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ORIGINAL ARTICLE

The relationship among neutrophil to lymphocyte ratio, stroke territory, and 3-month mortality in patients with acute ischemic stroke

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Abstract

Background Stroke therapy options have focused on limiting the infarct volume. Neutrophil to lymphocyte ratio (NLR) can be valuable to detect the patients that required intensive treatment at early stage by predicting infarct volume. The aim of this study is to evaluate the relationship between NLR and infarct volume according to the stroke territory, and to determine the prognostic value of NLR for predicting 3-month mortality in acute ischemic stroke (AIS) patients.

Methods A total of 107 patients with AIS were enrolled and followed up 3 months in terms of mortality. Study population was divided into two groups according to the stroke territory: anterior circulating stroke (ACS) and posterior circulating stroke (PCS). All patients underwent magnetic resonance imaging. The complete blood count and venous blood samples were obtained from the patients on admission to the emergency department.

Results There were no difference between ACS and PCS groups regarding baseline characteristics and co-morbid diseases. Also, C-reactive protein and NLR were similar between two groups. In correlation analyses, infarct volume was significantly correlated with CRP and NLR in ACS ($r = 0.350$, $p = 0.001$ and $r = 0.482$, $p \leq 0.001$, respectively), but not correlated with infarct volume in PCS. Also, NLR was correlated with NIHHS in only ACS group ($r = 0.326$, $p = 0.002$). Multivariate analysis showed that NLR was the only independent predictor of 3-month mortality (OR 1.186, 95% CI 1.032–1.363, $p = 0.016$).

Conclusion NLR is significantly correlated with ACS infarct volume, but not with PCS infarct volume in AIS. Also, NLR was an independent predictor of 3-month mortality in AIS patient.

Keywords Acute ischemic stroke · Infarct volume · Stroke territory · Neutrophil to lymphocyte ratio · Mortality

Introduction

Acute ischemic stroke (AIS) is the main cause of adult permanent disability, second most common cause of dementia, and third most common cause of mortality worldwide [1]. It also causes high treatment costs and labor losses. Ischemic infarct volume on imaging modality and clinic National Institutes of Health Stroke Scale/Score (NIHSS) are important factors in predicting the post-stroke prognosis of patients. Therefore, current treatment strategies for AIS including anti-aggregant therapy, intravenous or intraarterial recombinant tissue plasminogen activators, and mechanical endovascular therapies aim to limit the infarct volume [2]. In addition to these well-defined traditional prognostic factors, inflammatory markers are also associated with poor prognosis in AIS and may help to detect the patients that required intensive treatment at early stage.

Inflammation has a pivotal role in initiation and progression of atherosclerosis [3]. White blood cell (WBC) count and subtypes of WBC are commonly used inflammatory markers [4]. It was demonstrated that higher WBC and neutrophil counts were correlated with larger infarct volume and increased stroke severity in patients with AIS [5]. However, recently, neutrophil to lymphocyte ratio (NLR) has emerged as a novel marker of the systemic inflammation. It is an easily obtainable parameter from complete blood count and quite inexpensive [4]. Previous studies have reported that NLR was associated with poor outcomes and predict short-term mortality in patients with AIS [6, 7].

AIS can be classified into two groups according to stroke territory: anterior circulation stroke (ACS) and posterior circulation stroke (PCS) [8]. ACS accounts for 70–75% of all

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ischemic stroke cases, whereas the range of PCS is approximately 20–25%. Although the association between NLR and infarct volume has been investigated previously in patients with AIS, to our knowledge, no study so far evaluated the association of NLR with stroke volume according to the stroke territory. In this study, we aimed to investigate the link between NLR and infarct volume according to the stroke territory in patients with presenting AIS. In addition, we will evaluate the prognostic value of NLR for predicting 3-month mortality in these patients.

