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Association of Six Complex Inflammatory Indicators with Prognosis in Patients with Intravenous Thrombolysis Stroke

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Objective: The objective of this study is to examine the correlation between neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic immune inflammation index (SII), systemic inflammation response index (SIRI) and pan-immune-inflammation value (PIV) with the outcome following 3 months of thrombolysis in individuals diagnosed with acute ischemic stroke.

Methods: A retrospective analysis was conducted on a cohort of 762 patients who received intravenous thrombolysis between January 2019 and December 2022. The values of NLR, PLR, LMR, SII, SIRI and PIV were calculated based on relevant blood indices obtained upon admission. Logistic regression analysis using R software was employed to examine the correlation between SIRI, SII, PIV, and poor prognosis following 3 months of thrombolysis, with their distribution analyzed across the study population and various outcomes. Receiver operating characteristic (ROC) curves were utilized to analyze and evaluate their predictive efficacy for adverse outcomes.

Results: The unfavorable prognosis group exhibited significant differences from the favorable prognosis group in various hematological markers, including PLR, NLR, LMR, SII, SIRI, and PIV, as indicated by ROC values of 0.613 (95% confidence interval (CI), 0.564–0.661), 0.707 (95% CI, 0.663–0.751), 0.614 (95% CI, 0.567–0.662), 0.715 (95% CI, 672–0.758), 0.631 (95% CI, 0.584–0.679), and 0.569 (95% CI, 0.520–0.619) respectively. (4) Conclusions: PLR, NLR, LMR, SII, SIRI, and PIV demonstrated associations with adverse outcomes at the 3-month mark in patients who underwent intravenous thrombolysis, with NLR (ROC is 0.707) and SII (ROC is 0.715) showing the most pronounced significance and PIV (ROC is 0.569) exhibiting the least significance.

Keywords: acute ischemic stroke, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, systemic immune inflammation index, systemic inflammation response index

Introduction

Stroke is a significant contributor to morbidity, disability, and mortality on a global scale, with China bearing a particularly high burden and risk of stroke.[1,2] Approximately 70% of strokes are classified as acute ischemic stroke (AIS), with the primary mechanisms being ischemia, hypoxia, and neuroinflammatory responses within cerebral blood vessels. While intravenous thrombolysis remains the primary treatment for AIS within the initial 4.5-hour time frame,[3,4] it is associated with potentially severe complications including vascular perfusion injury and cerebral hemorrhage. Timely identification of patients with a poor thrombolytic prognosis and prompt intensification of treatment by healthcare providers have the potential to enhance patient outcomes following intravenous thrombolysis, mitigate the likelihood of disease recurrence and mortality, and optimize the utilization of medical resources.

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Research has demonstrated that neuroinflammation significantly influences the pathology, physiology, and prognosis of stroke. In the context of acute ischemic stroke, cerebral cells release inflammatory mediators that initiate a cascade of inflammation-associated responses, ultimately resulting in neuronal damage and leading to neurological deficits and adverse clinical outcomes in patients. Established inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR), which can be easily obtained from blood counts, have been shown to be reliable indicators of functional outcome in cases of acute ischemic stroke (AIS).[5,6] Following this, a number of new predictors have been introduced, including the systemic immune inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV).[7,8] Despite this, there is a limited amount of research that has simultaneously incorporated multiple inflammation indices, and even fewer studies have utilized these repetitive and practical composite inflammation ratio markers collectively to forecast outcomes in acute ischemic stroke patients following intravenous thrombolysis at the 3-month mark.

In this study, we conducted a comprehensive analysis of the relationship between PLR, NLR, LMR, SII, SIRI, and PIV composite inflammatory markers and the prognosis of AIS patients receiving intravenous thrombolysis therapy (IVT) at three months. Our aim was to enhance the predictive accuracy of existing models and facilitate more precise treatment strategies for the broader population.

Material and Methods

Study Population

The retrospective observational study conducted from January 2019 to December 2022 included patients with acute ischemic stroke who underwent intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA) at a national advanced stroke center. Retrospective studies Can lead to information bias due to poorly documented information, etc, thus we used chained equation multivariate estimation, interpolation to deal with missing values. Determination of sample size[9] Refer to the statistical formula: $n = (Z * \sigma / E)^2$ (n: represents the required sample size; Z: confidence level of Z statistic (Z statistic at 95% confidence level is 1.96). σ: overall standard deviation, generally 0.5; E: error margin (0.05). The result is n=385, and a sample size greater than 385 is sufficient. Ethics approval for the study was obtained from the Research Ethics Committee of the hospital (ethics approval number: 2022–063), and written informed consent was obtained from each patient or their guardian prior to participation.

The study's inclusion criteria consisted of individuals aged 18 years or older, meeting the indications for intravenous thrombolysis, and providing informed consent from patients or guardians, including re-stroke patients and patients under antiplatelet therapy. The exclusion criteria included individuals with a history of stroke with a modified Rankin Scale (m RS) score greater than 2 before the current episode, recipients of endovascular therapy, diagnosed with stroke-like illness post-admission, lacking essential test data necessary for analysis, and patients who were lost to follow-up.

