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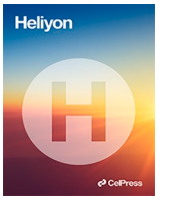

Research article

Value of the red blood cell distribution width (RDW) and neutrophil lymphocyte ratio (NLR) in the prediction of functional recovery and 3-month mortality following endovascular treatment for acute anterior circulation ischemic stroke

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ABSTRACT

Objectives: The red blood cell distribution width (RDW) and neutrophil to lymphocyte ratio (NLR) have been linked to poor prognosis in patients with ischaemic stroke. However, no study has yet evaluated the prognostic role of RDW and NLR, or their combined effect on reperfusion in patients with endovascularly-treated acute ischaemic stroke. This study therefore aimed to analyse the impact of RDW and NLR on poor functional outcomes and failed reperfusion following endovascular treatment in patients with acute **anterior circulation** ischaemic stroke.

Methods: A total of 275 patients with acute **anterior circulation** ischaemic stroke treated endovascularly between 2015 and 2018 were enrolled in this study. The relationships between RDW, NLR, and poor outcomes were analysed using univariate and multivariate logistic regression models and receiver operating characteristic (ROC) curve analysis. The Youden Index was applied to determine the cut-off value.

Results: Multivariate logistic regression analysis identified RDW ($p = 0.015$) and NLR ($p = 0.015$) as independent predictors of mortality at the 3rd month. ROC curve analysis of RDW revealed a cutoff value of 14.25 ($p = 0.009$) for poor clinical outcomes (modified Rankin scale [mRS] 3–6). Similarly, a cutoff value of 14.25 was found for mortality prediction ($p = 0.003$). The cutoff value for poor clinical outcome (mRS 3–6) in the NLR was determined as 5.93 ($p = 0.003$), whereas the cutoff value for mortality was set at 5.17 ($p = 0.028$). RDW also predicted failed reperfusion, with a cutoff value of 17.75 ($p = 0.048$).

Conclusions: High RDW and NLR upon admission were identified as independent indicators of mortality in endovascularly treated acute **anterior circulation** ischemic stroke patients. Furthermore, the RDW could potentially predict failed reperfusion.

1. Introduction

Acute ischaemic stroke (AIS) is a leading cause of disability and a significant contributor to mortality among adults worldwide [1]. Currently, revascularization treatments are being effectively utilised for the treatment of acute ischaemic stroke. Mechanical

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thrombectomy has become the gold standard treatment, particularly for large vessel occlusions [2–6]. Despite successful revascularization, expected clinical improvement is not achieved in some patients. Hence, the ability to predict prognosis is crucial for establishing an appropriate strategy for the treatment of patients with AIS. Although neuroimaging techniques have proven effective for the diagnosis, treatment, and prognosis of stroke, readily available blood biomarkers to assess crucial stroke pathophysiological processes, including neuronal death, inflammation, blood-brain barrier disruption, endothelial dysfunction, and haemostasis, are still lacking [7]. The post-cerebral infarction inflammatory response is a crucial factor in the pathophysiology of stroke, which has a significant impact on the outcomes of the recanalization procedure [8].

Biomarkers are defined as physiological characteristics or biological substances that can be objectively assessed and used as indicators of pathological processes, risk, and pharmacological responses to treatment [9]. Recent studies have identified numerous blood biomarkers to predict stroke prognosis. Red blood cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR) are among the most promising candidate biomarkers currently being investigated [7].

RDW, which represents the heterogeneity of circulating erythrocyte volume, is a biomarker potentially involved in endothelial dysfunction, oxidative stress, and inflammatory processes in vascular diseases [10]. A high RDW has been proposed as an independent predictor of poor outcomes in patients [11–15]. Owing to the accessibility of measurement in the peripheral blood, extensive research has also been conducted on NLR, which serves as an indicator of both innate (neutrophil) and adaptive (lymphocyte) immune responses [16]. A high NLR signifies an imbalance between stroke-induced central and peripheral inflammation [16,17]. High NLR has further been suggested to be associated with both stroke incidence and poor prognosis following stroke [18–20]. The clinical significance of the RDW and NLR in stroke, which are classified as inflammatory biomarkers, can be attributed to the significant role that inflammation plays in the onset of stroke, as well as in the progression and recovery of brain damage [7].