Methods

Study population

A total of 107 patients presenting with AIS between 01 January 2017 and 31 December 2017 were included in this study. The diagnosis of AIS was based on World Health Organization's definition [9]. Patients were etiologically classified according to the Trial of Org 10,172 in Acute Stroke Treatment (TOAST) criteria: cardioembolic, atherosclerotic, small vessel/lacunar, and cryptogenic/others [10]. Exclusion criteria for the patients were the following: (i) those patients with trauma or previous history of surgery; (ii) those with an active infection before stroke onset or within 72 h after admission; (iii) previously known hematologic disorders; (iv) severe hepatic or renal disease; (v) acute metabolic disease or intoxication; (vi) patients with cerebrovascular and/or coronary heart disease; (vii) a history of cancer or the use of steroids or immunosuppressant agent; (viii) those patients having both ACS and PCS together; and (ix) lacking of the medical, demographic, clinical, laboratory, and/or radiologic data. The study was conducted in full accordance with the Declaration of Helsinki and was approved by the local ethics committee. All patients provided written, informed consent before inclusion in this study.

Clinical data

Baseline clinical data including age, gender, and risk factors such as hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), heart failure, and atrial fibrillation (AF) were recorded on pre-prepared standard study forms for all patients. HT was defined as systolic blood pressure (BP) ≥ 140 mmHg, and/or diastolic BP ≥ 90 mmHg, taking anti-hypertensive medications, and/or previously diagnosed hypertension. DM was defined as fasting serum glucose of ≥ 126 mg/dL (7 mmol/L), a non-fasting glucose of ≥ 200 mg/dL (11.1 mmol/L), use of anti-diabetic medications, or a previously established diagnosis. HL was diagnosed if low-density lipoproteins (LDL)-cholesterol level is ≥ 100 mg/dL or use of lipid-lowering agents after being diagnosed with HL. Atrial fibrillation was defined as AF recorded at the time of the electrocardiography or any previously known episode of AF.

Laboratory methods

The complete blood count and venous blood samples including C-reactive protein (CRP) and creatinine were taken from the patients on admission to the emergency department. In addition, venous blood samples for cholesterol levels were obtained within 24 h after admission and after a 12-h overnight fasting period. All samples were collected in EDTA tubes, and were sent to the laboratory for analysis within 2 h after collection. Biochemical tests such as total cholesterol, LDL-cholesterol, high-density lipoproteins-cholesterol, triglycerides, and fasting glucose were measured spectrophotometrically. The mean platelet volume (MPV), red cell distribution width (RDV), and WBC counts were measured using a Cell-Dyne counter of Abbott Laboratories (Abbott Laboratories, IL). The NLR was obtained by dividing the neutrophil count to the lymphocyte count.

Magnetic resonance image acquisition and analysis

Magnetic resonance images (MRI) were performed with scanners of 1.5 T (Magnetom Avanto; Siemens, Erlangen, Germany) by using dedicated head coil. Patients were placed in the supine position. The scanning protocol included diffusion-weighted imaging (DWI) and apparent diffusion coefficient sequence with 5-mm section. All the MRI images were evaluated on a workstation (Leonardo; Siemens, Erlangen, Germany) by a neurologist. The infarct volume was calculated based on the DWI images. First, in DWI images with infarct, the infarct areas in every image were calculated separately and added to each other. Second, whole infarct areas were multiplied by section thickness. Whole infarct volumes were obtained as millimeter. Volume calculation on diffusion MRI was performed by a neurologist with 10-year experience. The infarct volume was calculated using the previously described formula [11]. Treatments were managed for all patients according to the previously described guidelines.

Stroke territory and severity

Stroke territory was classified according to MRI. PCS was defined as ischemia in the vascular territory of basilar, vertebral, or posterior cerebral arteries. ACS was defined as ischemia in the vascular territory internal carotid, middle, or anterior cerebral arteries [8]. Our study population was divided into two groups according to this classification: ACS (n =

84) and PCS ($n = 23$). Stroke severity was assessed based on the NIHSS [12].

Medications and follow-up

The study population was evaluated in terms of the therapy of stroke including anti-aggregant therapy, intravenous or intraarterial recombinant tissue plasminogen activator, and mechanical endovascular therapy. The hospital's electronic record system was assessed for evaluation of in-hospital and 3-month mortality after AIS and contacted by the telephone and national mortality record.

