivity (%)	Specificity (%)
Lymphocyte count (10^9/L)	0.752	(0.706,0.793)	0.000	1.51	67.66	69.65
Monocyte count (10^9/L)	0.828	(0.788,0.864)	0.000	0.38	89.05	59.70
HDL-C (mmol/L)	0.714	(0.667,0.758)	0.000	1.24	89.05	45.27
MHR	0.883	(0.848,0.913)	0.000	0.367	88.56	72.64
NLR	0.635	(0.586,0.682)	0.000	2.301	37.81	83.08
Rvalue (min)	0.805	(0.763,0.843)	0.000	5.0	73.63	77.61
K (min)	0.757	(0.712,0.798)	0.000	1.3	55.22	82.09
Angle (deg)	0.756	(0.711,0.797)	0.000	68.6	63.18	77.11
MA (mm)	0.807	(0.765,0.845)	0.000	63.2	75.62	68.66
G (d/sc)	0.804	(0.761,0.841)	0.000	8600	75.12	69.15
A30 (mm)	0.804	(0.762,0.842)	0.000	63.1	75.12	70.15

3.3. Analysis of Independent Risk Factors of ACI

The Logistic single factor regression analysis was conducted by using the above 6 factors with higher diagnostic efficiency: MHR, monocyte count, R value, MA, G, and A30. Re-segmented assignments were made based on the diagnostic cut-off value, and four factors, including monocyte count, MHR, R value, and A30, were screened out by the step-by-step forward method, and were included in the logistic multivariate regression analysis and modeled. The results showed that monocyte count>0.38×10^9/L, MHR>0.367, A30>63.1mm, R value<5.0min, are independent risk factors for ACI. Logistic regression analysis was used to establish the regression equation when the four indicators were used together in detection. The equation was as follows: logit(P)=-2.219+1.541*monocyte count-1.731*R+1.466*A30+2.040*MHR. (Detailed information was shown in Table 3,4).

Table 3. Monocyte count, MHR, R, MA, G, A30 were selected piecewise assignment by diagnostic critical value

Items	cut point (Diagnostic critical value)	Assign the value of 1	Assign the value of 0
Monocyte count (10^9/L)	0.38	>0.38	≤0.38
MHR	0.367	>0.367	≤0.367
R value (min)	5.0	>5.0	≤5.0
G (d/sc)	8600	>8600	≤8600

MA (mm)	63.2	>63.2	≤63.2
A30 (mm)	63.1	>63.1	≤63.1

Table 4. The results of logistic model predicting CI by using the four factors (monocyte count, MHR, R value and A30) (LR forward method)

Items	B	Significance	OR	95% CI of OR	
				Lower limit	Upper limit
Monocyte count	1.541	0.000	4.667	2.241	9.720
MHR	2.040	0.000	7.691	3.928	15.056
R value	-1.731	0.000	0.177	0.098	0.321
A30	1.466	0.000	4.334	2.394	7.844
Constant	-2.219	0.000	0.109	-	-

3.4. The Diagnostic Value of Combined use of Multiple Indicators for ACI

The ROC curve for the equation of combined use of indicators was plotted. The critical value of the predicted probability (P) of this model was 0.409. ACI was predicted to occur when P≥0.409. The AUC of ACI was 0.912 as predicted by this model, and the 0.95 confidence interval of AUC was (0.880, 0.938), which was higher compared with the detection using individual indicators. The sensitivity was 0.841 and the 0.95 confidence interval of the sensitivity was (0.783, 0.888),which was no significant difference between the detection by using individual indicator and combined use of indicators. The specificity was 0.861, and the 0.95 confidence interval for the specificity was (0.805, 0.905), which was significantly better than the detection by using individual indicator. The total coincidence rate of the internal validation using the existing samples by applying this model was 85.1%, and the overall effect was satisfactory. Detailed information was shown in Table 5 and Figure 1.

