Association between erythrocyte and platelet related parameters with the initial severity of acute ischemic stroke

[1]Chen Chen, [1]Weichao Zhu, [1]Tianshuo Sun, [1]Haixu Zhao, [1]Hui Liu, [1]Cui Zhang, [1]Mengyuan Hao, [1]Qian Liang, [2]Guodong Tian, [3]Donglai Jing, [4]Kangbo Li

[1]4th Department of Internal Medicine, Xiong'an New District Rongcheng People's Hospital, Baoding, China; [2]3rd Department of Internal Medicine, Xiong'an New District Rongcheng People's Hospital, Baoding, China; [3]Medical Administration Office, Xiong'an New District Rongcheng People's Hospital, Baoding, China; [4]School of Clinical Medicine, North China University of Science and Technology, Tangshan, China

Abstract

Background & Objective: The purpose of the present study was to evaluate the association between erythrocyte and platelet related parameters with the initial severity of acute ischemic stroke (AIS). *Methods:* This observational study included 113 patients with AIS in the 4th Department of Internal Medicine, Xiong'an New District Rongcheng People's Hospital. Erythrocyte and platelet related parameters including red blood cell distribution width (RDW), hematocrit value (HCT), platelet volume distribution width (PDW), and plateletcrit (PCT) were measured for all patients. In addition, modified Rankin Scale (mRS) was performed to assess the initial severity of AIS for all patients. Ordinal logistic regression analysis was used to investigate the association between the erythrocyte and platelet related parameters with mRS. *Results:* RDW was positively and significantly associated with mRS (Estimate = 0.532, P = 0.025, 95% CI: 0.067, 0.997) in patients with AIS. *Conclusion:* RDW is associated with the initial severity of AIS.

Keywords: Acute ischemic stroke, erythrocyte and platelet related parameters, modified Rankin Scale

INTRODUCTION

Stroke is an acute cerebrovascular disease characterized by focal neurological deficits. The prevalence of stroke is expected to rise significantly, a trend that can be attributed in part to ongoing demographic transformations, such as an aging population and evolving health dynamics in developing countries.[1] Indeed, stroke has become the leading cause of death in China[2], it was estimated that there were 3.4 million new cases of stroke among the Chinese population aged 40 and older, resulting in 2.3 million deaths in 2020. Ischemic stroke (IS) accounted for 15.5 million, representing 86.8% of all new stroke cases.[3] IS refers to a stroke caused by cerebral ischemia and hypoxia, resulting in necrosis and softening of the brain tissue due to cerebral blood supply disorder.[4] According to the statistics, the total number of deaths associated with IS reached 3.29 million,

representing 50.3% of deaths due to strokes in 2019.[5] The central goal of therapy for acute ischemic stroke (AIS) is to restore blood flow, and preserve tissue in the ischemic penumbra, an area where blood flow is reduced yet adequate enough to prevent the occurrence of infarction.[6] At present, the main therapies for AIS include intravenous thrombolysis, arterial thrombolysis, angioplasty, and mechanical thrombectomy. Notably, all of these procedures have strict time window restrictions.[7] Therefore, it is particularly important to evaluate the initial severity of AIS. In recent years, many studies have shown that erythrocyte and platelet-related parameters including red blood cell distribution width (RDW), hematocrit value (HCT), platelet volume distribution width (PDW), and plateletcrit (PCT) are closely related to the prognosis of stroke.[8-11] However, such studies lack the evaluation of the correlation between the above parameters and the

initial severity of AIS. Therefore, this study aims to investigate the correlation between the above parameters and the disease severity during the initial diagnosis of AIS.

METHODS

This study included 113 AIS patients admitted to the 4th department of internal medicine, Xiong'an New District Rongcheng People's Hospital from December 2022 to June 2023. Inclusion criteria: (1) diagnosed with AIS; (2) aged ≥ 18 years. Exclusion criteria: (1) concurrent with other major adverse cardiovascular events; (2) patients with cancer, or other diseases deemed unsuitable for research by the attending physician. (3) patients with incomplete relevant information.

Information on age, gender, body mass index, blood pressure, smoking history, drinking history, previous medical history (hypertension, diabetes, coronary heart disease) were collected by the trained nurses or physicians.

Peripheral venous blood was drawn from the patient and sent to the laboratory for routine blood tests and blood biochemistry tests. Erythrocyte and platelet related parameters include RDW, HCT, PDW, and PCT. Blood biochemistry includes serum creatinine, blood urea nitrogen, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, and fasting plasma glucose.

