Journal of Integrative Neuroscience

J. Integr. Neurosci. **2023**; 22(3): 78
https://doi.org/10.31083/j.jin2203078

Original Research

Red Cell Distribution Width and Futile Recanalization in Individuals with Acute Ischemic Stroke following Endovascular Treatment

Zhengyang Wang[1,*], Yin Liu[1,*]

[1]Jiangsu Taizhou People's Hospital, 225300 Taizhou, Jiangsu, China
*Correspondence: Wangzy19930201@163.com (Zhengyang Wang); lindaandtony@163.com (Yin Liu)
Academic Editor: Beata Sarecka-Hujar
Submitted: 31 July 2022 Revised: 24 August 2022 Accepted: 29 August 2022 Published: 19 May 2023

Abstract

Background: Previous studies reported that red cell distribution width (RDW) was related to acute ischemic stroke (AIS). Endovascular treatment (EVT) still faces a huge challenge: futile recanalization. The goal of our study was to investigate the relationship between futile recanalization and RDW in AIS patients receiving EVT. **Methods**: We retrospectively identified 188 AIS individuals with anterior circulation occlusion throughout EVT and obtained complete or near-total recanalization. The subjects were classified into futile recanalization group by their 3-month modified Rankin scale (mRS) score $\geq$3. The predictive value of RDW was calculated using receiver operating characteristic (ROC) curves, area under the curve (AUC) values, and logistic regression approaches. **Results**: One hundred and eleven (59.0%) patients were defined as futile recanalization. The RDW was observed as an novel factor of futile recanalization in the multivariate regression model ([OR, odd-ratio] = 5.233, 95% [CI, confidence interval] = 2.656–10.307; $p < 0.001$). According to the ROC, the model integrating RDW with other risk factors had a relatively higher AUC compared than the RDW alone model (0.944 *vs* 0.798; $p < 0.001$) via DeLong's test. **Conclusions**: Higher RDW is associated with poor functional outcome in anterior circulation AIS patients undergoing EVT at 3 months.

Keywords: red cell distribution width; acute ischemic stroke; prognosis; futile recanalization; endovascular treatment

1. Introduction

Acute ischemic stroke (AIS) is a leading cause of disability and mortality worldwide [1]. Clinical trials have proved that endovascular treatment (EVT) improves functional outcomes for large arterial occlusion patients regardless of prior intravenous thrombolysis (IVT) [2–4]. The patient's prognosis with similar characteristics may differ substantially. Indeed, futile recanalization, defined as poor clinical outcome despite early recanalization of an occluded artery, remains a significant challenge [5]. It could be associated to microvascular injury, poor collateral circulation and brain autoregulation [6].

As the peripheral blood index, red cell distribution width (RDW) is well-known to be a risk marker for vessel wall injury and cardiovascular disease [7,8]. Increased RDW correlates with increased risk for carotid atherosclerosis, which in turn promotes the incidence of stroke [9]. High RDW was found to be related to unfavorable outcomes in AIS patients [10]. So far, the relationship between poor outcome and RDW in AIS patients through complete recanalization remains unclear [11]. Therefore, this work aims to study whether RDW could be a risk indicator for futile recanalization in AIS patients following EVT.

2. Materials and Methods

2.1 Study Design

Between January 2018 and December 2021, we investigated 289 consecutive AIS patients treated with EVT alone or IVT with EVT at Taizhou People's Hospital. After mechanical thrombectomy, the modified Thrombolysis in Cerebral Infarction (mTICI) scores of 2b–3 were determined as recanalization [12]. A total of 211 patients were included in our cohort.

Inclusion criteria for patients

(1) Occlusion of a major anterior circulation artery, together with anterior cerebral artery (ACA), middle cerebral artery first segment (MCA M1), MCA second segment (MCA M2), internal carotid artery (ICA), ICA terminus (ICA-T), (2) Age over 18 years, (3) The pretreatment modified Rankin Scale (mRS) score of 0–2.

Exclusion criteria for patients

Patients were excluded who had an active internal hemorrhage, hematologic diseases or active bleeding indications, heart failure, cerebral aneurysm, recent cerebral hemorrhage, and intracranial tumor. We also excluded participants with insufficient clinical and follow-up information.