The roles of the RDW and NLR in patients with cerebrovascular disease have been the subject of numerous studies; however, no study has yet examined their influence on reperfusion in patients with endovascularly-treated ischaemic stroke, or their prognostic role. To address this knowledge gap, the present study aimed to determine how RDW and NLR affect the prognosis, 3-month survival, and reperfusion in patients with AIS following endovascular treatment **(EVT)**.

2. Material and methods

2.1. Study population

This study involved a retrospective evaluation of the prospectively-collected data of patients with anterior circulation strokes who underwent endovascular treatment at the **Neurology Clinic of Gaziantep University Şahinbey Research and Application Hospital** between January 2015 and December 2018. **A total of 275 patients who met the inclusion criteria were enrolled.** inclusion criteria were patients who experienced anterior circulation strokes, 1) age 18 years or older at the time of inclusion, 2) underwent groin puncture within the first 6 h following symptom onset, 3) were identified as having intracranial artery occlusion on digital subtraction angiography (DSA), and 4) underwent collection venous blood samples collected prior to the procedure. The exclusion criteria included: 1) patients admitted to the hospital 6 h following the onset of symptoms, 2) those with a recent stroke history of six months or pre-stroke disability, 3) those who had experienced an infection within the previous fortnight, 4) those receiving immunosuppressants or steroids prior to the occurrence of the stroke, 5) prior diagnosis with an immune disorder, 6) prior diagnosis with a haematological disorder, 7) a prior medical history of malignancy, 8) history of surgery or trauma within the previous two weeks, or 9) critical liver, kidney, or cardiac failure.

2.2. Ethical approval

This study was approved by the Ethics Committee of Atatürk University Faculty of Medicine, Turkey (B.30.2. ATA.0.01.00/72; number of meetings: 1; decision number: 34) on 26 January 2023. Explicit patient consent was deemed unnecessary due to the retrospective design of the study, which utilised data extracted from a medical records database.

2.3. Criteria for data collection and evaluation

Patient data including demographic information (age and sex), stroke risk factors, clinical data, imaging findings, and laboratory parameters were all collected. The following stroke risk factors were assessed and recorded: hypertension, diabetes, smoking, atrial fibrillation, coronary artery disease, and history of stroke. The diagnosis and treatment decisions regarding stroke were invariably rendered by two seasoned stroke neurologists. National Institutes of Health Stroke Scale (NIHSS) scores (with higher scores indicating more severe neurological deficits) and computed tomography (CT) images at the time of admission were also assessed. Additionally, the Alberta Stroke Program Early CT scores (ASPECTS) were calculated and recorded.

2.4. Localizations of occlusion, procedures of treatment, and clinical outcomes

Anterior circulatory intracranial artery occlusion was confirmed through DSA. Occlusion regions were classified as follows: tandem occlusion, internal carotid artery (ICA) distal (T-occlusion and L-occlusion), and middle cerebral artery (MCA) M1, MCA M2 and MCA M3-M4. EVT was performed by clinically certified neurointerventionalists. Three classes of endovascular treatment protocols were established: thrombectomy alone, thrombectomy in conjunction with intra-arterial tissue plasminogen activator (IA rtPA), and IA rtPA

alone. Recanalization after EVT was evaluated using the modified Thrombolysis in Cerebral Infarction Scale (mTICI). Successful recanalization was defined as an mTICI score of 2c-3. Symptomatic intracranial haemorrhage (sICH) was defined as a deterioration of ≥4 points in the NIHSS, in conjunction with haemorrhagic transformation (HT) following EVT, as determined by CT [21]. The discharge and the modified Rankin Scale (mRS) scores after 3 months were assessed and recorded (mRS ≤2 denoted a favourable outcome, ≥3 indicated an unfavourable outcome).