Table 5. Comparison of the diagnostic efficacy of using individual indicator and combined use of the indicators

Items	Sensitivity (0.95CI)	Specificity (0.95CI)	Coincidence rate (0.95CI)	AUC (0.95CI)
Monocyte	0.891 (0.839,0.930)	0.597 (0.526, 0.665)	0.744 (0.698, 0.768)	0.828 (0.788, 0.864)
MHR	0.886 (0.833 ,0.926)	0.726 (0.659, 0.787)	0.806 (0.764, 0.843)	0.883 (0.848, 0.913)
R value	0.736 (0.670, 0.796)	0.776 (0.712, 0.832)	0.756 (0.711, 0.797)	0.805 (0.763, 0.843)
A30	0.751 (0.686.0.809)	0.702 (0.633, 0.764)	0.726 (0.680, 0.769)	0.804 (0.762 0.842)
G	0.751 (0.686, 0.809)	0.692 (0.623, 0.755)	0.721 (0.675, 0.765)	0.804 (0.761, 0.841)
MA	0.756 (0.691, 0.814)	0.687 (0.618, 0.905)	0.721 (0.675, 0.765)	0.807 (0.765, 0.845)
Combined detection (P)	0.841 (0.783, 0.888)	0.861 (0.805, 0.905)	0.851 (0.812, 0.884)	0.912 (0.880, 0.938)

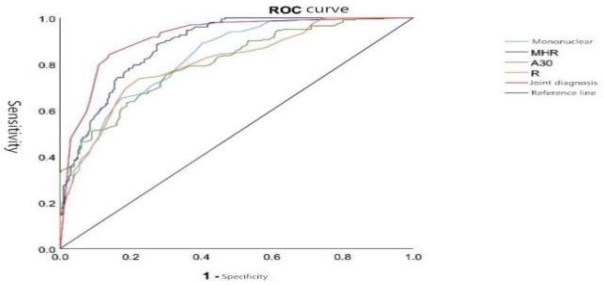

Figure 1. ROC curve of using individual indicator or combined use of the four indicators in detection (monocyte count count, MHR, A30, R value)

3.5. The Relationship between Each Individual Indicator and the NIHSS Score of the Patients with ACI

Table 6. The relationship between each individual index and the NIHSS score of patients with ACI

Items	Mild neurological deficit group (NIHS score≤5 branch)	Moderate to severe neurological deficit group(NIHSS score >5branch)	t	P
Number of cases	152	49		
Neutrophil count (10^9/L)	4.39±1.38	6.63±2.98	-5.086	0.000
Lymphocyte count (10^9/L)	1.96±0.70	1.61±0.69	3.055	0.003
Monocyte count (10^9/L)	0.52±0.14	0.72±0.26	-5.277	0.000
HDL-C (mmol/L)	1.03±0.20	0.86±0.17	5.362	0.000
MHR	0.51±0.16	0.87±0.38	-6.392	0.000
NLR	2.48±1.18	5.76±7.01	-3.258	0.000
Rvalue (min)	4.76±0.65	4.65±0.70	0.998	0.320
K (min)	1.41±0.32	1.32±0.33	1.752	0.081
Angle (deg)	68.93±4.81	70.92±4.62	-2.546	0.012
MA (mm)	65.88±4.37	68.89±5.62	-3.900	0.000
G (d/sc)	9790.42±2100.72	11546.33±2747.71	-4.103	0.000
A30 (mm)	65.59±4.45	68.79±5.62	-4.102	0.000

Statistical analysis was performed using 12 laboratory test indicators of different neurological deficit groups. There was no significant difference in R value and K value between the two groups (P>0.05). Table 6 The results show that the neutrophil count, monocyte count, MHR, NLR, Angle, MA, G, A30 in the moderate to severe neurological deficit group (NIHSS score>5) were higher than those in the mild neurological deficit group (NIHS score ≤ 5). Compared with the mild neurological deficit group, the lymphocyte count and HDL-C were decreased in the moderate to severe neurological deficit group. See Table 6 for details.

3.6. Correlation Analysis between Various Indicators and NIHSS Score of the Patients with ACI

A pearson analysis was performed using 12 clinical examination indicators and NIHSS scores in patients with ACI. The results showed that there was a positive correlation between NIHSS score and the neutrophil count, monocyte count ,MHR and NLR (P<0.001). Among them, the NIHSS score had the strongest correlation with MHR (r=0.674, P<0.001). See Table 7 and Figure 2-5 for details.