Upon admission, laboratory data of patients were acquired, including white blood cells (WBC), platelets (PLT), red blood cells (RBC), and red cell distribution width (RDW). Risk factors such as demographic characteristics, history of stroke or transient ischemic attack (TIA), pre-

existing comorbidities (such as diabetes, hyperlipidemia, hypertension, atrial fibrillation, coronary heart disease) as well as serum glucose and blood pressure were collected at baseline while onset to recanalization time (OTR) were documented at hospital records [13]. Using the Alberta Stroke Program Early CT Score (ASPECTS) on head computed tomographic angiography (CTA), the extension of ischemic lesion was assessed [14]. The neurological impairment proportion was estimated using the NIH Stroke Scale (NIHSS) score [15]. According to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification, subtypes of stroke were determined [16].

CT scans were examined during the hospitalization, the therapy was changed if hemorrhagic transformation (HT) was observed [17]. Through standardized telephone surveys, the follow-up data was gathered.

According to the mRS score at 3 months after EVT, the subjects were classified into the successful recanalization group (good prognosis, mRS score 0–2) and the futile recanalization group (poor prognosis, mRS score 3–6) [18,19].

This study was approved by our hospital's ethics committee, and informed consent requirement was waived owing to the retrospective nature.

2.2 Statistical Analysis

The SPSS 21.0 (IBM Corp, Armonk, NY, USA) was applied to analyze the statistical data in the present study, and $p < 0.05$ was regarded as significant statistically. To describe the normal distribution for continuous variables, the means $\pm$ standard deviation (SD) were utilized; and were examined through ANOVA analysis. Non-normally distributed continuous variables, on the other hand, were reviewed through Mann–Whitney U-test and stated as median (interquartile range [IQR]). The chi-square test was applied for categorical variables comparison. Binary stepwise logistic regression analysis was performed to find the independent predictors, which comprised variables with a $p < 0.05$ in univariate analysis. The predictive value of the models using RDW alone and RDW paired with additional parameters was measured through receiver-operating characteristic (ROC) curves. The area under the curve (AUC) was used to calculate the optimum cut-off values. MedCalc 9.0 (MedCalc Software Ltd, Ostend, Belgium) was used for comparisons of ROC curve AUC values.

3. Results

Following excluding 23 patients, the present work had 188 subjects (Fig. 1), with 70 median years old (IQR 60–77), while 39.4% were female patients. The mean RDW value was 13.0 $\pm$ 1.26. The median baseline NIHSS score was 16 (IQR 10–19). Almost 51.9 % (86/188) had good collateral flow (ASPECTS 8-10) to a certain degree [20]. The sites of obstruction including: ICA in 66 patients (35.1%), ICA-T in 4 patients (2.1%), MCA M1 in 86 patients (45.7%), MCA M2 in 31 patients (16.5%), and ACA in 1 patient (0.5%). Overall, 111 out of 188 (59.0%) patients finally had poor functional outcome at 3 months. All patients' clinical and baseline characteristics are given below in Table 1.

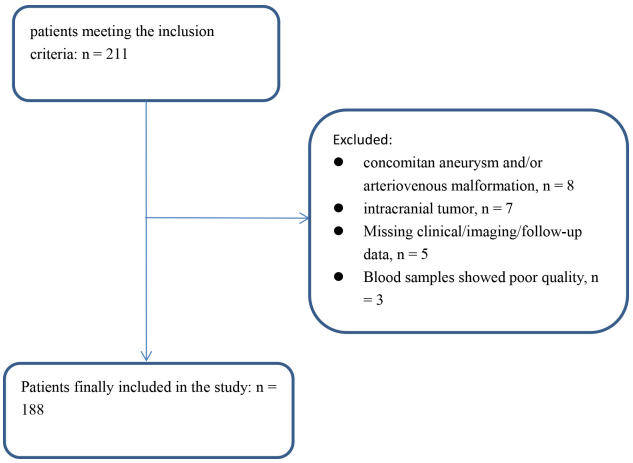

Fig. 1. Flowchart of inclusion and exclusion.

Age ($p = 0.017$), ASPECTS 8-10 ($p < 0.001$), the NIHSS score ($p < 0.001$), and HT ($p < 0.001$), as well as the subtype of stroke ($p = 0.012$), were all substantially different when comparing the two groups. In comparison with the significant recanalization group, the futile recanalization patients exhibited higher systolic blood pressure ($p = 0.007$), blood glucose ($p = 0.011$), and RDW value (13.4 $\pm$ 1.33 *vs* 12.5 $\pm$ 0.72; $p < 0.001$). The OTR time was not substantially associated with a 3-month futile recanalization ($p = 0.591$).