2.5. RDW and NLR

Laboratory records were examined prior to the initiation of EVT. RDW and NLR values were calculated by dividing the neutrophil count by the lymphocyte count in the venous blood samples taken at admission.

2.6. Statistical analysis

Data are presented as the mean, standard deviation; median, minimum, maximum; and the percentage and number. The Shapiro–Wilk test, Kolmogorov–Smirnov test, Q-Q plot, skewness, and kurtosis were used to examine the normal distribution of the continuous variables. When comparing two independent groups, if the condition for a normal distribution was met, the Independent Samples *t*-test was applied; otherwise, the Mann–Whitney *U* test was used. When comparing continuous variables with more than two independent groups, the ANOVA test was applied if the data were normally distributed; otherwise, the Kruskal Wallis test was **utilised. Both** multivariate and univariate logistic regression analyses were employed to identify variables that had an independent impact on functional recovery, 3-month mortality, and reperfusion among patients with AIS receiving endovascular treatment. Odds ratios (OR) and corresponding 95 % confidence intervals (CI) were calculated for each variable. In order to ascertain the diagnostic applicability of the continuous variable, **receiver operating characteristic (ROC)** curve analysis was performed to ascertain the diagnostic applicability of continuous variables. In addition, the cutoff value was ascertained using the Youden index. The results of the ROC analyses were reported in terms of the sensitivity and specificity. Analyses were conducted utilizing the statistical analysis program IBM SPSS 20. Statistical significance was set at $p < 0.05$.

Table 1
Baseline and clinical characteristics of the study population.

Variable	n = 275
Demographic data	
Mean age, y, SD	64.4 ± 13.3
Females, n (%)	146 (53.1)
Medical history	
Hypertension, n (%)	192 (69.8)
Diabetes mellitus, n (%)	105 (38.2)
Atrial fibrillation, n (%)	92 (33.5)
Coronary artery disease, n (%)	70 (25.5)
Smoking, n (%)	89 (32.4)
Previous stroke or TIA, n (%)	25 (9.1)
Clinical data	
Median NIHSS, points (IQR)	16 (5–29)
Median ASPECTS, points (IQR)	9 (5–10)
Pretreatment with intravenous thrombolysis, n (%)	37 (13.5)
Occlusion site, n (%)	
Tandem occlusion	63 (22.9)
ICA	38 (13.8)
MCA M1	98 (35.7)
MCA M2	38 (13.8)
MCA M3-M4	38 (13.8)
Operation modes, n (%)	
Intraarterial thrombolysis	33 (12)
Mechanical Thrombectomy	75 (27.3)
Mechanical Thrombectomy and Intraarterial thrombolysis	167 (60.7)
Recanalization outcomes, n (%)	
mTICI 2b-3	237 (86.2)
mTICI 2c-3	188 (68.4)
Clinical outcomes	
Hemorrhagic transformation, n (%)	91 (33.1)
Symptomatic intracranial haemorrhage, n (%)	46 (16.7)
mRS 3–6 at 3 month, n (%)	181 (65.8)
Mortality at 3 month, n (%)	95 (34.5)
Laboratory data	
RDW	14.30 (1.90)
NLR	4.53 (5.03)

3. Results

3.1. Basic characteristics and clinical results

The study population comprised 275 patients with large vessel occlusion (LVO) who received endovascular treatment and met all of the aforementioned the inclusion criteria. The mean age was 64.4 ± 13.3, with 146 (53.1 %) being female. At admission, the mean ASPECT score was 9.0 ± 1.1 (range: 5–10, median: 9.0) and the mean NIHSS score was 16.1 ± 5 (range: 5–29, median: 16). The mean NLR was 6.06 ± 5.53 (range: 0.56–46.33; median: 4.53) and the mean RDW prior to EVT was 14.82 ± 2.18 (range: 9.90–24.90; median: 14.30). Recanalization was successfully accomplished in 188 patients (68.4 %) following EVT (mTICI 2c-3). At the 3rd month following the occurrence of stroke, a poor clinical outcome (mRS 3–6) was observed in 181 patients (65.8 %), with 46 patients (16.7 %) developing sICH. A summary of the baseline demographic and clinical characteristics of the patients is shown in Table 1.