Stroke patients were classified into anterior or posterior circulation groups based on the location of lesion infarction. The etiological diagnosis was categorized according to the classic 1993 TOAST typology proposed by Adams et al.[10] This typology includes subtypes such as atherosclerotic large artery disease, small artery occlusion, cardiogenic embolism, stroke of undetermined etiology, and stroke of other known etiology.

Patients with acute ischemic stroke (AIS) were primarily admitted to our institution for cranial CT scans to exclude cerebral hemorrhage. Subsequently, patients received treatment with intravenous thrombolysis using rt-PA at the standard dose of 0.9 mg/kg (Boehringer Ingelheim, Germany, in 20- and 50-mg sizes) within 4.5 hours post-onset. A fraction of 10% of the total dose was administered intravenously over 1 minute, while the remaining dose was infused through intravenous pumping using a continuous micropump over a 60-minute period.[11] The maximum administered dose of rt-PA did not exceed 90 mg.

Data Acquisition

Upon admission, we gathered the patient's clinical information, encompassing gender, age, weight, height, diastolic blood pressure (DBP), systolic blood pressure (SBP), onset-to-treatment time (OTT), and door-to-needle time (DNT), National Institutes of Health Stroke Scale (NIHSS) score, the NIHSS score ahead thrombolysis (ANIHSS), post-

thrombolysis NIHSS score (PNIHSS), Modified Rankin Scale (m RS) score,[12] vascular risk factors (such as hypertension, diabetes mellitus (DM)), atrial fibrillation, coronary artery disease(CHD), prior strokes, hyperlipidemia, and a history of smoking and alcohol consumption), and pre-existing medications (including antiplatelet agents, statins, and anticoagulants).

Upon admission to the hospital, laboratory tests were conducted to assess baseline blood glucose levels, hemoglobin (Hb) count, white blood cell count(WBC), platelet count (P), neutrophil count(N), lymphocyte (L) count, monocyte (M) count, eosinophil (E) count, international normalized ratio, prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), brain natriuretic peptide (BNP) for heart failure measurements, lactate dehydrogenase (LDH), creatinine (CR), and uric acid (UA).

Definition of Inflammation Indicators

Upon the patient's admission to the emergency room, a venous blood sample was promptly obtained for the purpose of measuring neutrophil count, lymphocyte count, platelet technique, and monocyte count. These data are subsequently utilized in the calculation of a composite inflammatory biomarker as outlined in previous studies:[13,14]

PLR = platelet counts/lymphocyte counts, NLR = neutrophil counts/lymphocyte counts, LMR = lymphocyte counts/monocyte counts, SII = platelet counts * (neutrophil counts/lymphocyte counts), SIRI = neutrophil count * monocyte count/lymphocyte counts, and PIV = neutrophil counts * platelet count * monocyte counts/lymphocyte counts.

Prognostic Assessment

All patients with acute ischemic stroke (AIS) underwent clinical assessment three months post-intravenous thrombolysis treatment using the modified Rankin Scale (mRS). These patients were stratified into groups based on their prognosis, with a favorable outcome defined as an mRS score of 2 or lower, and an unfavorable outcome as an mRS score greater than 2. Clinical prognostic information was gathered through telephone follow-ups and in-person evaluations at the three-month mark, with assessments conducted by two experienced senior neurologists who were blinded to the patients' personal information. In instances of disagreement, a third senior physician was consulted for further evaluation.

Statistical Analysis

Data analysis was conducted using R software (version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria). The normal distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Continuous data were reported as the median and interquartile range (IQR), while categorical data were presented as frequency and percentage (%). The chi-square test was used to compare categorical data across different groups, and the Mann–Whitney *U*-test was employed to compare continuous data. Variables with a significance level of $P<0.05$ in univariate regression analysis were selected for inclusion in subsequent multivariate logistic regression analysis and subjected to screening through backward regression. Variables that maintained a significance level of $P<0.05$ following multivariate logistic regression analysis were deemed to be statistically significant.

The density histogram sentiment was demonstrated for the distribution of six indicators (PLR, NLR, LMR, SII, SIRI, and PIV) within the overall study population. Violin plots were utilized to display the distribution of these indicators within the subgroups of good prognosis and poor prognosis, with adjustments made for modeling. Additionally, the ROCR package was employed to generate receiver operating characteristic (ROC) curves, assessing the discriminatory ability of the six indicators in predicting prognosis.