The modified Rankin Scale (mRS) was performed to assess the initial severity (the level of disability) of AIS for all patients in the current study. A score of 0 indicates the absence of disability. a score of 2 indicates a mild level of disability; the individual is unable to perform all prior activities but can manage personal affairs independently. A score of 3 indicates a moderate level of disability; the individual requires some assistance yet is capable of walking unaided. A score of 4 indicates a moderately severe level of disability; the individual cannot walk without support and is unable to attend to personal hygiene and bodily needs without help. A score of 5 indicates severe disability; the individual requires constant nursing care and attention. A score of 6 denotes dead.[12]

Statistical analysis

The data were analyzed using SPSS 26 statistical software package. The quantitative data were described as mean ± standard deviation, and the qualitative data were described as frequency and percentage. Ordered logistic regression was used

to analyze the relationship between erythrocyte and platelet related parameters and mRS. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 113 patients (77 males) with AIS were included in this study. The mean age was 62.87 ± 13.61 years. Among them, 44 patients (38.94%) had mRS of 0; 28 patients (24.78%) had mRS of 1; 11 patients (9.73%) had mRS of 2; 5 patients (4.42%) had mRS of 3; 24 patients (21.24%) had mRS of 4; 1 patient (0.88%) had mRS of 5. There was no patient have mRS of 6 (Table 1).

Ordinal Logistic regression analysis

The dependent variable was mRS for all analyses. When setting age, gender and RDW as independent variables, the results showed that

Table1: Baseline characteristics

Variables	
Age (years)	62.87 ± 13.61
Male, n (%)	77 (68.14%)
Current smokers, n (%)	44 (38.94%)
Current drinkers, n (%)	21 (18.58%)
Hypertension, n (%)	73 (64.60%)
Diabetes, n (%)	34 (30.09%)
CAD, n (%)	17 (15.04%)
BMI (kg/m^2)	24.48 ± 3.92
RDW (%)	12.89 ± 0.78
HCT (%)	41.91 ± 4.84
PDW (fL)	16.36 ± 2.13
PCT (%)	0.21 ± 0.06
Scr (μmol/L)	75.60 ± 34.25
BUN (mmol/L)	6.24 ± 2.30
TC (mmol/L)	4.72 ± 1.27
HDL-C (mmol/L)	1.07 ± 0.53
LDL-C (mmol/L)	2.79 ± 1.04
FBG (mmol/L)	6.82 ± 3.05
SBP (mmHg)	149.42 ± 22.26
DBP (mmHg)	89.52 ± 13.92

CAD: coronary artery disease; BMI: body mass index; RDW: red blood cell distribution width; HCT hematocrit value; PDW: platelet volume distribution width; PCT: plateletcrit; mRS: modified Rankin Scale; Scr: serum creatinine; BUN: blood urea nitrogen; TC: total cholesterol; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; FBG: fasting plasma glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure.

RDW was significantly and positively correlated with mRS (Estimate = 0.532, *P* = 0.025, 95% CI: 0.067, 0.997) (Table 2). When setting age, gender and HCT as independent variables, the results showed that HCT was negatively correlated with mRS, but with no statistical significance (Estimate = -0.061, *P* = 0.134, 95% CI: -0.141, 0.019) (Table 3). When setting age, gender and PDW as independent variables, the results showed that PDW was positively correlated with mRS, but with no statistical significance (Estimate = 0.014, *P* = 0.860, 95% CI: -0.142, 0.170) (Table 4). When setting age, gender and PCT as independent variables, the results showed that

Table 2: Ordinal logistic regression analysis between RDW and mRS

	mRS	Estimate	SE	Wald	*P* Value	95% CI
Threshold	0	7.543	2.974	6.431	0.011	1.713, 13.373
	1	8.653	3.001	8.314	0.004	2.771, 14.534
	2	9.135	3.014	9.188	0.002	3.228, 15.042
	3	9.387	3.021	9.659	0.002	3.467, 15.308
	4	12.91	3.220	16.08	<0.001	6.600, 19.221
Location	Age	0.014	0.014	1.088	0.297	-0.012, 0.041
	Gender (female)	-0.804	0.382	4.436	0.035	-1.553, -0.056
	RDW	0.532	0.237	5.031	0.025	0.067, 0.997

RDW: red blood cell distribution width; mRs: modified Rankin Scale.

Table 3: Ordinal logistic regression analysis between HCT and mRS

	mRS	Estimate	SE	Wald	*P* Value	95% CI
Threshold	0	-2.132	2.251	0.897	0.344	-6.544, 2.280
	1	-1.063	2.245	0.224	0.636	-5.464, 3.338
	2	-0.590	2.243	0.069	0.792	-4.987, 3.807
	3	-0.336	2.243	0.022	0.881	-4.731, 4.060
	4	3.204	2.430	1.739	0.187	-1.558, 7.967
Location	Age	0.012	0.014	0.766	0.382	-0.015, 0.040
	Gender (female)	-0.401	0.382	1.100	0.294	-1.151, 0.349
	HCT	-0.061	0.041	2.241	0.134	-0.141, 0.019

HCT hematocrit value; mRs: modified Rankin Scale.