The binary logistic regression analyses included variables with a $p < 0.05$ in the univariate analysis, as shown in Table 2. Systolic blood pressure (odds ratio (OR), 1.028; 95% confidence interval (CI), 1.008–1.049; $p = 0.028$), hemorrhagic transformation (OR, 5.701; 95% CI, 1.991–16.324; $p = 0.001$), NIHSS score (OR, 1.106; 95% CI, 1.017–1.203; $p = 0.019$), ASPECTS 8–10 (OR, 0.045; 95% CI, 0.016–0.128; $p < 0.001$) were all important risk factors. The higher RDW (OR = 5.233, 95% CI: 2.656–10.307, $p < 0.001$) patients, even after complete recanalization, there is a considerably increased probability of a poor 3-month outcome.

As shown with ROC analysis (Fig. 2), the RDW was found as a respective predictor of futile recanalization, having an AUC of 0.798 and an optimal cut-off value of 13.25 (specificity 87% and sensitivity 60%). Variables discovered through regression analysis were incorporated into an integrated model. The combined model had a significantly higher AUC compared with the RDW alone model (0.944 *vs* 0.798; $p < 0.001$). Thus, it was more effective significantly.

Table 1. Detailed Baseline and Clinical Features of the Patients.

Variables	Total (n = 188)	Futile Recanalization (n = 111)	Successful Recanalization (n = 77)	*p* value
Demographics				
Age (median, IQR)	70 [60–77]	71 [64.5–77.5]	68 [52–75]	0.017
Females, n (%)	74 (39.4)	43 (38.7)	31 (40.3)	0.834
Medical history				
Current smoker, n (%)	34 (18.1)	16 (14.4)	18 (23.4)	0.116
Drinking, n (%)	28 (14.9)	15 (13.5)	13 (16.9)	0.523
Hypertension, n (%)	105 (55.9)	67 (60.4)	38 (49.4)	0.135
Diabetes mellitus, n (%)	30 (16.0)	20 (18.0)	10 (13.0)	0.354
Hyperlipidemia, n (%)	75 (39.9)	43 (38.7)	32 (41.6)	0.698
Coronary heart diseases, n (%)	20 (10.6)	13 (11.7)	7 (9.1)	0.567
Atrial fibrillation, n (%)	99 (52.7)	62 (55.9)	37 (48.1)	0.292
Previous stroke or TIA, n (%)	31 (16.5)	19 (17.1)	12 (15.6)	0.781
Clinical assessment on admission				
systolic blood pressure (mean, SD)	143 ± 23.4	146 ± 23.81	140 ± 21.8	0.007
dyastolic blood pressure (mean, SD)	85 ± 13.6	89 ± 13.65	83 ± 13.3	0.066
Glucose, mmol/L, median (IQR)	7.0 [6.4–8.1]	7.0 [6.6–9.2]	6.8 [5.8–7.6]	0.011
NIHSS SCORE, median (IQR)	16 [10–19]	16 [14–20]	12 [8–16]	<0.001
ASPECTS 8-10, n (%)	80 (42.6)	19 (17.1)	61 (79.2)	<0.001
OTR time (min) (mean ± SD)	420 ± 212.5	420 ± 188.8	400 ± 243.9	0.591
Occlusion site				0.131
ICA, n (%)	66 (35.1)	43 (38.7)	23 (29.9)	
ICA-T, n (%)	4 (2.1)	1 (0.9)	3 (3.9)	
MCA M1, n (%)	86 (45.7)	53 (47.7)	33 (42.9)	
MCA M2, n (%)	31 (16.5)	14 (12.6)	17 (22.1)	
ACA, n (%)	1 (0.5)	0 (0.0)	1 (1.3)	
Stroke etiology				0.012
Atherosclerotic, n (%)	78 (41.4)	48 (43.2)	30 (39.0)	
Cardioembolic, n (%)	96 (51.2)	60 (54.1)	36 (46.8)	
Undetermined or others, n (%)	14 (7.4)	3 (2.7)	11 (14.3)	
Laboratory data				
WBC (mean, SD)	8.20 ± 2.76	8.04 ± 2.96	8.32 ± 2.45	0.508
Neutrophils (mean, SD)	6.43 ± 2.85	6.62 ± 3.10	5.80 ± 2.40	0.179
Lymphocytes (mean, SD)	1.01 ± 0.84	0.85 ± 0.71	1.19 ± 0.97	0.019
Monocytes (mean, SD)	0.39 ± 0.24	0.33 ± 0.24	0.41 ± 0.24	0.057
RBC (mean, SD)	4.41 ± 0.69	4.34 ± 0.76	4.42 ± 0.58	0.579
PLT (mean, SD)	166.5 ± 68.06	160.0 ± 66.92	171.0 ± 70.01	0.592
RDW (mean, SD)	13.0 ± 1.26	13.4 ± 1.33	12.5 ± 0.72	<0.001
Prior IVT, n (%)				0.669
YES	47 (25.0)	29 (26.1)	18 (23.4)	
NO	141 (75.0)	82 (73.9)	59 (76.6)	
Hemorrhagic transformation, n (%)				<0.001
YES	77 (41.0)	59 (53.2)	18 (23.4)	
NO	111 (59.0)	52 (46.8)	59 (76.6)	