Results

Baseline Patient Characteristics

A total of 860 patients diagnosed with acute ischemic stroke (AIS) were initially admitted for the study. Ultimately, 762 patients were included in the statistical analyses. At the 3-month follow-up, 580 patients (76.1%) exhibited a favorable prognosis, while 182 patients (23.9%) had a unfavorable prognosis ((Figure 1)). The baseline characteristics of the patients in both outcome groups are presented in Table 1(Table 1). In the distribution of the two groups, in which age,

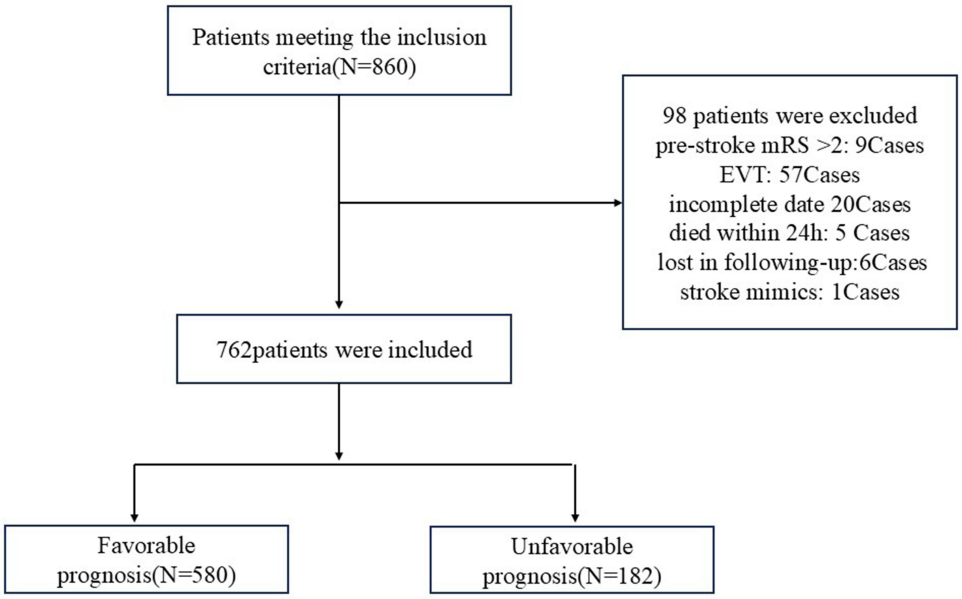

Figure 1 Study flowchart.

TOAST, SBP, DBP, Diabetes, Atrial fibrillation, N, M, E, BNP, PLR, NLR, LMR, SII, SIRI and PIV and SBP are differentiated($p<0.05$).MRS distribution of patients in the favorable and unfavorable prognosis groups (Figure 2). Density histogram of the distribution of PLR,NLR,LMR,SII,SIRI and PIV composite inflammatory indicators in the study population (Figure 3).

Table 1 Baseline Characteristics of AIS Patients with Different Prognoses

Variables	Total (n = 762)	Favorable prognosis group (N=580)	Unfavorable prognosis group (N=182)	P value
Age, year, Median (Q1, Q3)	65 (55, 71)	64 (55, 71)	67 (56.25, 73.75)	0.003*
Gender, n (%)				0.054
Female	371 (48.7)	291 (50.2)	80 (44.0)	
Male	391 (51.3)	289 (49.8)	102 (56.0)	
Height, centimeter, Median (Q1, Q3)	170 (162, 173)	170 (162, 173)	170 (162, 173)	0.463
Weight, kilogram, Median (Q1, Q3)	70 (60, 78)	70 (62.38, 78)	68 (60, 78)	0.053
Anterior /Posterior circulation n (%)				0.530
Anterior	575 (75)	434 (75)	141 (77)	
Posterior	187 (25)	146 (25)	41 (23)	
TOAST, n (%)				0.018*
LAA	460 (60.4)	341 (58.8)	119 (65.4)	
SAO	151 (19.8)	120(20.7)	31(17.0)	
CE	142 (18.6)	112 (19.3)	30 (16.5)	
SOE	6(0.8)	4(0.7)	2 (1.1)	
SUE	3(0.4)	3(0.5)	0(0.0)	
SBP, Median (Q1, Q3)	5 (2, 11)	4 (2, 9)	10 (5, 15)	< 0.001*
DBP, Median (Q1, Q3)	3 (2, 10)	3 (1, 7)	9 (4, 14)	< 0.001*
ANIHSS, Median (Q1, Q3)	146 (135, 159)	145 (134, 158)	150 (137, 162)	0.003*
Post thrombolysis, NIHSS Median (Q1, Q3)	82 (76, 89)	82 (76, 89)	82 (76, 89)	0.882
OTT, min, Median (Q1, Q3)	128.5 (92, 176)	128 (90, 174.25)	132 (97, 180)	0.247
DNT, min, Median (Q1, Q3)	46 (34, 65)	47 (34, 65.25)	45.5 (34, 65)	0.838

(*Continued*)

Table 1 (Continued).