Table 4: Ordinal logistic regression analysis between PDW and mRS

	mRS	Estimate	SE	Wald	*P* Value	95% CI
Threshold	0	0.802	1.595	0.253	0.615	-2.323, 3.927
	1	1.858	1.602	1.345	0.246	-1.282, 4.999
	2	2.321	1.607	2.085	0.149	-0.829, 5.471
	3	2.567	1.610	2.542	0.111	-0.588, 5.723
	4	6.061	1.889	10.292	0.001	2.358, 9.764
Location	Age	0.023	0.013	3.054	0.081	-0.003, 0.048
	Gender (female)	-0.611	0.369	2.732	0.098	-1.335, 0.113
	PDW	0.014	0.080	0.031	0.860	-0.142, 0.170

PDW: platelet volume distribution width; mRS: modified Rankin Scale.

Table 5: Ordinal logistic regression analysis between PCT and mRS

	mRS	Estimate	SE	Wald	*P* Value	95% CI
	0	1.828	1.163	2.471	0.116	-0.451, 4.108
	1	2.887	1.182	5.962	0.015	0.570, 5.204
Threshold	2	3.351	1.193	7.895	0.005	1.014, 5.688
	3	3.599	1.198	9.018	0.003	1.250, 5.948
	4	7.105	1.564	20.636	<0.001	4.039, 10.170
	Age	0.025	0.013	3.544	0.060	-0.001, 0.052
Location	Gender (female)	0.533	0.379	1.982	0.159	-0.209, 1.275
	PCT	2.522	3.080	0.670	0.413	-3.516, 8.559

PCT: plateletcrit; mRS: modified Rankin Scale.

PCT was positively correlated with mRS, but with no statistical significance (Estimate = 2.522, *P* = 0.413, 95% CI: -3.516, 8.559) (Table 5). When setting age, gender, RDW, HCT, PDW, and PCT as independent variables, the results showed that RDW was still significantly and positively correlated with mRS (Estimate = 0.514, *P* = 0.036, 95% CI: 0.033, 0.995) (Table 6).

DISCUSSION

This study investigated the relationship between erythrocyte and platelet related parameters in relation to the severity of the disease during the early phase of ASI. The findings indicated that RDW exhibited a significant positive correlation with the severity of ASI. Consequently, the utilization of RDW may assist in evaluating the severity of ASI.

The RDW is a parameter that reflects the heterogeneity of red blood cell volume.[13] In the past, the coefficient of variation of the measured red blood cell volume, RDW-CV (RDW-coefficient of variation) and the standard deviation of the red blood cell distribution width, RDW-SD (RDW-standard deviation), were used for the classification and differential diagnosis of anemia.[14] In recent years, a large number of studies have shown that RDW is closely related to the risk and prognosis of cardiovascular disease.[15] Consistent with our results, Xue *et al.* retrospectively studied 629 patients with AIS and found that elevated RDW was significantly associated with moderate to severe AIS (OR = 2.21, 95% CI: 1.30, 3.75, *P* = 0.003) and elevated mRS (3-6 scores) (OR = 1.86, 95% CI: 1.02, 3.41, *P* = 0.044).[16] Additionally, both Kara *et al.* and Mohindra *et al.* reported that

Table 6: Ordinal logistic regression analysis among RDW, HCT, PDW, PCT and mRS

	mRS	Estimate	SE	Wald	*P* Value	95% CI
	0	4.910	4.014	1.496	0.221	-2.957, 12.776
	1	6.032	4.027	2.243	0.134	-1.862, 13.925
Threshold	2	6.523	4.034	2.614	0.106	-1.384, 14.429
	3	6.782	4.038	2.821	0.093	-1.132, 14.696
	4	10.349	4.179	6.134	0.013	2.159, 18.539
	Age	0.006	0.015	0.135	0.713	-0.025, 0.036
	Gender (female)	0.623	0.407	2.345	0.126	-0.174, 1.420
Location	RDW	0.514	0.245	4.394	0.036	0.033, 0.995
	HCT	-0.055	0.042	1.719	0.190	-0.136, 0.027
	PDW	0.030	0.080	0.144	0.705	-0.127, 0.187
	PCT	0.065	3.234	<0.001	0.984	-6.274, 6.404

RDW: red blood cell distribution width; HCT hematocrit value; PDW: platelet volume distribution width; PCT: plateletcrit; mRS: modified Rankin Scale.

