Neurology Asia 2025; 30(2) : 391 – 402

Dynamic changes of systemic immune-inflammation index and systemic inflammation response index after mechanical thrombectomy and their predictive value for functional outcomes in patients with acute ischemic stroke

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Abstract

Objective: To investigate the dynamic changes in the systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI) after mechanical thrombectomy (MT) and their ability to predict 90-day functional outcomes in acute ischemic stroke (AIS) patients. *Methods:* This retrospective cohort study included 423 AIS patients who underwent MT treatment at a single center between January 2018 and February 2024. SII and SIRI were measured at admission, Day 1, and Day 3 post-MT. The primary outcome was poor functional outcome (modified Rankin Scale score > 2) at 90 days. Receiver operating characteristic curve (ROC) analysis and multivariable logistic regression were used to assess the predictive performance and independent associations of SII and SIRI with outcomes. The relationships between SII, SIRI, and 90-day mRS scores were explored using Spearman correlation analysis and multivariable linear regression models. *Results:* The poor outcome group had significantly higher SII and SIRI at all time points compared to the good outcome group (all $P < 0.001$). ROC analysis showed that SII and SIRI on day3 had the strongest predictive power (SII: AUC=0.80; SIRI: AUC=0.82). After adjusting for potential confounders, multivariable logistic regression analysis indicated that SII and SIRI on day3 were independently associated with poor outcomes at 90 days (Both $P < 0.001$). Multivariable linear regression analysis further confirmed that SII and SIRI on day3 were significantly positively correlated with mRS scores (both $P < 0.01$). *Conclusion:* SII and SIRI levels after MT (especially on day3) can serve as effective predictors of 90-day functional outcomes in AIS patients.

Keywords: Acute ischemic stroke, Mechanical thrombectomy, Systemic immune-inflammation index, Systemic inflammation response index, Prognosis.

INTRODUCTION

Acute ischemic stroke (AIS) is one of the leading causes of mortality and disability worldwide, imposing a substantial burden on patients' quality of life, healthcare systems, and socioeconomic well-being.[1] The World Stroke Organization's latest report projects that annual global stroke deaths will increase from 6.6 million to 9.7 million between 2020 and 2050, a staggering 50% rise. Concurrently, disability-adjusted life years (DALYs) attributable to stroke are expected to surge from 144.8 million to 189.3 million. Mechanical thrombectomy (MT) has emerged as the standard treatment for large vessel occlusion AIS.[2] However, despite achieving timely and complete reperfusion, approximately half of

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Date of Submission: 14 February 2025; Date of Acceptance: 3 March 2025

https://doi.org/10.54029/2025ukj

the patients undergoing MT still experience poor outcomes at 3 months.[3] Therefore, it is of paramount importance to thoroughly investigate the factors associated with MT outcomes to facilitate early identification of high-risk patients and optimize clinical management strategies.

Inflammatory response plays a pivotal role in the pathophysiological processes of ischemic stroke, spanning the entire spectrum from ischemic injury to tissue repair.[4-6] Patients with AIS receiving MT treatment may experience a more intense inflammatory response, not only due to reperfusion injury but also potentially related to the MT procedure itself.[7-9] Consequently, a comprehensive understanding of the dynamic changes in the inflammatory response following MT and its relationship with clinical outcomes is of great clinical significance. The systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI), as novel integrated inflammatory indices, incorporate information from four types of inflammatory and immune cells: lymphocytes, neutrophils, monocytes, and platelets, reflecting the balance between immune and inflammatory states.[11,12] These indices were initially used to predict tumor prognosis and identify high-risk patients, and have now been shown to be associated with the severity and adverse outcomes of various diseases, including various cancers, heart failure, and cardiovascular disorders.[11-14] Compared to single inflammatory markers, SII and SIRI may more comprehensively reflect the overall inflammatory status of the body.[15,16] However, research on the predictive value of SII and SIRI in AIS patients remains limited, particularly in the population undergoing MT treatment. More importantly, the dynamic changes of these inflammatory indices after stroke onset and their relationship with prognosis have not been fully elucidated. The dynamic changes of inflammatory markers may have higher predictive value than measurements at a single time point.