Variables	Total (n = 762)	Favorable prognosis group (N=580)	Unfavorable prognosis group (N=182)	P value
Smoking, n (%)				0.548
No	406 (53)	305 (53)	101 (55)	
Yes	356 (47)	275 (47)	81 (45)	
Drinking, n (%)				0.238
No	515 (68)	385 (66)	130 (71)	
Yes	247 (32)	195 (34)	52 (29)	
Diabetes, n (%)				0.001*
No	592 (78)	471 (81)	121 (66)	
Yes	170 (22)	109 (19)	61 (34)	
Hypertension, n (%)				0.934
No	289 (38)	219 (38)	70 (38)	
Yes	473 (62)	361 (62)	112 (62)	
Hyperlipidemia, n (%)				0.694
No	753 (99)	572 (99)	181 (99)	
Yes	9 (1)	8 (1)	1 (1)	
Atrial fibrillation, n (%)				0.001*
No	665 (87)	520 (90)	145 (80)	
Yes	97 (13)	60 (10)	37 (20)	
Previous stroke, n (%)				0.099
No	658 (86)	508 (88)	150 (82)	
Yes	104 (14)	72 (12)	32 (18)	
CHD, n (%)				0.056
No	590 (77)	459 (79)	131 (72)	
Yes	172 (23)	121 (21)	51 (28)	
WBC counts ×109/L, Median (Q1, Q3)	7.38 (5.98, 9)	7.19 (5.83, 8.68)	8.12 (6.5, 9.8)	< 0.001*
HGB, g/L Mean ± SD	144 (133, 155.75)	145 (133, 156)	142 (131, 154.75)	0.182
PLTconut×109/L, Median (Q1, Q3)	217 (180, 256)	216.5 (180, 253.25)	222 (175, 271.75)	0.28
Ncount×109/L, Median (Q1, Q3)	4.48 (3.43, 5.92)	4.18 (3.27, 5.5)	5.76 (4.31, 7.36)	< 0.001*
Lcount×109/L, Median (Q1, Q3)	1.86 (1.36, 2.49)	2 (1.47, 2.63)	1.52 (1.18, 2.1)	< 0.001*
Mcount×109/L, Median (Q1, Q3)	0.49 (0.38, 0.62)	0.48 (0.38, 0.61)	0.52 (0.4, 0.65)	0.063
Ecount×109/L, Median (Q1, Q3)	0.1 (0.05, 0.17)	0.11 (0.05, 0.18)	0.08 (0.03, 0.14)	0.001*
PT, s, Median (Q1, Q3)	10.8 (10.3, 11.5)	10.7 (10.2, 11.4)	11.05 (10.5, 11.8)	< 0.001*
APTT, s Median (Q1, Q3)	26.4 (24.6, 28.8)	26.4 (24.6, 28.63)	26.2 (24.6, 29.3)	0.823
INR2, Median (Q1, Q3)	0.93 (0.88, 0.99)	0.92 (0.88, 0.98)	0.95 (0.9, 1.01)	< 0.001*
GLU, μ mol/L Median (Q1, Q3)	6.85 (5.8, 8.89)	6.67 (5.7, 8.45)	7.66 (6.35, 10.46)	< 0.001
BNP, p g/mL Median (Q1, Q3)	32.36 (10.85, 116)	27.95 (9.78, 95.53)	59.2 (15.48, 160.5)	< 0.001*
LDH, U/L Median (Q1, Q3)	396.76 (229, 489.5)	386 (210.3, 477.25)	424.06 (307, 511.99)	< 0.001*
Cr, μ mol/L Median (Q1, Q3)	67.22 (57.52, 79.07)	66.8 (57.48, 78.39)	69.25 (57.73, 79.96)	0.293
UA, μ mol/L Median (Q1, Q3)	323.02 (263.29, 394.5)	327.15 (267.96, 397.42)	316.8 (253.93, 372.15)	0.052
PLR, Median (Q1, Q3)	116.58 (84.34, 157.96)	108.18 (78.61, 149.91)	135.68 (103.66, 191.35)	< 0.001*
NLR, Median (Q1, Q3)	2.25 (1.5, 3.86)	2 (1.36, 3.39)	3.36 (2.4, 5.17)	< 0.001*
LMR, Median (Q1, Q3)	4.01 (2.88, 5.29)	4.32 (3.05, 5.56)	3.24 (2.34, 4.07)	< 0.001*
SII, Median (Q1, Q3)	497.09 (320.85, 829.62)	419.29 (280.59, 743.21)	725.98 (528.75, 1172.39)	< 0.001*
SIRI, Median (Q1, Q3)	1.09 (0.74, 1.74)	1 (0.66, 1.54)	1.46 (1.02, 2.33)	< 0.001*
PIV, Median (Q1, Q3)	244.86 (147.11, 425.95)	207.3 (127.74, 371.67)	381.42 (263.37, 596.25)	< 0.001*

Note: *P < 0. 05, statistically significant.

Distribution of Complex Inflammatory Indicators

Violin plots were utilized to display the distribution of PLR, NLR, LMR, SII, SIRI, and PIV composite inflammatory indicators in both favorable and unfavorable prognosis groups, following adjustment for modeling (Figure 4). The figures