Poor outcomes, which include a 3-month low mRS score (3–6), mortality by the third month, sICH, and failed recanalization (mTICI 0–2b), are detailed in Table 2. Significant differences were observed in age, NIHSS score, ASPECT score, RDW, and NLR values among patients who had poor clinical outcomes at the 3rd month (mRS 3–6, mortality) ($p < 0.5$ for all). Significantly higher RDW (14.7 vs. 14.2, $p = 0.048$), NIHSS score (18 vs. 15, $p < 0.001$), and age (71 vs. 66, $p = 0.019$) were observed in patients who experienced failed recanalization (mTICI 0–2b). Significantly higher NIHSS (18 vs. 16; $p = 0.000$) and ASPECTS (8 vs. 9; $p = 0.004$) scores were observed in patients with sICH.

3.2. Univariate and multivariate logistic regression analysis

The 3rd month mRS (3–6), 3rd month mortality, sICH, and failed recanalization (mTICI 0–2b) were determined as dependent variables associated with adverse outcomes. Independent variables included age, admission NIHSS score, ASPECT score, RDW, and NLR. Using these variables, univariate analysis revealed that the admission NIHSS score, ASPECTS score, and NLR were associated with poor prognosis at the 3rd month, as indicated by an mRS score of 3–6. Similarly, the NIHSS score at admission, RDW, and NLR were found to be associated with mortality at the 3rd month. Furthermore, the admission NIHSS score was associated with both symptomatic intracranial haemorrhage (sICH) and failed reperfusion (mTICI 0–2b), as presented in Table 3. In the context of multivariate analysis, it was observed that the NIHSS (OR, 0.818; 95 % CI, 0.765–0.876; $p = 0.000$) and ASPECTS (OR, 1.722; 95 % CI, 1.266–2.341; $p = 0.001$) scores at admission were indicative of the 3rd month poor prognosis (mRS 3–6); The admission NIHSS score (OR, 1.283; 95 % CI, 1.193–1.380; $p = 0.000$), RDW (OR, 1.176; 95 % CI, 1.031–1.340; $p = 0.015$), and NLR (OR, 1.064; 95 % CI, 1.012–1.119; $p = 0.015$) were also found to be associated with the 3rd month mortality. The admission NIHSS score remained significantly associated with sICH (odds ratio [OR], 1.124; 95 % CI, 1.051–1.202; $p = 0.001$) and failed reperfusion (mTICI 0–2b) (OR, 0.858; 95 % CI, 0.809–0.910; $p = 0.000$). RDW and NLR have been identified as potential independent risk factors for prediction of the 3rd month mortality. Furthermore, the admission NIHSS score was identified as a notable independent risk factor for the 3rd month

Table 2
Comparison of the clinical characteristics and outcomes in patients undergoing EVT.