Table 2. Association between baseline characteristics and futile recanalization.

Variables	OR	95% CI	β	p value
Systolic blood pressure	1.028	1.008–1.049	0.028	0.007
Hemorrhagic transformation	5.701	1.991–16.324	1.741	0.001
RDW	5.233	2.656–10.307	1.655	<0.001
NIHSS SCORE	1.106	1.017–1.203	0.101	0.019
ASPECTS 8-10	0.045	0.016–0.128	–3.104	<0.001

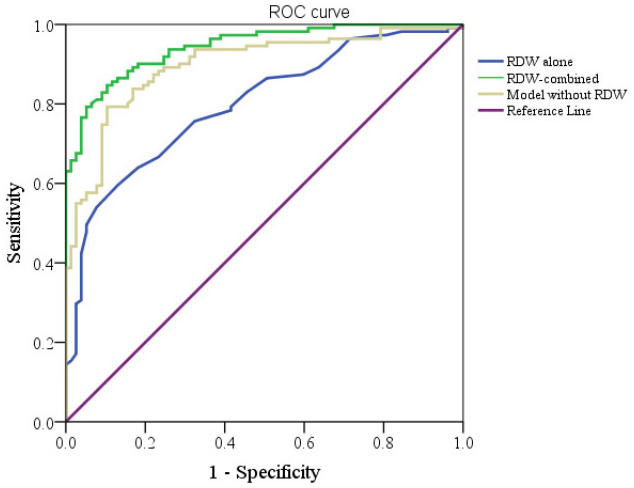

Fig. 2. ROC curve of RDW-combined, without RDW and RDW alone model.

4. Discussion

The clinical impact of EVT in treating AIS patients has been documented; however, not all fully recanalized patients will be capable of achieving premorbid functionality. Futile recanalization eventually brings physical disability as well as broader pressure to stroke survivors. The prediction of recanalization is pivotal to select patients prior to EVT. In clinical settings, RDW is a readily available and easily assessed blood parameter. Several studies have linked higher RDW levels with ischemic stroke morbidity and mortality [21–23]. In addition, recent investigations have revealed the importance of RDW as a risk marker of long-term survival in AIS patients receiving IVT [24]. In our prior study, we observed the association between RDW and the 1-year prognosis of anterior circulation ischemic stroke patients following EVT, yet, the respect to futile recanalization remains unclear.

This retrospective observational research showed that RDW could independently contributed to 3-month poor outcome. The model integrating RDW with other risk markers plays a significant role in determining unfavorable functional outcome in AIS patients with successful recanalization.

Different factors have been found to increase the risk of the stroke prognosis such as hyperglycemia, oxidative stress, inflammation, or alterations in brain perfusion [11,25]. Abnormal elevated RDW indicates the damage of microcirculatory blood flow being implicated as a key pathological feature of stroke [26]. This may account for its association with the severity of vascular lesions partially, which results in futile recanalization following EVT. The association of oxidation with RDW has also been found in an animal model [27]. An imbalance between anti-oxygen implicated in ischemic stroke lesions and the oxygen-free radical production systems causes lipid peroxidative damage [28]. The level of RDW was associated with C-reactive protein (CRP) level in a large population study, suggesting RDW's fundamental function in increasing inflammatory stress [29]. In turn, inflammation may influence erythrocyte deformability, erythrocyte circulatory half-life, and erythropoiesis, promoting anisocytosis and increasing RDW level [30]. Interestingly, our study observed no statistical difference in WBC counts between two groups. The latent link of inflammation and oxidative stress with RDW may explain the results.