Based on this background, this study aims to investigate the predictive value of SII and SIRI at multiple key time points for 90-day functional outcomes in AIS patients receiving MT. This will help elucidate the dynamic changes of early inflammatory indices in MT patients and provide important information for prognostic assessment. By gaining a deeper understanding of the relationship between the dynamic changes of SII and SIRI and AIS prognosis, we hope to provide new insights for risk stratification and personalized treatment decisions in clinical practice, ultimately improving the long-term prognosis of AIS patients.

METHODS

This study is a single-center retrospective cohort study aimed at evaluating the predictive value of SII and SIRI at different time points for 90-day functional outcomes in AIS patients receiving MT treatment. We consecutively enrolled 423 AIS patients who underwent MT treatment at the Stroke Center of Zhongshan Hospital, Xiamen University, between January 2018 and February 2024. The inclusion criteria were: (1) age ≥ 18 years; (2) clinical presentation and imaging examinations consistent with the diagnosis of AIS;[17] and (3) CT angiography at admission confirming the presence of intracranial large vessel occlusion (including internal carotid artery, middle cerebral artery M1 or M2 segment, basilar artery, or posterior cerebral artery P1 segment). The exclusion criteria were: (1) intracranial hemorrhage on baseline CT or magnetic resonance imaging (MRI); (2) pre-stroke modified Rankin Scale (mRS) score ≥ 2; (3) severe systemic diseases (such as renal failure, severe liver dysfunction, or malignant tumors); (4) presence of infectious diseases, inflammatory disorders, immune system disorders, or ongoing immunotherapy at admission; (5) concomitant diseases that may affect inflammatory markers (such as tumors, myocardial infarction, trauma, recent surgery, or allergic reactions); (6) lack of complete laboratory examination data; and (7) loss to follow-up or lack of follow-up data.

We extracted patients' demographic characteristics and clinical data from the hospital's electronic medical record system using a pre-designed standardized form. The collected data included age, sex, smoking and drinking status, medical history (hypertension, diabetes, previous stroke or transient ischemic attack, coronary artery disease, valvular heart disease, and atrial fibrillation), blood pressure at admission, baseline National Institutes of Health Stroke Scale (NIHSS) score, Glasgow Coma Scale (GCS) score, location of vessel occlusion, and stroke etiology (TOAST classification). Additionally, we collected information related to MT treatment, including time from symptom onset to femoral artery puncture, time from symptom onset to reperfusion, time from puncture to reperfusion, number of retrieval attempts, retrieval techniques, and vessel reperfusion status. The degree of reperfusion after the procedure was assessed using the modified Thrombolysis in Cerebral Infarction (mTICI) score, based on the final digital

subtraction angiography, with mTICI 2b-3 defined as successful reperfusion.[18]

We collected venous blood samples from patients in the fasting state on the morning of admission (Day 0), the first day after the procedure (Day 1), and the third day after the procedure (Day 3). The hospital's laboratory center used an automated hematology analyzer to determine complete blood cell counts, including white blood cell count, neutrophil count, lymphocyte count, monocyte count, and platelet count. Simultaneously, an automated biochemical analyzer was used to measure serum biochemical indicators, including total protein, albumin, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, creatinine, and uric acid levels.

The main exposure variables in this study were SII and SIRI, calculated using the following formulas: SII = platelet × neutrophil / lymphocyte; SIRI = (neutrophil × monocyte) / lymphocyte count.

The primary outcome was poor functional outcome at 90 days, defined as an mRS score of 3-6 at 3 months; an mRS score ≤ 2 was defined as a good outcome. Follow-up data were obtained through the National Cerebrovascular Disease Big Data Platform (Stroke Center Construction Information Management System). Specially trained follow-up staff completed the follow-up assessments by telephone, using the mRS to evaluate functional outcomes and promptly recording the results in the system. To ensure data accuracy and completeness, all data were independently collected and recorded by two professionally trained neurologists following a standardized procedure and subsequently cross-checked by other researchers.

Statistical analysis

Statistical analyses were performed using R software (version 4.2.2). The normality of continuous variables was tested using the Shapiro-Wilk test. Normally distributed continuous variables were expressed as mean ± standard deviation (mean ± SD), and comparisons between groups were performed using the independent samples t-test. Non-normally distributed continuous variables were expressed as median and interquartile range [median (Q1, Q3)], and comparisons between groups were performed using the Mann-Whitney U test. Categorical variables were expressed as frequency and percentage [n (%)], and comparisons between groups were performed using Pearson's chi-square test or Fisher's exact test.