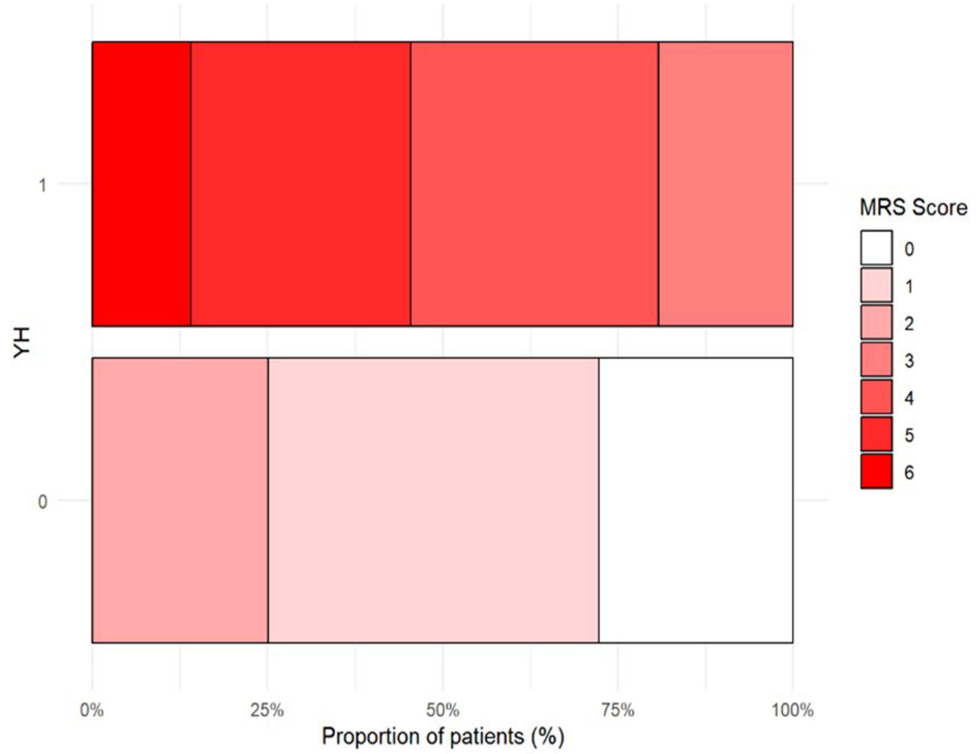

Figure 2 MRS distribution map in the study population. 0: Favorable prognosis; 1: Unfavorable prognosis.

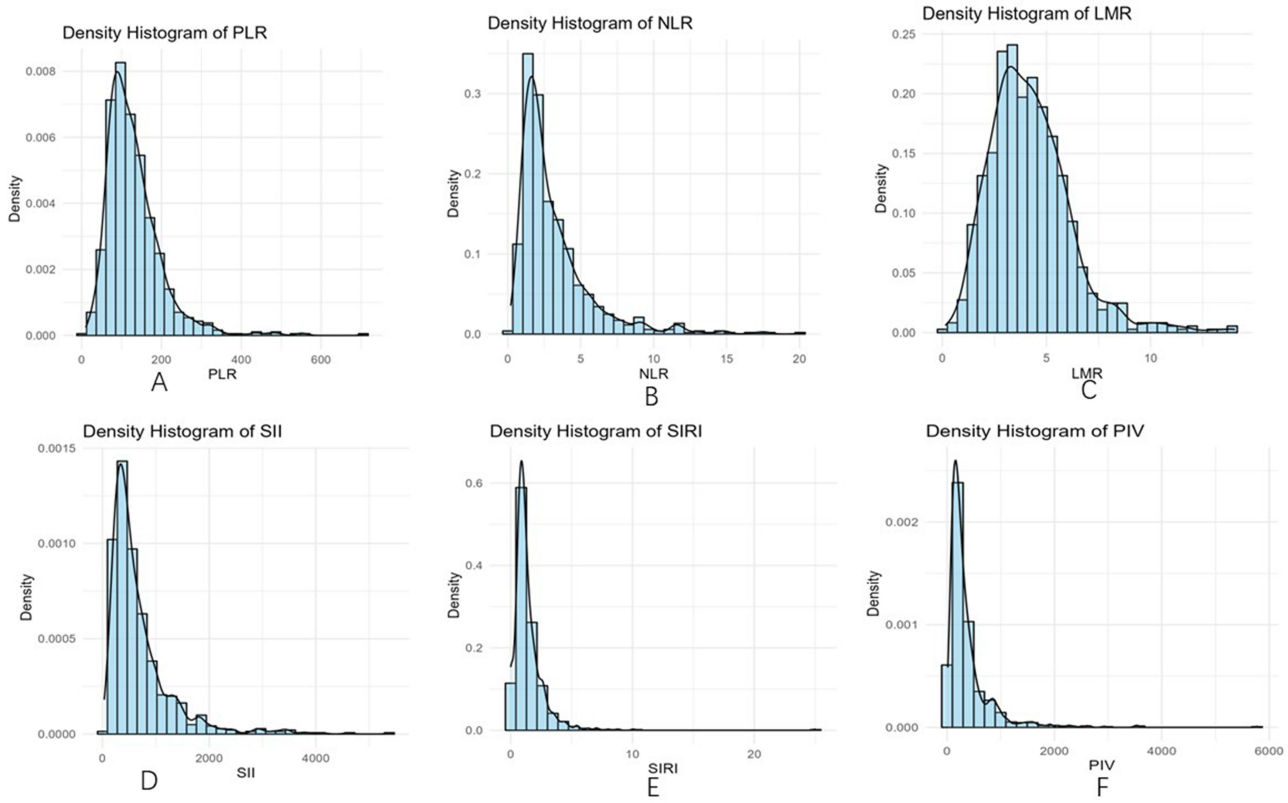

Figure 3 Histogram of the distribution density of PLR (**A**), NLR(**B**), LMR(**C**), SII (**D**), SRI(**E**) And PIV(**F**) in the study population.