Statistical analysis

Statistical analyses were performed using the SPSS Statistics 24.0 software (SPSS Inc., Chicago, IL). Continuous data were presented as the mean value ± standard deviation or median with interquartile range (IQR; 25th and 75th) according to distribution normality using the Kolmogorov–Smirnov test. Student's t test was used for comparisons of parametric variables, and Mann–Whitney U test was used for comparisons of non-parametric variables. Categorical data were expressed as percentage, and compared using the chi-squared test. Pearson's and Spearman's rank correlation coefficients were used for correlation analysis. Variables which had unadjusted p value of < 0.1 in univariate analysis were considered as a potential risk predictors and included in the full multivariate model. Multivariate logistic regression analysis was performed to determine the independent predictors of 3-month mortality. Receiver operating characteristic (ROC) curve analysis was used to obtain the sensitivity and specificity of the NLR for predicting 3-month mortality. A p value < 0.05 was defined as statistically significant.

Results

A total of 107 patients were enrolled in this study and followed up 3 months in terms of mortality. The mean age of the study population was 67 (55–74) years, and 53.3% of study population was male. Eighty-four patients (78.5%) had ACS, whereas 23 patients (21.5%) had PCS. Baseline characteristics of the study groups were shown in Table 1. There were no significant differences between two groups regarding the age, sex, and co-morbid diseases including DM, HT, HL, heart failure, and AF. The ACS group was treated mostly with endovascular/thrombolytic, while PCS was treated mostly with anti-aggregant therapy ($p = 0.023$). In addition, infarct volume was significantly higher in patients with ACS group compared to PCS group ($p = 0.005$).

The laboratory parameters of the study group were listed in Table 2. Biochemical and laboratory parameters including neutrophil, lymphocyte, NLR, and CRP were similar between ACS and PCS groups ($p > 0.05$ for all).

In correlation analysis, infarct volume was positively correlated with NIHSS ($r = 0.609$, $p < 0.001$), ASPECT ($r = 0.742$, $p < 0.001$), CRP ($r = 0.350$, $p = 0.001$), and NLR ($r = 482$, $p \leq 0.001$) in ACS group, but it was only correlated with NIHSS ($r = 0.593$, $p = 0.003$) in PCS group (Table 3). In contrary to ACS group, there was no significant correlation between infarct volume and NLR in PCS group. In addition, NLR was positively correlated with NIHSS score in ACS group ($r = 0.326$, $p = 0.002$), while no significant correlation was detected between these two parameters in PCS group.

The 3-month mortality rate was 20.6% in study population. Patients in dead group were significantly older ($p = 0.024$) and had higher CRP level ($p = 0.004$), higher NLR level ($p < 0.001$), and higher frequency of AF ($p = 0.002$) compared to patients in surviving group (Table 4). Univariate and multivariate logistic regression analyses were performed to determine the independent predictors of 3-month mortality. In univariate analysis, age, the presence of AF, NIHSS, CRP, and NLR were found to be associated with increased risk of 3-month mortality. Multivariate logistic regression analysis demonstrated that NLR was the only independent predictor of 3-month mortality. ROC curve analysis was used to detect the sensitivity and specificity of the NLR for predicting 3-month mortality (Table 5). NLR ≥ 4.7 predicted 3-month mortality with a specificity of 76.5%, sensitivity of 63.6%, positive predictive value of 41.2%, and negative predictive value of 89% (Fig. 1).

Discussion

This study revealed that NLR was significantly related to ACS infarct volume, but not related to PCS infarct volume. Also, NLR was the independent predictor of 3-month mortality in patients with AIS. The results point out that a higher NLR can indicate stroke severity on admission, and can help to make the decision of the necessity of endovascular intervention particularly in ACS.

It has been well recognized that inflammatory response is implicated in all stages of AIS [13]. Inflammatory mediators are expressed at low levels in normal brain tissue. However, an ischemic condition could provide the release of proinflammatory cytokines and recruitment of immune cells, which represent an important mechanism of secondary progression of brain lesion [14]. Studies showed that elevated WBC count is associated with poor outcomes in patients with AIS [15]. However, every WBC subtypes have different prognostic role [16]. Neutrophils are the first WBC subtype recruited to the damaged brain area [17]. Activated neutrophils cause the release of proteolysis

Table 1 Comparison of clinical and demographic features of patients with anterior and posterior circulation stroke