Characteristics	Patients (N = 275)	Favourable (N =)	Unfavourable (N =)	P-Value
		mRS 0–2 (N = 94)	mRS 3–6 (N = 181)	
Median age, years	67 (28–100)	60 (28–100)	69 (33–90)	< **0.001**
Median NIHSS, points (IQR)	16 (5–29)	12 (5–24)	18 (6–29)	< **0.001**
Median ASPECTS, points (IQR)	9 (5–10)	10 (7–10)	9 (5–10)	< **0.001**
RDW	14.30 (9.90–24.90)	13.90 (9.90–21.70)	14.60 (10.00–24.90)	**0.006**
NLR	4.53 (0.56–46.33)	3.53 (0.86–28.04)	4.84 (0.56–46.33)	**0.002**
		Mortality (No) (N = 95)	**Mortality (Yes) (N = 180)**	
Median age, years	67 (28–100)	66 (28–100)	69 (34–90)	**0.030**
Median NIHSS, points (IQR)	16 (5–29)	14 (5–26)	19 (8–29)	< **0.001**
Median ASPECTS, points (IQR)	9 (5–10)	9 (5–10)	9 (5–10)	**0.006**
RDW	14.30 (9.90–24.90)	14.00 (9.90–21.70)	14.80 (11.40–24.90)	**0.004**
NLR	4.53 (0.56–46.33)	4.09 (0.73–28.04)	5.24 (0.56–46.33)	**0.042**
		sICH (No) (N = 56)	**sICH (Yes) (N = 46)**	
Median age, years	67 (28–100)	67 (28–100)	68 (40–90)	0.188
Median NIHSS, points (IQR)	16 (5–29)	16 (5–29)	18 (10–28)	< **0.001**
Median ASPECTS, points (IQR)	9 (5–10)	9 (5–10)	8 (6–10)	**0.004**
RDW	14.30 (9.90–24.90)	14.20 (9.90–24.90)	14.80 (11.40–23.90)	0.121
NLR	4.53 (0.56–46.33)	4.49 (0.56–28.04)	5.28 (0.70–46.33)	0.381
		Successful reperfusion (N = 188)	**Unsuccessful reperfusion (N = 87)**	
Median age, years	67 (28–100)	66 (28–100)	71 (34–90)	**0.019**
Median NIHSS, points (IQR)	16 (5–29)	15 (5–26)	18 (6–29)	< **0.001**
Median ASPECTS, points (IQR)	9 (5–10)	9 (5–10)	9 (5–10)	0.342
RDW	14.30 (9.90–24.90)	14.20 (10.00–23.50)	14.70 (9.90–24.90)	**0.048**
NLR	4.53 (0.56–46.33)	4.20 (0.86–46.33)	4.80 (0.56–34.98)	0.138

Table 3
Results of univariate and multivariate logistic regression analysis.

		Univariate Analysis			Multivariate Analysis		
		OR	95%CI	P	OR	95%CI	P
mRS	Age	0.978	0.957–1.000	0.051			
	NIHSS	0.821	0.765–0.881	0.000	0.818	0.765–0.876	0.000
	ASPECTS	1.635	1.197–2.234	0.002	1.722	1.266–2.341	0.001
	RDW	0.871	0.757–1.002	0.053			
	NLR	0.938	0.880–0.999	0.048	0.939	0.882–1.000	0.051
Mortality	Age	1.013	0.991–1.037	0.254			
	NIHSS	1.271	1.180–1.369	0.000	1.283	1.193–1.380	0.000
	ASPECTS	0.904	0.698–1.172	0.446			
	RDW	1.169	1.025–1.334	0.020	1.176	1.031–1.340	0.015
	NLR	1.062	1.010–1.117	0.018	1.064	1.012–1.119	0.015
sICH	Age	1.009	0.983–1.035	0.515			
	NIHSS	1.102	1.027–1.182	0.007	1.124	1.051–1.202	0.001
	ASPECTS	0.805	0.611–1.060	0.122			
	RDW	1.054	0.909–1.223	0.488			
	NLR	1.036	0.984–1.092	0.178			
Reperfusion	Age	0.982	0.961–1.004	0.101			
	NIHSS	0.854	0.812–0.918	0.000	0.858	0.809–0.910	0.000
	ASPECTS	0.957	0.751–1.220	0.724			
	RDW	0.940	0.830–1.064	0.326			
	NLR	0.994	0.947–1.042	0.790			

poor clinical outcome (mRS score of 3–6), mortality, sICH, and failed reperfusion (mTICI score of 0–2b).