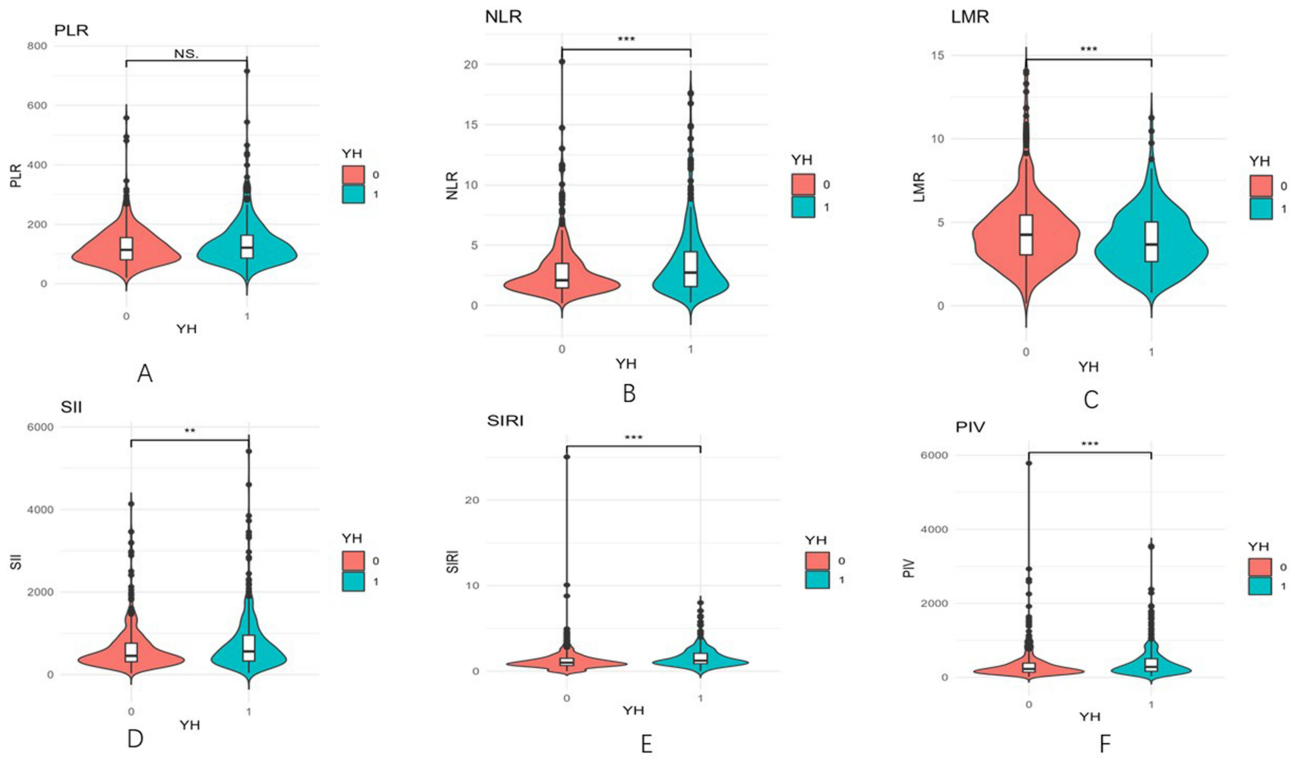

Figure 4 Violin plots of the distribution of PLR (**A**), NLR(**B**), LMR(**C**), SII (**D**), SIRI(**E**) and PIV(**F**) inflammation ratios. 0: Favorable prognosis group; 1: Unfavorable prognosis group.

illustrate notable distinctions in PLR and NLR levels between the two groups, with elevated levels observed in the unfavorable prognosis group compared to the favorable prognosis group.

Logistic Regression Analysis Results

Table 2 shows the results of the multivariate logistic regression model for the strong prognosis and unfavorable prognosis groups after thrombolysis (Table 2).

Model 1 was a univariate and multivariate analysis. It was seen that PLR (odds ratio(OR), 1.001; 95% CI 1.000–1.003, P=0.012), NLR (OR, 1.122; 95% CI 1.089–1.201, P=0.028), LMR (OR, 1.023; 95% CI 1.021–1.025,

Table 2 Multifactorial Analysis of PLR, NLR, LMR, SII, SIRI, and PIV in Relation to 3-Month Unfavorable Prognosis in Patients with AIS

	Model 1		Model 2	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
PLR	1.001 (1.000–1.003)	0.012	1.001 (1.000–1.002)	0.013
NLR	1.122 (1.089–1.201)	0.028	1.123 (1.088–1.204)	0.029
LMR	1.023 (1.021–1.025)	<0.001	1.025 (1.020–1.024)	<0.001
SII	1.325 (1.260–1.401)	<0.001	1.326 (1.257–1.406)	<0.001
SIRI	1.999 (1.989–2.050)	0.037	1.999 (1.997–2.010)	0.038
PIV	1.101 (1.100–1.110)	0.096	1.101 (1.089–1.121)	0.081

Notes: Model 1 was a univariate and multivariate analysis; Model 2 adjusted for sex, age, randomized glucose, admission NIHSS score, smoking, alcohol history, premorbid mRS, TOAST, and comorbidities.