	All patients ($n = 107$)	Anterior circulation stroke ($n = 84$)	Posterior circulation stroke ($n = 23$)	p
Age (years)	67 (55–74)	68 (57–75)	60 (47–73)	0.065
Male gender, *n* (%)	57 (53.3)	43 (51.2)	14 (60.9)	0.410
Diabetes mellitus, *n* (%)	33 (30.8)	25 (29.8)	8 (34.8)	0.644
Hypertension, *n* (%)	67 (62.6)	51 (60.7)	16 (69.6)	0.437
Hyperlipidemia, *n* (%)	38 (35.5)	30 (35)	8 (34.7)	0.785
Heart failure, *n* (%)	5 (4.7)	5 (6)	0	0.583
Atrial fibrillation, *n* (%)	13 (12.1)	11 (13.1)	2 (8.7)	0.730
Stroke subtypes, *n* (%)				
Cardioembolic	31 (29)	28 (33.3)	3 (13)	*0.016*
Atherosclerotic	18 (16.8)	15 (17.9)	3 (13)	
Small vessel/lacunar	16 (15)	7 (8.3)	9 (39.1)	
Cryptogenic/others	42 (39.3)	34 (40.5)	8 (34.8)	
Therapy strategy, *n* (%)				
Endovascular/thrombolytic	23 (21.5)	22 (26.2)	1 (4.3)	*0.023*
Anti-aggregant only	84 (78.5)	62 (73.8)	22 (95.7)	
NIHSS	10 (10–15)	10 (7–16)	8 (7–12)	0.308
ASPECTS		8 (6–9)	–	–
Infarct volume, cm^3	4.30 (0.24–19.3)	6.63 (0.58–25.9)	0.6 (0.52–9.12)	*0.005*
Medications, *n* (%)				
ACE-ARB	43 (40.2)	35 (41.7)	8 (34.8)	0.551
CCB	26 (24.3)	18 (21.4)	8 (34.8)	0.186
β blocker	17 (15.9)	14 (16.7)	3 (13)	0.920
Anti-aggregants	25 (23.4)	21 (25)	4 (17.4)	0.445
Anti-diabetics	33 (30.8)	25 (29.8)	8 (34.8)	0.644
Oral anti-coagulant	7 (6.5)	6 (7.1)	1 (4.3)	0.537
Statins	36 (33.6)	29 (34.5)	7 (30.4)	0.659

Nonparametric variables are expressed as median (interquartile range)

NIHSS National Institutes of Health Stroke Scale/Score, ASPECTS Alberta Stroke Program Early CT Score, ACE-ARB angiotensin-converting enzyme inhibitor /angiotensin receptor blocker, CCB calcium channel blockers, $P<0.05$ was considered as statistically significant

enzymes such as acid phosphatase or reactive oxygen products, and exacerbate ischemic brain injury. Early neutrophilia has been reported to be associated with larger infarct volumes [5]. In addition, it has been demonstrated that infarct volume is significantly reduced when neutrophil infiltration is inhibited [18]. In contrast to neutrophils, the role of lymphocytes in AIS is controversial. Nevertheless, it has been demonstrated that lymphocyte counts decreased after AIS, and this reduction in lymphocytes is associated with poor prognosis [16, 19]. Therefore, recent studies have demonstrated that NLR which reflects the balance between neutrophils and lymphocytes is a more useful marker than other WBC subtypes for risk prediction.

Increased NLR has been generally reported to be associated with poor prognosis and predict short-term mortality in patients with AIS [6, 7, 20–22]. Similar to previous studies, we also showed that NLR was an independent predictor of 3-month mortality in AIS patients and NLR ≥ 4.7 predicted 3-month mortality with a specificity of 76.5% and sensitivity of 63.6%. We think that the possible underlying mechanism of the relationship between higher NLR and mortality in patients may be explained as follows: NLR may increase as a result of inflammatory response in AIS or be a marker indicating the severity/extent of necrotic tissue and its associated biochemical pathways. Previous studies have shown that increased neutrophils release cytokins, chemokines, free oxygen radicals, and other inflammatory mediators, which result in blood-brain barrier disruption, neuronal cell death, and hemorrhagic transformation after AIS. All these occurred changes are associated with poor outcome and may contribute to the mortality of AIS [20]. Our results confirm that elevated NLR on the hospital admission is an easy and strong predictor of poor outcomes in AIS patients. Therefore, we can conclude that a higher NLR should be