3.3. Prognostic analysis of RDW and NLR in patients undergoing EVT

The cutoff value of RDW which could be used to predict the 3-month prognosis in patients undergoing EVT, was 14.25 (AUC = 0.595; 95 % CI, 0.526–0.655; p = 0.009) for poor clinical outcomes (mRS 3–6), and 14.25 (AUC = 0.608; 95 % CI, 0.537–0.679; p = 0.003) for mortality (Table 4). The cut-off value of NLR for a poor clinical outcome (mRS 3–6) was 5.93 (AUC = 0.609; 95 % CI, 0.540–0.679; p = 0.003), and the cut-off value for mortality was 5.17 (AUC = 0.580; 95 % CI, 0.508–0.653; p = 0.028) (Table 4). With a cutoff value of 17.75, RDW also predicted failed reperfusion (AUC = 0.574; 95 % CI, 0.501–0.647; p = 0.048) (Table 4). Age was further found to be a predictor of poor clinical outcome (mRS 3–6), 3-month mortality, and failed reperfusion (Table 4), while the independent variables of admission NIHSS and ASPECTS scores predicted poor clinical outcome (mRS 3–6), 3-month mortality, and sICH.

4. Discussion

Our study is one of few studies with such a large sample size to jointly assess the prognostic role of RDW and NLR in patients who

Table 4
Diagnostic efficacy of markers related to unfavourable outcomes.

	Prediction	AUC	95%CI	Cut off	Sensitivity (%)	Specificity (%)	Youden Index	p
mRS	Age	0.641	0.573–0.709	64.50	65.9	61.1	0.270	**0.000**
	NIHSS	0.764	0.705–0.823	14.50	76.0	65.3	0.412	**0.000**
	ASPECTS	0.322	0.257–0.387	8.50	56.4	14.7	−0.288	**0.000**
	RDW	0.595	0.526–0.655	14.25	57.5	63.2	0.207	**0.009**
	NLR	0.609	0.540–0.679	5.93	41.9	77.9	0.198	**0.003**
Mortality	Age	0.587	0.517–0.656	67.50	58.3	58.1	0.164	**0.018**
	NIHSS	0.788	0.734–0.842	15.50	85.4	59.8	0.452	**0.000**
	ASPECTS	0.397	0.325–0.468	8.50	53.1	26.3	−0.206	**0.005**
	RDW	0.608	0.537–0.679	14.25	64.6	57.5	0.221	**0.003**
	NLR	0.580	0.508–0653	5.17	53.1	63.1	0.163	**0.028**
sICH	Age	0.561	0.474–0.648	55.50	87.2	25.4	0.127	0.189
	NIHSS	0.664	0.591–0.737	16.50	72.3	60.5	0.329	**0.000**
	ASPECTS	0.374	0.289–0.459	9.50	25.5	52.6	−0.218	**0.007**
	RDW	0.572	0.483–0.660	14.50	57.4	59.2	0.167	0.121
	NLR	0.541	0.449–0.632	5.26	51.1	61.4	0.125	0.381
Reperfusion	Age	0.588	0.516–0.660	68.50	55.2	62.2	0.174	**0.019**
	NIHSS	0.691	0.624–0.758	14.50	80.5	47.3	0.278	**0.000**
	ASPECTS	0.466	0.391–0.542	8.50	60.9	30.9	−0.082	0.370
	RDW	0.574	0.501–0.647	17.75	49.4	66.5	0.159	**0.048**
	NLR	0.556	0.484–0.628	3.78	66.7	46.3	0.129	0.138