Table 7. Correlation analysis between NIHSS score and the indicators

Items	r	P value
Neutrophil count (10^9/L)	0.599	P<0.001
Lymphocyte count (10^9/L)	-0.237	0.001
Monocyte count (10^9/L)	0.601	P<0.001
HDL-C (mmol/L)	-0.279	P<0.001
MHR	0.674	P<0.001
NLR	0.651	P<0.001
Angle (deg)	0.227	0.001
MA (mm)	0.297	P<0.001
G (d/sc)	0.333	P<0.001
A30 (mm)	0.318	P<0.001

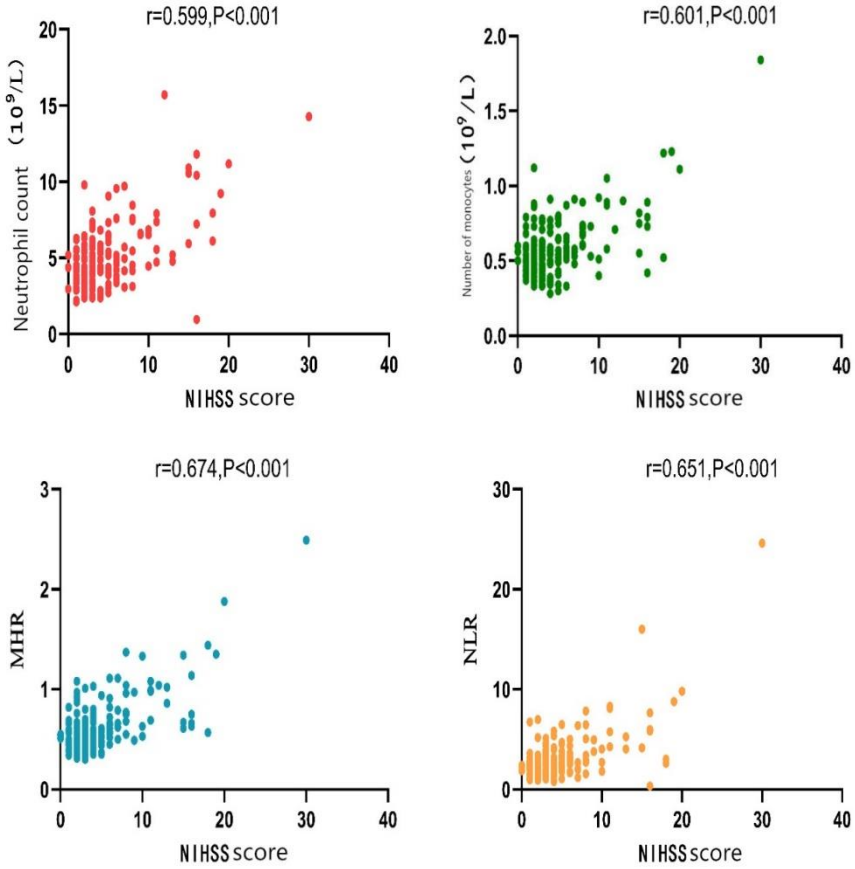

Figure 2. Correlation analysis between NIHSS score and neutrophil count、monocyte count、MHR and NLR

4. DISCUSSION

Vasculopathy is the pathogenesis of ischemic cardiovascular and cerebrovascular diseases. Studies have shown that inflammation plays a pivotal role in the entire pathophysiological process of CI [11]. During ischemic stroke, immune cells including monocytes, neutrophils, and lymphocytes in the peripheral blood can migrate to and accumulate in the injured site [5, 12-14] . Monocytes can be activated and form macrophages which serve an important role [15]. After vascular endothelial cells are injured, platelets can be activated and induce inflammatory reactions. Monocytes can bind with the adhesion molecules expressed on the injured vascular endothelial cells, migrate to the sublayer of vascular endothelium, and convert into macrophages [15]. The