Table 2 Comparison of laboratory parameters of patients with anterior and posterior circulation stroke

	All patients ($n = 107$)	Anterior circulation stroke ($n = 84$)	Posterior circulation stroke ($n = 23$)	p
Creatinine (mg/dL)	0.8 (0.7–1.08)	0.83 (0.7–1.07)	0.8 (0.68–1.1)	0.692
Total cholesterol (mg/dL)	181 (154–201)	179 (151–194)	195 (162–211)	0.066
LDL cholesterol (mg/dL)	110 (91–121)	110 (90–119)	110 (91–134)	0.695
HDL cholesterol (mg/dL)	38 (31–42)	38 (31–42)	38 (31–44)	0.875
Triglyceride (mg/dL)	158 (104–192)	155 (102–174)	164 (132–306)	0.084
Hemoglobin (g/dL)	13.2 ± 1.8	13.2 ± 1.9	13.4 ± 2.1	0.709
Platelet count (10^3/mm^3)	259 (216–316)	262 (217–315)	256 (214–322)	0.991
White blood cell count (10^3/mL)	10.9 ± 3.1	11.0 ± 3.2	10.7 ± 2.8	0.740
Neutrophil count (10^3/mL)	7.5 (5.6–9.6)	7.5 (5.8–9.7)	7 (5.3–9.6)	0.527
Lymphocyte count (10^3/mL)	2.1 (1.3–2.8)	2.09 (1.31–2.67)	2.1 (1.30–2.90)	0.973
Neutrophil to lympocyte ratio	3.68 (2.34–5.07)	3.68 (2.32–5.28)	3.68 (2.36–5.08)	0.818
Mean platelet volume (fL)	7.6 ± 1.4	7.7 ± 1.4	7.5 ± 1.4	0.496
Red cell distribution width	12.8 ± 1.8	12.6 ± 1.7	13.5 ± 2.1	0.058
CRP (mg/dL)	1.2 (0.58–1.86)	1.24 (0.58–1.89)	0.7 (0.4–1.8)	0.497

Parametric variables are expressed as mean ± SD, and nonparametric variables are expressed as median (interquartile range)

LDL low-density lipoprotein, HDL high-density lipoprotein, CRP C reactive protein

taken into consideration in patients with AIS and these patients should be followed more closely in terms of poor outcomes. On the other hands, RDW and MPV were also found to be associated with AIS in the previous studies [23, 24]. However, we found no association among RDW, MCV, and mortality. This may be due to our small patient population.

Infarct volume is a good predictor of the severity of neurological deficits, functional outcomes, and short-term mortality after stroke [6, 25]. The NIHSS is a neurologic severity scale that is a valid, reliable, and reproducible scale, and it is correlated with infarct volume [12]. It is also showed that NLR is positively correlated with infarct volume and NIHSS [7]. However, these studies included all stroke patients and did not classify the patients according to the stroke territory. In this study, we divided patients into two groups as ACS and PCS according to the stroke territory. Consistent with previous findings in literature, we found that NIHHS was positively correlated with both ACS and PCS infarct volumes. We also detected that NLR was significantly correlated with ACS infarct volume. However, there was no significant correlation between NLR and PCS infarct volume. This unexpected situation between the NLR and PCS infarct volume may possibly be explained as follows. A very small infarct in posterior circulation can be fatal such as pontine infarct which causes severe inflammatory response involving cardio-respiratory system. Thus, the association between NLR and mortality may be based on different mechanisms in the ACS and PCS groups (i.e., extent of tissue necrosis, autonomic derangement, or another mechanism). Our results suggest that both infarct volume and autonomic distress may be related to mortality in ACS, whereas only autonomic distress due to severe deficits, impairment of consciousness, and direct damage to autonomic pathways may be associated with mortality in PCS. To our knowledge, this is the first study that investigates the association of NLR with ACS and PCS infarct volumes. We think that our results will need to be validated in larger prospective studies.