To evaluate the predictive value of SII and SIRI for poor functional outcomes at 90 days before the procedure (Day 0), on the first day after the procedure (Day 1), and on the third day after the procedure (Day 3), we constructed receiver operating characteristic (ROC) curves and calculated the area under the curve (AUC), sensitivity, specificity, and accuracy. The optimal cut-off values were determined using the Youden index. The DeLong test was used to compare the differences in AUC between ROC curves at different time points.

We constructed four multivariate logistic regression models to investigate the association between SII and SIRI at different time points and 90-day functional outcomes. The crude model was unadjusted; model 1 was adjusted for age, hyperlipidemia, and atrial fibrillation; model 2 was further adjusted for baseline NIHSS score, GCS score, and the number of mechanical thrombectomy attempts based on model 1; and model 3 was further adjusted for baseline white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM), red blood cell (RBC), and platelet (PLT) based on model 2. The selection of covariates was based on variables with P values < 0.05 in the univariate analysis and factors associated with AIS prognosis reported in previous literature. We calculated odds ratios (ORs) and 95% confidence intervals (CIs) to assess the strength of the association between SII and SIRI and poor outcomes at 90 days.

To further investigate the correlation between SII and SIRI at different time points and 90-day mRS scores, we used Spearman's rank correlation analysis. Additionally, we constructed four multivariate linear regression models, with the selection and adjustment of covariates being the same as in the logistic regression models. All statistical analyses were two-sided, and P values < 0.05 were considered statistically significant.

RESULTS

Baseline characteristics and clinical features of patients

A total of 423 AIS patients who received MT treatment were included in this study, of which 168 (39.72%) had good functional outcomes (mRS 0-2) and 255 (60.28%) had poor functional outcomes (mRS 3-6) at 90 days. The baseline characteristics and clinical features of the two groups are detailed in Table 1.

Table 1: Baseline characteristics and clinical features of patients between good and poor outcome groups

Variables	Total (n=423)	Good outcome (n=168)	Poor outcome (n=255)	*P*
Age, year	68.00 (57.00,76.00)	64.00 (55.00, 71.75)	70.00 (59.00, 78.00)	**<.001**
Sex, male, n (%)	281 (66.43)	116 (69.05)	165 (64.71)	0.355
Current smoker, n (%)	148 (34.99)	68 (40.48)	80 (31.37)	0.055
Alcohol consumption, n (%)	93 (21.99)	41 (24.40)	52 (20.39)	0.330
Baseline NIHSS score	15.00 (11.00, 19.00)	13.00 (8.00, 16.00)	17.00 (13.00, 20.00)	**<.001**
Baseline GCS score	12.00 (9.00, 14.00)	14.00 (11.00, 15.00)	11.00(8.00, 14.00)	**<.001**
Systolic Blood pressure	148.00(133.00,164.00)	148.00(133.00,162.00)	149.00(132.50,166.00)	0.641
Diastolic Blood pressure	87.00 (77.00, 97.00)	87.00 (76.75, 97.25)	87.00 (77.00, 96.00)	0.330
Medical history, n (%)				
Diabetes mellitus	126 (29.79)	42 (25.00)	84 (32.94)	**0.081**
Hypertension	291 (68.79)	110 (65.48)	181 (70.98)	0.232
Dyslipidemia	101 (23.88)	50 (29.76)	51 (20.00)	**0.021**
Prior stroke or TIA	66 (15.60)	24 (14.29)	42 (16.47)	0.545
Atrial Fibrillation	173 (40.90)	57 (33.93)	116 (45.49)	**0.018**
Coronary artery disease	52 (12.29)	16 (9.52)	36 (14.12)	0.159
Valvular heart disease	53 (12.53)	19 (11.31)	34 (13.33)	0.538
Stroke etiology, n (%)				0.209
Large-artery atherosclerosis	220 (52.01)	96 (57.14)	124 (48.63)	
Cardioembolism	183 (43.26)	64 (38.10)	119 (46.67)	
Other determined etiology	20 (4.73)	8 (4.76)	12 (4.71)	
Occluded vessel, n (%)				
Anterior circulation	356 (84.16)	142 (84.52)	214 (83.92)	0.868
Posterior circulation	72 (17.02)	25 (14.88)	47 (18.43)	0.342
Treatment characteristics				
Intravenous thrombolysis, n (%)	173 (40.90)	72 (42.86)	101 (39.61)	0.506
Onset-to-puncture time, min	378.00(263.50,595.00)	368.50(233.75,661.25)	385.00(275.00,579.00)	0.457
Puncture-to-recanalization time, min	98.00(61.00,155.50)	94.50 (54.75,141.50)	100.00(67.50,165.00)	0.060
Onset-to-recanalization time, min	499.00(363.00,737.50)	494.00(319.50,755.25)	500.00(377.50,723.50)	0.422
Number of thrombectomy attempts	2.00 (1.00, 2.00)	1.00 (1.00, 2.00)	2.00 (1.00, 3.00)	**0.001**
mTICI score 2b-3, n (%)	125 (29.55)	58 (34.52)	67 (26.27)	**0.069**
Thrombectomy technique, n (%)				
Stent retriever	105 (24.82)	43 (25.60)	62 (24.31)	0.765
Aspiration	24 (5.67)	9 (5.36)	15 (5.88)	0.819
Combined	260 (61.47)	104 (61.90)	156 (61.18)	0.880
90-day morality	86 (20.33)	0 (0.00)	86 (33.73)	**<.001**
90-day mRS score	3.00 (1.00, 5.00)	1.00 (0.00, 2.00)	4.00 (4.00, 6.00)	**<.001**