macrophages can differentiate into foam cells which enhance local inflammatory responses, accelerate the formation, growth, and rupture of plaques, induce atherosclerosis, and participate in the pathogenesis of ischemic cardiovascular and cerebrovascular diseases [16]. HDL-C can reversely transport cholesterol and inhibit endothelial cell inflammation, oxidative stress, and anti-thrombosis. Therefore, monocytes and HDL-C have a negative regulatory relationship in regulating atherosclerosis (Wang et al., 2021) (Petrone et al., 2019). Studies have shown that MHR (monocyte/HDL-C ratio), a new inflammatory index combining the two indicators, can dynamically reflect the inflammatory response status in atherosclerotic plaques including the activation of pro-inflammatory factors and the suppression of anti-inflammation factors (Gilbert, Bissell, Santiago, & Rech, 2020). MHR serves an assistive role in assessing the severity and prognosis of coronary heart disease (Guo, Han, Wang, & Liu, 2019). This study showed that monocyte count, lymphocyte count, HDL-C, MHR, and NLR can be used as independent indicators to predict ACI. Various inflammatory factors are involved in the occurrence and development of ACI, and can be used as laboratory indicators for predicting ACI. Among all the inflammatory indicators, MHR has the highest diagnostic efficiency. The cutoff value of MHR in predicting ACI is 0.367, the area under the curve 0.883, the sensitivity 88.56%, and the specificity 72.64%. The specificity of MHR is significantly higher than that of the monocyte count, HDL-C, and the sensitivity is significantly higher than NLR.

In ACI, atherosclerosis and lipid plaque shedding occur, vascular endothelial cells are injured, platelets are activated, blood clotting reaction is initiated, and thrombus is finally formed. The results of this study demonstrated that compared with the control group, the R value and K value were decreased and the Angle, MA, G, and A30 were increased in patients with CI. All these indictors can be used as independent factors in predicting ACI. R value reflects the comprehensive effect of the coagulation factors participating in the coagulation initiation process. K value and Angle reflect the function of fibrinogen. MA, G, and A30 all reflect the quality and quantity of platelets, indicating that the blood is in a hypercoagulable state and fibrinogen and platelet function are enhanced in ACI. In CI, the inner wall of the blood vessel is injured, coagulation factors are activated, platelet aggregates and fibrinogen increases, and thus blood is in a hypercoagulable state (J. Li, Wu, Hao, & Yao, 2019). Atherosclerosis, hypercoagulable state and hemodynamic changes are three important factors contributing to CI (Amtul, 2016). Studies have shown that inflammation and oxidative stress played an important role in thrombogenesis in arteriosclerosis (Vivarelli et al., 2005). The interaction between platelets and neutrophils can also lead to enhanced blood coagulation, trigger the formation of micro-thrombosis and ultimately contribute to CI.

Logistic regression analysis showed that monocyte count>0.38×109/L, MHR>0.367, A30>63.1mm, R value<5.0min were independent risk factors for ACI. In detecting the predictive effects of individual indicator, the diagnostic coincidence rate and area under the curve (AUC) of MHR was the highest (0.806 and 0.883, respectively) among all the indicators, the sensitivity of

monocytes was the highest (0.891), and the specificity of the R value was the highest (0.776). This suggested that it was necessary to integrate the results tested by individual indicator in predicting the occurrence of ACI. The equation model established by combining the four indicators greatly improved the specificity of the detection, the diagnostic coincidence rate and the accuracy without reducing the sensitivity, and the overall effect was satisfactory. This results demonstrated that the regression equation prediction model constructed in this study showed a better predictive efficiency in predicting ACI.