Abbreviations: OR, odds ratio; CI, confidence interval.

P<0.001),SII (OR, 1.325; 95% CI 1.260–1.401, P<0.001), SIRI (OR, 1.999; 95% CI 1.989–2.050, P=0.037), and PIV (OR, 1.101; 95% CI 1.100–1.110, P=0.096) were identified as unfavorable prognostic factors.

Model 2 adjusted for sex, age, randomized glucose, admission NIHSS score, smoking, alcohol history, premorbid mRS, TOAST, and comorbidities. It was seen that PLR (OR, 1.001; 95% CI 1.000–1.002, P=0.013), NLR (OR, 1.123; 95% CI 1.088–1.204, P=0.029), LMR (OR, 1.025; 95% CI 1.020–1.024, P<0.001),SII (OR, 1.326; 95% CI 1.257–1.406, P<0.001), SIRI OR, 1.999; 95% CI 1.997–2.010, P=0.038), and PIV (OR, 1.101; 95% CI 1.089–1.121, P=0.081) were identified as unfavorable prognostic factors.

ROC Values of Composite Inflammatory Markers for Adverse Outcomes

The area under the receiver operating characteristic curve (AUC-ROC) values for PLR, NLR, LMR, SII, SIRI, and PIV were as follows: 0.613 (95% CI, 0.564–0.661), 0.707 (95% CI, 0.663–0.751), 0.614 (95% CI, 0.567–0.662), 0.715 (95% CI, 0.672–0.758), 0.631 (95% CI, 0.584–0.679), and 0.569 (95% CI, 0.520–0.619) (Figure 5). Among these, SII and NLR demonstrated the highest significance in predicting unfavorable prognosis in patients 3 months post intravenous thrombolysis for stroke, while PIV showed the least predictive ability for unfavorable prognosis.

Discussion

This study represents a novel contribution to the existing literature as it is the first to utilize a relatively large sample size in examining the relationship between multiple composite inflammation ratios and 3-month prognostic outcomes in patients following thrombolysis. Our findings indicate that elevated levels of PLR, NLR, LMR, SII, SIRI, and PIV are correlated with unfavorable prognostic outcomes at the 3-month mark in patients who have undergone intravenous thrombolysis. We conducted a univariate analysis followed by a multivariate multifactorial regression analysis, identifying PLR, NLR, LMR, SII, SIRI, and PIV as independent predictors of poor prognosis in patients undergoing intravenous thrombolysis, even after adjusting for potential confounding variables. Furthermore, the study revealed that SII and NLR exhibited the highest receiver operating characteristic (ROC) values and demonstrated superior diagnostic accuracy with values of 0.707 (95% CI, 0.663–0.751) and 0.715 (95% CI, 0.672–0.758), respectively, in predicting unfavorable prognosis.

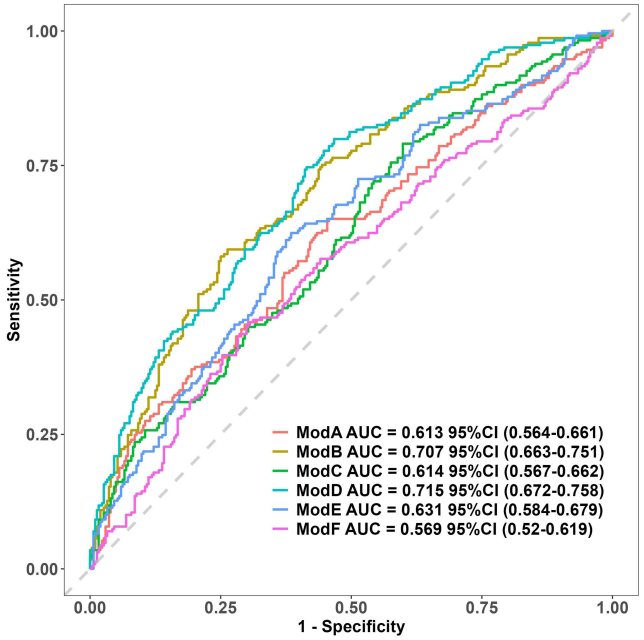

Figure 5 Receiver operating characteristic curves (ROC) for PLR (Mod A), NLR (Mod B), LMR (Mod C), SII (Mod D), SIRI (Mod E) and PIV (Mod F) to predict unfavorable prognosis in AIS patients at 3 months. Area under the curve (AUC) values can be used to measure predictive accuracy.