Table 3 The correlation of anterior and posterior infarct volumes with clinical scores and laboratory parameters

		NIHSS	ASPECTS	NLR	CRP	MPV	RDW
ACS infarct volume	r	0.609	0.742	0.482	0.350	−0.150	0.098
	p	< 0.001	< 0.001	< 0.001	0.001	0.173	0.377
PCS infarct volume	r	0.593	–	0.186	0.276	−0.050	0.371
	p	0.003	–	0.396	0.202	0.822	0.082

ACS anterior circulation stroke, PCS posterior circulation stroke, NIHSS National Institutes of Health Stroke Scale, ASPECTS Alberta Stroke Program Early CT Score, NLR neutrophil to lymphocyte ratio, CRP C reactive protein, MPV mean platelet volume, RDW red cell distribution width

Table 4 Comparison of clinical, demographic, and laboratory features in surviving and dead patients

	Surviving patients ($n = 85$)	Dead patients ($n = 22$)	p
Age (years)	65 (52–73)	68.5 (64.7–79)	*0.024*
Male gender, *n* (%)	48 (56.5)	9 (40.9)	0.192
Diabetes mellitus, *n* (%)	25 (29.4)	8 (36.4)	0.529
Hypertension, *n* (%)	55 (64.7)	12 (54.5)	0.380
Hyperlipidemia, *n* (%)	30 (35)	8 (34.7)	0.785
Heart failure, *n* (%)	3 (3.5)	2 (9.1)	0.271
Atrial fibrillation, *n* (%)	6 (7.1)	7 (31.8)	*0.002*
Therapy strategy, *n* (%)			0.621
Endovascular/thrombolytic	18 (21.2)	5 (22.7)	
Anti-aggregant only	67 (78.8)	17 (77.3)	
Stroke territory, *n* (%)			
Anterior circulation stroke	66 (77.6)	18 (81.8)	
Posterior circulation stroke	19 (22.4)	4 (18.2)	0.671
NIHSS	9 (6–15)	13 (8–16)	0.072
Infarct volume, cm^3	4.27 (0.23–17.8)	5.86 (0.46–21.5)	0.697
CRP	1 (05–1.75)	1.84 (1.12–2.15)	*0.004*
NLR	3.04 (2.09–4.6)	5.3 (3.5–10.1)	*< 0.001*
MPV	7.4 (6.9–8.4)	7.4 (6.8–8.0)	0.579
RDW	12.3 (11.3–13.4)	12.9 (12–14.6)	0.061

NIHSS National Institutes of Health Stroke Scale, CRP C reactive protein, NLR neutrophil to lymphocyte ratio, MPV mean platelet volume, RDW red cell distribution width, *P<0.05* was considered as statistically significant

Early risk stratification in patients with AIS is important to determine the appropriate treatment and improve outcomes. Therefore, risk assessment should be performed as soon as possible after patient's admission. NLR is a simple marker and easily obtain from complete blood count. A higher NLR can indicate more severe form of AIS and be a clinically beneficial tool for risk stratification. Therefore, we suggest that NLR can identify the higher-risk patients that required endovascular intervention particularly in ACS patients.

This study has several limitations. First, the study conducted with limited time and sample size was relatively small. It could be interesting to evaluate long-term prognostic value of NLR with a larger sample size in AIS patients. Second, although we excluded patients with active infection, many diseases and factors that might affect inflammatory markers may

Table 5 Univariate and multivariate logistic regression analyses showing the independent predictors of 3-month mortality

	Univariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Age	1.049	1.008–1.092	0.019	1.015	0.971–1.061	0.515
Male gender	1.874	0.723–4.855	0.196			
Hypertension	1.528	0.591–3.950	0.382			
Diabetes mellitus	0.729	0.272–1.955	0.530			
Heart failure	0.366	0.057–2.338	0.288			
Atrial fibrillation	6.144	1.810–20.858	0.004	2.426	0.574–10.261	0.228
NIHHS	1.082	0.990–1.183	0.082	1.025	0.927–1.134	0.628
Stroke territory	1.295	0.391–4.291	0.672			
Therapy strategy	0.913	0.297–2.813	0.875			
Infarct volume	0.994	0.980–1.008	0.388			
CRP	2.345	1.248–4.408	0.008	2.046	0.991–4.221	0.053
NLR	1.245	1.090–1.421	0.001	1.186	1.032–1.363	*0.016*