the RDW levels of patients with more severe AIS were significantly higher than those with milder AIS.[8,17] Furthermore, Akpinar *et al*. collected 205 patients with AIS to explore the relationship between RDW and poor functional outcome. The results showed that elevated RDW was closely related to functional impairment in AIS (when RDW >16%, OR = 2.873, 95% CI: 1.342, 6.151; *P* = 0.007).[18] Xie *et al*. reported that the RDW values for patients with IS and hemorrhagic stroke following a transient ischemic attack (TIA) were notably elevated compared to those of patients who experienced a TIA alone. (13.35 ± 1.59 v.s. 13.32 ± 1.08 v.s. 12.84 ± 1.19, $P \le 0.001$). The results of multivariate logistic regression showed that RDW was closely associated with IS after TIA (OR = 2.52, 95% CI: 1.46, 3.35, $P = 0.002$) and hemorrhagic stroke after TIA (OR = 1.511, 95% CI: 1.101, 2.074, $P = 0.011$).[19]

The HCT is the percentage of red blood cells in the whole blood volume.[20] Recent research has suggested a potential positive correlation between HCT levels and cardiovascular risk factors.[21] Regarding its relationship with IS, Allport *et al*. studied the correlation between HCT and infarct size in 64 AIS patients. The results showed that HCT level was significantly and negatively correlated with reperfusion level. Elevated HCT was a significant predictor of infarct growth (OR = 1.26, 95% CI: 1.00, 1.59).[22] In addition, Gotoh *et al*. followed up 2585 individuals in a Japanese community for 19 years. The participants were categorized into four groups based on the sex-specific quartiles of HCT measured at baseline. The findings indicated that the risk of IS was greater in both the lowest and highest quartiles compared to the third quartile, which served as the reference (Q1, HR = 1.55, 95% CI: 0.99, 2.43; Q2, HR = 1.44, 95% CI: 0.93, 2.23; Q4, HR = 1.62, 95% CI: 1.06, 2.50).[23] Furthermore, Kellert *et al*. studied 217 patients with stroke who received intravenous thrombolysis. The results showed that reduced HCT was significantly associated with mortality in stroke patients three months later (OR = 1.12, 95% CI, 1.01, 1.23; $P = 0.027$).[9] Li *et al*. studied the levels of hemoglobin, HCT and mRS of 858 patients with acute cerebral infarction. The results showed that HCT value decreased by 1 percentage point was associated with an OR for mortality of 1.047, 95% CI: 1.003, 1.093, $P = 0.037$.[24]

The PDW is the coefficient of variation that reflects the volume of platelets.[25] Previous studies have demonstrated that PDW is significantly associated with the extent of coronary artery disease.[25] Regarding its association with IS, Gao *et al*. studied the relationship between PDW values and clinical prognosis in 82 AIS patients. The results showed that PDW < 16.05% was significantly associated with poor clinical prognosis (OR = 6.68, 95% CI: 1.69, 26.49, $P = 0.007$).[26] Additionally, Lyu *et al*. studied 150 patients with atrial fibrillation. The results showed that PDW can be regarded as a risk factor for atrial fibrillation complicated by stroke (OR: 1.56, $P = 0.002$).[27] Furthermore, Sarkar *et al*. reported that PDW was significantly associated with motor function deficits in AIS patients.[10]

The PTC is the total mass of platelets as a percentage of the blood volume they occupy.[28] A recent study indicated that patients exhibiting elevated levels of PCT are at an increased risk for acute myocardial infarction and myocardial damage.[29] In regards to strokes, Mohamed et al. studied 157 patients with IS, among whom the PCT of patients with poor prognosis was significantly higher than that of patients with good prognosis ($0.28 \pm 0.1\%$ v.s. $0.25 \pm 0.1\%$, $P = 0.04$).[11] Additionally, Aslan *et al*. conducted a study involving 230 patients who exhibited more than 50% stenosis of the carotid artery, aiming to assess the effectiveness of PTC in predicting major adverse cardiac and cerebrovascular events (MACCE). MACCE was defined as a combination of all-cause mortality, cardiovascular death, myocardial infarction, stroke, hemorrhage, acute kidney injury, carotid revascularization, and hospitalization due to worsening heart failure. The findings indicated that patients experiencing MACCE had significantly elevated PTC levels (0.247 vs. 0.213, $P < 0.001$). Multivariate regression analysis revealed that PTC was independently linked to MACCE (OR = 2.196, 95% CI: 1.200, 4.018, $P = 0.011$). However, although a higher incidence of stroke was noted among patients in the elevated PCT group, the results did not reach statistical significance.[30]

In conclusion, this study is the first to investigate the correlation between erythrocyte and platelet related parameters with the initial severity of AIS. The results showed that RDW is positively and significantly associated with the severity of ASI in the initial stage. However, this study is a cross-sectional study with a small sample size, further largescale studies are needed to clarify this relationship and to better understand the underlying mechanisms involved in RDW and initial severity of AIS.

DISCLOSURE

Conflict of interest: None

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