Consistent with our results, RDW in the futile recanalization group were significantly higher than in the successful recanalization group. In addition, the logistic regression analysis observed RDW as a risk indicator of poor prognosis in AIS patients following EVT. These findings support the notion that inflammation plays a central contributor to the stroke pathology and can influence the clinical prognosis [31].

According to ROC curves analysis, we found that the admission RDW had a significant prognostic ability of poor 3-month outcome, having an AUC of 0.798 and the optimal cut-off value of 13.25 (specificity 87% and sensitivity 60%). The primary novel creation was developing a model that combined the RDW with other risk factors. The integrated model outperformed the RDW-only model in terms of predictive value. It could be helpful to take RDW value into account during the preoperative evaluation.

This study was based on actual clinical practice, nevertheless, it has also some limitations. The retrospective single center data collection could have influenced the results, the discriminative value of RDW in terms of specificity and sensitivity was relatively low. Besides, no dynamic changes in RDW were seen, suggesting that the evolution of RDW values over time rather than at a single time, maybe more predictive of prognosis in patients after EVT.

5. Conclusions

In this study, we demonstrated that RDW is an independent indicator of futile recanalization in anterior circulation AIS patients following EVT. Further prospective longitudinal multicenter trials should be performed to corroborate these findings.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

Conceptualizing and designing the study—YL and ZW. Extracting, analyzing and interpreting the data, Tables and Figures—ZW. Drafting the manuscript—ZW. Critical revision of the manuscript—YL and ZW. Supervision—YL and ZW. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Jiangsu Taizhou People's Hospital issued approval KY_2022_005_01. Due to the retrospective nature of this study, no written informed consent was obtained.

Acknowledgment

We thank all the participants in the study.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Krishnamurthi RV, Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, *et al*. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. The Lancet Global Health. 2013; 1: e259–e281.

[2] Turc G, Bhogal P, Fischer U, Khatri P, Lobotesis K, Mazighi M, *et al*. European Stroke Organisation (ESO)- European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke. Journal of NeuroInterventional Surgery. 2019; 11: 535–538.

[3] Muir KW, Ford GA, Messow C, Ford I, Murray A, Clifton A, *et al*. Endovascular therapy for acute ischaemic stroke: the Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE) randomised, controlled trial. Journal of Neurology, Neurosurgery and Psychiatry. 2017; 88: 38–44.

[4] Bracard S, Ducrocq X, Mas JL, Soudant M, Oppenheim C, Moulin T, *et al*. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. The Lancet Neurology. 2016; 15: 1138–1147.

[5] Menon BK, Al-Ajlan FS, Najm M, Puig J, Castellanos M, Dowlatshahi D, *et al*. Association of Clinical, Imaging, and Thrombus Characteristics with Recanalization of Visible Intracranial Occlusion in Patients with Acute Ischemic Stroke. JAMA. 2018; 320: 1017–1026.

[6] Horn N, Kniep H, Leischner H, McDonough R, Deb-Chatterji M, Broocks G, *et al*. Predictors of poor clinical outcome despite complete reperfusion in acute ischemic stroke patients. Journal of Neurointerventional Surgery. 2021; 13: 14–18.

[7] Lappegård J, Ellingsen TS, Vik A, Skjelbakken T, Brox J, Mathiesen, EB, *et al*. Red cell distribution width and carotid atherosclerosis progression The Tromsø Study. Thrombosis and Haemostasis. 2015; 113: 649–654.

[8] Song SY, Hua C, Dornbors III D, Kang RJ, Zhao XX, Du X, *et al*. Baseline red blood cell distribution width as a predictor of stroke occurrence and outcome: A comprehensive meta-analysis of 31 studies. Frontiers in Neurology. 2019; 10: 01237.

[9] Jia H, Li H, Zhang Y, Li C, Hu Y, Xia C. Association between red blood cell distribution width (RDW) and carotid artery atherosclerosis (CAS) in patients with primary ischemic stroke. Archives of Gerontology and Geriatrics. 2015; 61: 72–75.

[10] Lorente L, Martín MM, Abreu-González P, Pérez-Cejas A, González-Rivero AF, Ramos-Gómez L, *et al*. Early mortality of brain infarction patients and red blood cell distribution width. Brain Sciences. 2020; 10: 196.

[11] Piedade GS, Schirmer CM, Goren O, Zhang H, Aghajanian A, Faber JE, *et al*. Cerebral Collateral Circulation: a Review in the Context of Ischemic Stroke and Mechanical Thrombectomy. World Neurosurgery. 2019; 122: 33–42.