OR odds ratio, CI confidence interval, NIHSS National Institutes of Health Stroke Scale, CRP C reactive protein, NLR neutrophil to lympocyte ratio, *P<0.05* was considered as statistically significant

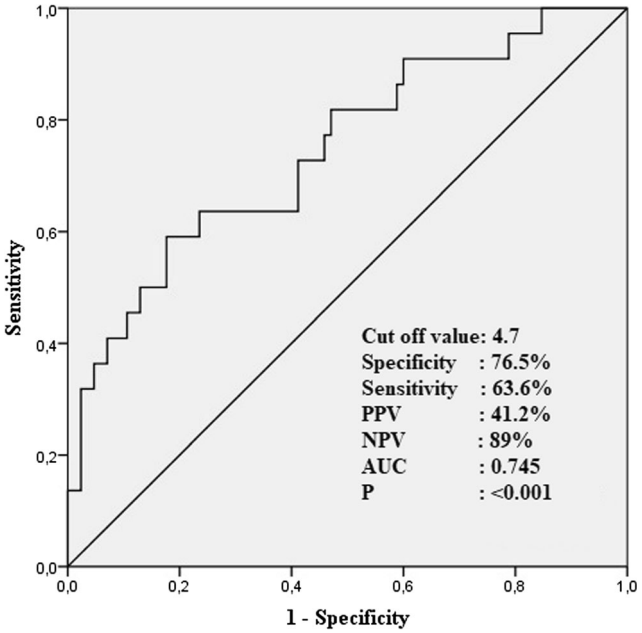

Fig. 1 ROC curve of neutrophil to lymphocyte ratio ≥ 4.7 for predicting 3-month mortality. PPV positive predictive value, NPV negative predictive value

not be taken into consideration. Larger studies with long-term follow-up are required to better elucidate the prognostic role of NLR in AIS patients according to stroke territory.

In conclusion, NLR is significantly correlated with ACS infarct volume, whereas not correlated with PCS infarct volume. In addition, it is an independent predictor of 3-month mortality in AIS patients. Therefore, it may guide the physician deciding the necessity of endovascular intervention particularly in ACS patients.

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Compliance with ethical standards