underwent endovascular treatment for AIS. This study showed that high RDW and NLR values at admission were associated with the 3rd month poor clinical outcomes in the third month of EVT, and could also serve as independent risk factors, particularly for mortality. In addition, high RDW values may act as an indicator of failed reperfusion. Endovascular treatment is of the utmost importance in managing AIS because of its substantial socioeconomic burden, high mortality, and morbidity. Nevertheless, successful reperfusion may not be achievable with EVT in certain patients, while favourable clinical outcomes may not be achieved in certain patients despite successful reperfusion. For the aforementioned reasons, it is important to develop a way to predict patient prognosis prior to deciding on EVT, which is a costly and invasive procedure. Although advanced neuroimaging techniques are valuable for treatment decision making and prognosis prediction, they are difficult to obtain, prohibitively expensive, and time consuming. As such, rapid, inexpensive, and readily available biomarkers are gaining importance. One recent meta-analysis that examined six prospective biomarkers, including RDW and NLR [7], centred on these biomarkers. The initial definition and reporting of the relationship between the RDW and cardiovascular were described by Tonelli et al. Their study demonstrated a relationship between a high RDW and heightened susceptibility to stroke [22]. Subsequent studies have confirmed that high RDW values increase the risk of AIS [23,24]. Recent studies have further emphasised the relationship between the RDW and prognosis. For example, one study conducted by Fan et al. demonstrated a relationship between high RDW values and poor prognosis among patients with AIS [11]. Similarly, Zhao et al. recently demonstrated that the RDW is associated with all-cause mortality in patients with AIS, and could be used a prognostic factor [25]. Research has further examined the relationship between RDW and prognosis in patients receiving intravenous thrombolytic treatment and demonstrated that RDW can accurately predict poor functional outcomes [15,26]. Indeed, two recently published studies [14,27] indicated that RDW may serve as an independent predictor of mortality and poor prognosis among patients with endovascularly treated AIS. Our findings are consistent with those of previous studies. Furthermore, logistic regression analysis revealed that high RDW could serve as a mortality risk factor for patients with endovascularly treated AIS. The pathophysiological processes of AIS are influenced by the NLR, as demonstrated by numerous studies and recent meta-analyses. Furthermore, a high NLR has been identified as an indicator of poor prognosis in AIS in many studies [7,11,16–18].

Several recent studies have further examined the association between high NLR and poor prognosis and mortality in patients undergoing endovascular treatment. For example, Duan et al. demonstrated that the initial NLR independently predicted 3-month functional outcomes, and showed a trend towards an association with mortality in patients with acute anterior circulation large-vessel occlusion following EVT [28]. Goyal et al. further demonstrated that a high NLR upon admission was an independent predictor of 3-month mortality in patients undergoing mechanical thrombectomy for large-vessel occlusion [20]. In a recent study, Li et al. also examined prognostic biomarkers following mechanical thrombectomy. Their findings demonstrated that NLR, as determined by the new peripheral blood cell ratios, could serve as a practical prognostic biomarker and an independent risk factor for poor 3-month prognosis [19]. The findings of our study, which are consistent with the literature, demonstrated that NLR is associated with mortality and poor prognosis. Logistic regression analysis showed that a high NLR may be an independent risk factor for mortality in patients with endovascularly treated AIS, and ROC curve analyses demonstrated the predictive value of NLR for poor clinical outcomes and mortality.