Bold P-values indicate statistical significance (P < 0.05). **Abbreviations:** NIHSS, National Institutes of Health Stroke Scale; GCS, Glasgow Coma Scale; TIA, Transient Ischemic Attack; mTICI, modified Thrombolysis in Cerebral Infarction; mRS, modified Rankin Scale.

Compared with the good outcome group, patients in the poor outcome group were significantly older ($P < 0.001$) and had more severe neurological deficits [NIHSS: 17 (13-20) vs. 13 (8-16), $P < 0.001$; GCS: 11 (8-14) vs. 14 (11-15), $P < 0.001$]. There were no statistically significant differences between the two groups in terms of gender composition, smoking and drinking percentages, and blood pressure levels at admission ($P > 0.05$).

Regarding medical history, the proportion of patients with atrial fibrillation was significantly higher in the poor outcome group than in the good outcome group ($P = 0.018$), while the proportion of patients with hyperlipidemia was lower ($P = 0.021$). Although diabetes was more common in the poor outcome group (32.94% vs. 25.00%), the difference did not reach statistical significance ($P = 0.081$). The prevalence of other common risk factors (such as hypertension, previous stroke/transient ischemic attack, coronary artery disease, and valvular heart disease) was similar between the two groups. According to the TOAST classification, the main stroke etiologies in both groups were large artery atherosclerosis and cardiogenic embolism, with no significant difference in subtype composition ($P = 0.209$). Vascular imaging assessments showed that the proportions of patients with anterior or posterior circulation large vessel occlusion were also essentially consistent between the two groups.

Regarding treatment, there were no statistical differences between the two groups in the proportion of patients receiving intravenous thrombolysis and the median values of key process indicators (such as time from symptom onset to arterial puncture, time from puncture to reperfusion, and time from symptom onset to reperfusion). However, the poor outcome group required more retrieval attempts during the thrombectomy procedure [2 (1-3) vs. 1 (1-2), $P = 0.001$] and had a relatively lower proportion of patients achieving mTICI 2b-3 reperfusion (26.27% vs. 34.52%, $P = 0.069$). In terms of retrieval strategies, both groups mainly used stent retrieval combined with aspiration catheters, and there was no statistically significant difference in the composition of various methods. It is worth noting that the all-cause mortality rate at 90 days was significantly higher in the poor outcome group than in the good outcome group ($P < 0.001$), and the median mRS score was also significantly higher [4 (4-6) vs. 1 (0-2), $P < 0.001$].