The study was in compliance with the Declaration of Helsinki principles and was approved by the Institutional Review Boards and Ethical Committee, and all patients involved gave their written informed consent.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, Creager MA, Culebras A, Eckel RH, Hart RG, Hinchey JA, Howard VJ, Jauch EC, Levine SR, Meschia JF, Moore WS, Nixon JV, Pearson TA, American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Epidemiology and Prevention, Council for High Blood Pressure Research, Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research (2011) Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 42:517–584
2. Li W, Yin Q, Xu G, Liu X (2016) Treatment strategies for acute ischemic stroke caused by carotid artery occlusion. Interv Neurol 5(3–4):148–156
3. Libby P, Ridker PM, Maseri A (2002) Inflammation and atherosclerosis. Circulation 105:1135–1143
4. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, Renlund DG, Muhlestein JB, Intermountain Heart Collaborative Study Group (2005) Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 45:1638–1643
5. Buck BH, Liebeskind DS, Saver JL, Bang OY, Yun SW, Starkman S, Ali LK, Kim D, Villablanca JP, Salamon N, Razinia T, Ovbiagele B (2008) Early neutrophilia is associated with volume of ischemic tissue in acute stroke. Stroke 39:355–360
6. Xue J, Huang W, Chen X, Li Q, Cai Z, Yu T, Shao B (2017) Neutrophil-to-lymphocyte ratio is a prognostic marker in acute ischemic stroke. J Stroke Cerebrovasc Dis 26(3):650–657
7. Tokgoz S, Kayrak M, Akpinar Z, Seyithanoğlu A, Güney F, Yürüten B (2013) Neutrophil lymphocyte ratio as a predictor of stroke. J Stroke Cerebrovasc Dis 22:1169–1174
8. Dorňák T, Král M, Hazlinger M, Herzig R, Veverka T, Buřval S, Šaňák D, Zapletalová J, Antalíková K, Kaňovský P (2015) Posterior vs. anterior circulation infarction: demography, outcomes, and frequency of hemorrhage after thrombolysis. Int J Stroke 10: 1224–1228
9. Stroke-Recommendations on stroke prevention, diagnosis, and therapy (1989) Report of the WHO task force on stroke and other cerebrovascular disorders. Stroke 20:1407–1431
10. Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL et al (1993) Classification of subtype of acute ischemic stroke: definitions for use in a multicenter clinical trial: TOAST trial of org 10172 in acute stroke treatment. Stroke 24:35–41
11. Sims JR, Gharai LR, Schaefer PW, Vangel M, Rosenthal ES, Lev MH et al (2009) ABC/2 for rapid clinical estimate of infarct, perfusion, and mismatch volumes. Neurology 2:2104–2110
12. Brott T, Adams HP, Olinger CP, Marler JR, Barsan WG, Biller J et al (1989) Measurements of acute cerebral infarction: a clinical examination scale. Stroke 20:864–870
13. Worthmann H, Tryc AB, Deb M, Goldbecker A, Ma YT, Tountopoulou A, Lichtinghagen R, Weissenborn K (2010) Linking infection and inflammation in acute ischemic stroke. Ann N Y Acad Sci 1207:116–122
14. Wang Q, Tang XN, Yenari MA (2007) The inflammatory response in stroke. J Neuroimmunol 184:53–68
15. Grau AJ, Boddy AW, Dukovic DA, Buggle F, Lichy C, Brandt T, Hacke W, CAPRIE Investigators (2004) CAPRIE investigators. Leukocyte count as an independent predictor of recurrent ischemic events. Stroke 35:1147–1152
16. Kim J, Song TJ, Park JH, Lee HS, Nam CM, Nam HS, Kim YD, Heo JH (2012) Different prognostic value of white blood cell subtypes in patients with acute cerebral infarction. Atherosclerosis 222: 464–467
17. Hallenbeck JM (1996) Significance of the inflammatory response in brain ischemia. Acta neurochir (Suppl) 66:27–31
18. Garau A, Bertini R, Colotta F, Casilli F, Bigini P, Cagnotto A et al (2005) Neuroprotection with the CXCL8 inhibitor repertaxin in transient brain ischemia. Cytokine 30:125–131

19. Chiu NL, Kaiser B, Nguyen YV, Welbourne S, Lall C, Cramer SC (2016) The volume of the spleen and its correlates after acute stroke. J Stroke Cerebrovasc Dis 25(12):2958–2961
20. Qun S, Tang Y, Sun J, Liu Z, Wu J, Zhang J, Guo J, Xu Z, Zhang D, Chen Z, Hu F, Xu X, Ge W (2017) Neutrophil-to-lymphocyte ratio predicts 3-month outcome of acute ischemic stroke. Neurotox Res 31:444–452
21. Zhang J, Ren Q, Song Y, He M, Zeng Y, Liu Z, Xu J (2017) Prognostic role of neutrophil-lymphocyte ratio in patients with acute ischemic stroke. Medicine (Baltimore) 96(45):e8624
22. Zhao L, Dai Q, Chen X, Li S, Shi R, Yu S, Yang F, Xiong Y, Zhang R (2016) Neutrophil-to-lymphocyte ratio predicts length of stay and acute hospital cost in patients with acute ischemic stroke. J Stroke Cerebrovasc Dis 25:739–744
23. Söderholm M, Borné Y, Hedblad B, Persson M, Engström G (2015) Red cell distribution width in relation to incidence of stroke and carotid atherosclerosis: a population-based cohort study. PLoS One 10(5):e0124957
24. Arévalo-Lorido JC, Carretero-Gómez J, Álvarez-Oliva A, Gutiérrez-Montaño C, Fernández-Recio JM, Najarro-Díez F et al (2013) Mean platelet volume in acute phase of ischemic stroke, as predictor of mortality and functional outcome after 1 year. J Stroke Cerebrovasc Dis 22:297–303
25. Yoo AJ, Chaudhry ZA, Nogueira RG, Lev MH, Schaefer PW, Schwamm LH, Hirsch JA, González RG (2012) Infarct volume is a pivotal biomarker after intra-arterial stroke therapy. Stroke 43: 1323–1330