Studies have shown that neutrophil count increases and lymphocyte count decreases in the early phase, which are related with the severity of stroke, size of the infarction area, and worse prognosis. This study showed that neutrophil count, monocyte count, MHR, and NLR were higher in the moderate-to-severe neurological deficit group than those in the mild neurological deficit group. The lymphocyte count was lower in the moderate-to-severe neurological deficit group than that in the mild neurological deficit group. This result supported previous studies. In the ischemic stroke, immune cells are activated to secrete cytokines and chemokines, triggering local and systemic inflammatory responses. The infiltration of peripheral inflammatory cells into the brain parenchyma can induce neuro-inflammatory responses, which further contributes to neuronal dysfunction and cell death. During acute ischemic stroke, large quantities of neutrophils are the first type of cells migrating into the injured brain tissue and aggravate ischemic brain injury via clogging micro-vessels, interacting with platelets, and releasing harmful substances or inflammatory mediators. Research has presented that the possible mechanism of lymphopenia was that lymphocytes exerted protective effect in ischemic brain regions. Certain protective subtypes of lymphocytes, such as $CD4^+CD25^+$ regulatory T cells, can secret anti-inflammatory cytokines and maintain immune homeostasis. $CD4^+CD25^+$ regulatory T cell, a kind of immune-regulatory T cell, plays an antagonistic role against immune injury during atherosclerosis and atherosclerotic CI. Another possible mechanism of lymphopenia is sympathetic tone and the increased serum level of cortisol in the process of stress response, which lead to the apoptosis of lymphocytes in peripheral blood and is related to the generation of pro-inflammatory cytokines . After stroke, the cerebral cortex is extensively damaged, leading to imbalance of controlling the autonomic nervous system, reduced parasympathetic nerve activity, the conversion of autonomic innervation to the sympathetic innervation, the weakening of high-level center inhibition, and abnormal spinal cord afferent stimulation. These changes can result in neurological deficits. Hypercholesterolemia increases the permeability of the blood-brain barrier, triggers apoptosis of neurons and induces changes in the signal coupling between neurons and astrocytes, which leads to neurological damage. HDL-C can reversely transport cholesterol, and thus it can regulate the dynamic balance of cholesterol in brain tissue. HDL can also protect brain tissue from I-R damage via inhibiting NLRP3 activation, and low HDL-C levels can lead to the formation of atherosclerotic plaque. Therefore, the level of HDL-C was lower in the moderate-to-severe neurological deficit group in our experiment. Angle, MA, G, and A30 were higher in the group with higher NIHSS score, while the difference of R and K values between the two groups was not statistically significant. Theses results indicated that the severity of neurological damage in

ACI might be related with the quality and quantity of platelets.

Pearson correlation analysis showed that NIHSS score was positively correlated with neutrophil count, monocyte count, MHR, and NLR. NLR is a composite index for inflammation, and the correlation between NLR and NIHSS score was better than neutrophil count and monocyte count, which can effectively reflect the severity of cerebrovascular damage. Studies have demonstrated that it can be used to reflect the prevalence of intracranial atherosclerosis, and predict the prognosis of stroke. Among all the indicators, the correlation between MHR and NIHSS was the strongest ($r=0.674$, $P<0.001$). The possible underlying mechanism might be that the in-situ macrophages in brain tissue were activated and recruited the circulating immune cells (e.g. neutrophils, lymphocytes, monocytes, eosinophils, etc.) to the injured site in the acute phase of ischemic stroke. Among all these cells, monocyte-derived macrophages play an essential role. HDL-C inhibits the activation of p38 and the activity of phosphoinositide kinase, reduces the expression levels of F actin, monocyte CD11b and endothelial cell adhesion molecules, and ameliorates monocyte proliferation, activation, and adhesion. HDL-C is negatively related with monocytes function. Combined use of the two indicators improves the correlation of MHR with ACI. Therefore, MHR can be used as a new inflammatory indicator in assess the severity of neurological damage in patients with ACI and predict the development of ACI.

5. CONCLUSION

In summary, MHR and TEG indicators are closely related to the occurrence and development of ACI. The combined use of the two indicators shows high accuracy, sensitivity, and specificity in the diagnosis of ACI. Therefore, it serves an early warning role for the patients with atypical clinical symptoms of CI, thereby decreasing missed diagnosis and misdiagnosis. Furthermore, it can assist in assessing the severity of the disease. Blood routine and blood lipid are the most common examination indicators in clinical practice. TEG is also a commonly used indicator in detecting blood coagulation function, which is simple and easy to obtain. Thus, these indicators can be widely used in early identification and diagnosis showing a high value in clinical application . If MHR, mononuclear count, and A30 increase and R value decreases, ACI might occur and imaging and other related examinations should be conducted as soon as possible, and intervention and treatment should be provided in time to improve the prognosis. If MHR is increased, there might be symptoms related with severe neurological deficit.

Studies have shown that MHR is also closely related to the size of the infarction area and prognosis of ACI. Larger infarction area is related with worse prognosis and higher MHR, which can be further investigated in future research.

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Competing interests

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