Research has demonstrated that immunity and inflammation play crucial roles in the pathophysiology of stroke, with inflammatory signaling being a prominent feature during the onset of acute ischemic stroke (AIS) and throughout the cerebral ischemic cascade. Following cerebral ischemia,[15] the release of neurotoxic substances such as inflammatory cytokines, chemokines, and reactive oxygen species (ROS) by damaged brain cells can lead to disruption of the blood-brain barrier and trigger an inflammatory cascade, resulting in neuronal damage and subsequent impairment of neurological function. Neutrophils,[16,17] influenced by inflammatory cytokines and chemokines originating from ischemic tissues, are the initial immune cells to migrate to ischemic brain regions. These neutrophils release proinflammatory mediators, proteases, reactive oxygen species (ROS), and extracellular matrix metalloproteinases (MMPs), leading to the generation of free radicals and consequent damage to ischemic tissues. Monocytes are recognized as a potential source of MMP-9, exacerbating brain tissue injury, while lymphocytes are believed to exhibit neuroprotective properties. Acute ischemic stroke is initiated by the excessive activation of platelets,[18] leading to thrombosis and vascular obstruction with deleterious outcomes.

Studies have demonstrated that the administration of tissue plasminogen[19] activator (tPA) following intravenous thrombolysis in a rat model induces endothelial cell injury, facilitating the adhesion and migration of neutrophils and T cells, thereby eliciting a cascade of inflammatory reactions. These findings suggest that intravenous thrombolysis may provoke an inflammatory response. It has been proposed that[20] elevated levels of neutrophil-lymphocyte ratio (NLR) upon admission could serve as a valuable indicator for predicting unfavorable short-term outcomes following intravenous thrombolysis in patients with mild acute ischemic stroke (AIS). WU et al discovered that NLR[21] and its fluctuations were correlated with 3-month outcomes and mortality in AIS patients after receiving intravenous thrombolysis. Additionally, both NLR and lymphocyte-monocyte ratio (LMR)[22] were linked to outcomes in patients with acute ischemic stroke who underwent mechanical thrombectomy (MT). Gong et al discovered that[5] NLR, PLR, and LMR were correlated with early functional decline following thrombolysis, with NLR and PLR serving as predictive factors for early functional deterioration in patients post-thrombolysis.

Research has also indicated that[23] in-hospital ischemic stroke patients with Neutrophil-to-Lymphocyte Ratio (NLR) exceeding 5.5 points and Systemic Immune-Inflammation Index (SII) surpassing 2120 points exhibit more intricate clinical characteristics and elevated mortality rates. Zhang et al further substantiated that an elevated Systemic Inflammatory Response Index (SIRI) is correlated with an increased likelihood of mortality and sepsis, as well as a heightened severity of stroke. They also found that SIRI shows promise as a low-grade inflammatory marker for predicting stroke prognosis, demonstrating superior predictive capabilities compared to NLR, PLR, and LMR.[7] Additionally, Platelet-Inflammatory Value (PIV),[24] a composite marker derived from four blood cell counts, has been investigated and shown to be linked to unfavorable 3-month outcomes in patients undergoing intravenous thrombolytic therapy, along with other inflammatory factors such as PLR, NLR, and Systemic Immune-Inflammation Index (SII).

Our study demonstrates significant advantages due to its historical significance. Specifically, we utilized a large sample size and for the first time, incorporated multiple composite inflammatory ratios simultaneously, including PLR, NLR, LMR, SII, SIRI, and PIV. These ratios, based on various hematocrits, play a crucial role in the inflammatory processes of ischemic stroke patients and can accurately predict the prognosis of patients undergoing intravenous thrombolysis. This provides clinicians with a comprehensive and precise prognostic tool. Furthermore, these six composite inflammatory ratios can be derived from the patient's blood cell count, a straightforward and cost-effective procedure that alleviates the financial strain on patients.

Our study is subject to several potential limitations. Firstly, it is important to note that this was a retrospective analysis conducted at a regional advanced stroke center, rather than a multicenter clinical study.[25] Future research should consider conducting a multicenter prospective study to minimize information bias and other potential confounding factors. Secondly, it is crucial to recognize that patients' composite inflammation ratios may fluctuate significantly throughout their hospitalization. Therefore, it is imperative to monitor these ratios dynamically, rather than solely focusing on the ratios in the immediate prethrombolytic admission period. Finally, traditional algorithms are currently employed for analysis, however, in light of advancements in artificial intelligence[26] and big data, there is a necessity to employ sophisticated artificial intelligence machine learning[27] algorithms in order to forecast future neurological outcomes in medical research for the betterment of society.

Conclusions

In summary, our research substantiates the association between PLR, NLR, LMR, SII, SIRI, and PIV with the three-month prognostic outcomes of acute ischemic stroke patients following intravenous thrombolysis, as determined through multivariate analysis. Notably, NLR and SII exhibited significant predictive capabilities. Clinicians can utilize these accessible predictors to early identify and manage risk factors, implement timely interventions, reduce adverse outcomes, apply precision medicine, and optimize healthcare resources.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics Statement

This study is in accordance with the principles established in the Helsinki Declaration and has been approved by the Ethics Committee of the Baoding No.1 Central Hospital (ethical batch number: 2022-063). Informed consent was obtained from all subjects participating in the study, and written informed consent to publish this article was obtained from patients.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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