[12] Yoo AJ, Simonsen CZ, Prabhakaran S, Chaudhry ZA, Issa MA, Fugate JE, *et al*. Refining Angiographic Biomarkers of Revascularization. Stroke. 2013; 44: 2509–2512.

[13] Xu H, Jia B, Huo X, Mo D, Ma N, Gao F, *et al*. Predictors of Futile Recanalization after Endovascular Treatment in Patients with Acute Ischemic Stroke in a Multicenter Registry Study. Journal of Stroke and Cerebrovascular Diseases. 2020; 29: 105067.

[14] Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. the Lancet. 2000; 355: 1670–1674.

[15] Wityk RJ, Pessin MS, Kaplan RF, Caplan LR. Serial assessment of acute stroke using the NIH Stroke Scale. Stroke. 1994; 25: 362–365.

[16] Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, *et al*. 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. 1993; 24: 35–41.

[17] Zhang X, Yuan K, Wang H, Gong P, Jiang T, Xie Y, *et al*. Nomogram to Predict Mortality of Endovascular Thrombectomy for Ischemic Stroke despite Successful Recanalization. Journal of the American Heart Association. 2020; 9: e014899.

[18] Nie X, Pu Y, Zhang Z, Liu X, Duan W, Liu L. Futile Recanalization after Endovascular Therapy in Acute Ischemic Stroke. BioMed Research International. 2018; 2018: 5879548.

[19] Broderick JP, Adeoye O, Elm J. Evolution of the Modified Rankin Scale and its Use in Future Stroke Trials. Stroke. 2017; 48: 2007–2012.

[20] Choi JY, Kim EJ, Hong JM, Lee SE, Lee JS, Lim YC, *et al*. Conventional Enhancement CT: a Valuable Tool for Evaluating Pial Collateral Flow in Acute Ischemic Stroke. Cerebrovascular Diseases. 2011; 31: 346–352.

[21] Turcato G, Cervellin G, Cappellari M, Bonora A, Zannoni M, Bovi P, *et al*. Early function decline after ischemic stroke can

be predicted by a nomogram based on age, use of thrombolysis, RDW and NIHSS score at admission. Journal of Thrombosis and Thrombolysis. 2017; 43: 394–400.

[22] Fan L, Gui L, Chai E, Wei C. Routine hematological parameters are associated with short- and long-term prognosis of patients with ischemic stroke. Journal of Clinical Laboratory Analysis. 2018; 32: e22244.

[23] Duchnowski P, Hryniewiecki T, Kuśmierczyk M, Szymański P. Red cell distribution width is a prognostic marker of perioperative stroke in patients undergoing cardiac valve surgery. Interactive CardioVascular and Thoracic Surgery. 2017; 25: 925–929.

[24] Ye WY, Li J, Li X, Yang XZ, Weng YY, Xiang WW, *et al*. Predicting the one-year prognosis and mortality of patients with acute ischemic stroke using red blood cell distribution width before intravenous thrombolysis. Clinical Interventions in Aging. 2020; 15: 255–263.

[25] Lattanzi S, Norata D, Divani AA, Napoli MD, Broggi S, Rocchi C, *et al*. Systemic Inflammatory Response Index and Futile Recanalization in Patients with Ischemic Stroke Undergoing Endovascular Treatment. Brain Sciences, 2021, 11: 1164.

[26] Saft M, Gonzales-Portillo B, Park YJ, Cozene B, Sadanandan N, Cho J, *et al*. Stem cell repair of the microvascular damage in stroke. Cells. 2020; 9: 2075.

[27] Ghaffari S. Oxidative Stress in the Regulation of Normal and Neoplastic Hematopoiesis. Antioxidants and Redox Signaling. 2008; 10: 1923–1940.

[28] Lorente L, Martín MM, Abreu-González P, Sabatel R, Ramos L, Argueso M, *et al*. Serum Malondialdehyde Levels and Mortality in Patients with Spontaneous Intracerebral Hemorrhage. World Neurosurgery. 2018; 113: e542–e547.

[29] Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between Red Blood Cell Distribution Width and Inflammatory Biomarkers in a Large Cohort of Unselected Outpatients. Archives of Pathology and Laboratory Medicine. 2009; 133: 628–632.

[30] Weiss G, Goodnough LT. Anemia of Chronic Disease. New England Journal of Medicine. 2005; 352: 1011–1023.

[31] Iadecola C, Anrather J. The immunology of stroke: From mechanisms to translation. Nature Medicine. 2011; 17: 796–808.