Inflammation plays a key role in numerous pathophysiological processes [19]. Previous studies have demonstrated that increased levels of inflammatory biomarkers, including C-reactive protein (CRP) and interleukin-6 (IL-6), are associated with the poor outcomes following AIS. Furthermore, the prognosis of AIS has been shown to be predominantly influenced by the magnitude of the inflammatory reaction [29,30]. Studies have further demonstrated that RDW and NLR act as inflammatory markers, and are associated with established inflammatory markers, including CRP and erythrocyte sedimentation rate (ESR) [11]. Thus, the prognostic value of the NLR and RDW in relation to AIS may be mediated by the inflammatory response. The precise mechanism by which high RDW contributes to increased mortality in patients with AIS remains unknown. The RDW may also be associated with inflammation and oxidative stress in the vascular system [14]. High RDW values result in thickening of the carotid intima, a condition that progresses to atherosclerosis and is a significant risk factor for ischemic stroke [31]. Inflammation and oxidative stress can also impair erythropoiesis and increase RDW, which is indicative of anisocytosis. A high RDW has the potential to negatively affect the integrity of blood cells by inducing membrane injury. Impaired microcirculation could, in turn, lead to the aggravation of ischaemia, penumbral loss, and ultimately poor functional consequences [32–34]. The NLR, a novel biomarker, offers significant insights into the destructive effects of neutrophils and the protective effects of lymphocytes during inflammatory processes, enabling a more comprehensive assessment of both the innate (lymphocytic) and adaptive (neutrophil) immune responses [16,35]. Lymphocytes and neutrophils are involved in the pathophysiological process of AIS from its onset [36]. Neutrophils accumulate in the infarcted region in the early stages of AIS. The release of cell-adhesion molecules, free oxygen radicals, and proteases may directly or indirectly exacerbate brain damage. Furthermore, they could increase the expression of matrix metalloproteinase-9 (MMP9), a protein that disrupts the blood-brain barrier (BBB), and potentially induce secondary brain damage [28,36,37]. Lymphocytes, which are involved in various inflammatory processes, exert anti-inflammatory effects during the late phase [38]. As such, they can reduce neurological deficits and infarct volume, thereby playing a neuroprotective function [35,39,40]. One study that examined the correlation between NLR and infarct volume demonstrated that NLR was an independent predictor of 3-month mortality, and was associated with infarct volume in patients with anterior circulation stroke [41]. The role of NLR in pathologies such as COVID, where inflammation is an important trigger, has been examined in numerous studies conducted during the COVID pandemic. The potential benefits of successful thrombectomy may further be negated by the severe neuroinflammatory stress response associated with COVID-19, while a high NLR has been associated with worse outcomes and increased mortality [42,43]. The results of one recent study have further demonstrated that positive changes in follow-up NLR values and NLR measurements at admission are associated with a positive functional outcome. Additionally, the NLR is a valuable marker for identifying patients at risk of poor functional outcomes [44].

A major finding of our study was that high RDW values could serve as a predictor of failed reperfusion. Unfortunately, the existing

literature on failed reperfusion in patients with AIS is scarce. Previous studies have primarily examined the clinical and technical aspects of failed reperfusion, including vascular anatomy, occlusion localisation, and procedure selection [45]. However, the relationship between the inflammatory markers NLR and platelet lymphocyte ratio (PLR) and reperfusion was examined in one study that demonstrated that these markers could be used to predict failed reperfusion [46]. However, to the best of our knowledge, no studies have yet evaluated the efficacy of RDW reperfusion in AIS. A high RDW may appear to be associated with poor prognosis, particularly because of the harm it causes to microcirculation; however, the precise mechanism by which it diminishes reperfusion success remains unclear [32,45].

Our study has the following limitations: it was a retrospective, single-centre investigation with a relatively small number of subjects; RDW and NLR values were only recorded at the time of admission; there were no follow-up values; and the prognostic evaluation was restricted to 3 months.

5. Conclusion

Overall, the present study demonstrated that RDW and NLR, which are readily available, inexpensive, and simple to measure from peripheral blood, can assist in prognostic prediction when deciding on EVT, an invasive and costly treatment method for ischaemic stroke, a disease which inflicts a significant socioeconomic burden. Furthermore, we demonstrated that RDW could be used to predict failed reperfusion. However, further investigation is required to understand the potential utility of these biomarkers in predicting the prognosis and procedural success in endovascularly treated patients.

Ethical statement

This study was approved by the Ethics Committee of Atatürk University Faculty of Medicine, Turkey (B.30.2. ATA.0.01.00/72; number of meetings: 1; decision number: 34) on 26 January 2023. Explicit patient consent was deemed unnecessary due to the retrospective design of the study, which utilised data extracted from a medical records database.

Data availability statement

Data are available from the authors upon reasonable request.

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CRediT authorship contribution statement

Alper Eren: Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Semih Giray:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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