Laboratory parameters in relation to outcome in patients

The laboratory parameters and inflammatory marker results are detailed in Table 2. Regarding the complete blood count, the poor outcome group had significantly higher white blood cell and neutrophil counts at all time points compared to the good outcome group ($P < 0.05$). Conversely, the lymphocyte and platelet counts in the poor outcome group were significantly lower than those in the good outcome group at all three time points (all $P < 0.001$). The monocyte count was higher in the poor outcome group than in the good outcome group only on Day 3 ($P < 0.001$), with no statistically significant differences at other time points. Biochemical indicators (including total protein, albumin, lipid profile, creatinine, and uric acid levels) showed no significant differences between the two groups ($P > 0.05$).

We focused on evaluating the dynamic changes of SII and SIRI at different time points and their relationship with prognosis (Figure 1). The results showed that the SII and SIRI levels in the poor outcome group were significantly higher than those in the good outcome group at all three time points (all $P < 0.001$). Further analysis revealed that the median SII and SIRI in the poor outcome group reached peak values on the first day after the procedure [SII: 2294.15 (1537.52, 3525.99) vs. 1520.98 (969.29, 2094.43); SIRI: 6.85 (4.40, 10.53) vs. 3.79 (2.53, 5.94), both $P < 0.001$]. Although they decreased on the third day after the procedure, they still remained at relatively high levels [SII: 2009.58 (1456.36, 3111.40) vs. 1043.81 (680.77, 1496.19); SIRI: 7.55 (4.90, 11.90) vs. 2.84 (1.52, 4.54), both $P < 0.001$].

Receiver operating characteristic curves of SII and SIRI

Both SII day 3 and SIRI day 3 showed strong predictive ability for poor functional outcomes at 90 days (Table 3, Figure 2).

The AUC of SII day 3 for predicting poor functional outcomes at 90 days was 0.80 (95% CI: 0.76-0.84), significantly higher than that on the first day after the procedure [0.70 (0.65-0.75)] and at admission [0.62 (0.56-0.67)]. The optimal cut-off value for SII on Day 3 was 1508.035, corresponding to an accuracy of 0.74 (0.70-0.79), sensitivity of 0.77 (0.70-0.83), and specificity of 0.73 (0.67-0.78). SIRI showed a similar trend to SII in predicting poor outcomes at 90 days, with its predictive performance on Day 3 [AUC: 0.82 (0.78-0.86), accuracy: 0.77, sensitivity: 0.80,

Table 2: Laboratory parameters and inflammatory markers in relation to outcome in patients

Variables	Total (n=423)	Good outcome (n=168)	Poor outcome (n=255)	P
WBC day0	8.53 (6.74,10.98)	8.18 (6.65.10.09)	8.80(6.75.11.94)	**0.028**
WBC day1	11.71 (9.80, 14.01)	10.58 (8.66. 12.57)	12.49 (10.34,14.69)	**<.001**
WBC day3	10.62(8.39, 13.66)	8.75 (7.05, 10.66)	12.13 (9.66, 15.60)	**<.001**
Neutrophil day0	6.09(4.36,8.57)	5.45 (4.01, 7.42)	6.44 (4.58, 9.74)	**<.001**
Neutrophil day1	9.99(8.02,12.03)	8.55 (6.91, 10.57)	10.73(8.83,12.93)	**<.001**
Neutrophil day3	8.60(6.39, 11.41)	6.38 (4.97,8.24)	10.07(8.11,13.85)	**<.001**
Lymphocyte day0	1.49(1.04,2.17)	1.75 (1.21.2.42)	1.37 (0.94, 1.97)	**<.001**
Lymphocyte day1	1.05 (0.74,1.38)	1.23 (0.92,1.62)	0.93 (0.70,1.21)	**<.001**
Lymphocyte day3	1.16 (0.86, 1.48)	1.37 (1.15, 1.69)	1.02 (0.73, 1.27)	**<.001**
Monocyte day0	0.45 (0.35.0.58)	0.43 (0.35, 0.58)	0.46 (0.35,0.56)	0.898
Monocyte day1	0.60 (0.46,0.74)	0.58 (0.46,0.71)	0.61 (0.46.0.79)	0.113
Monocyte day3	0.68 (0.49.0.85)	0.61 (0.45,0.77)	0.72 (0.54,0.91)	<.001
Platelet count day0	206.00(167.00,242.50)	213.00(180.75,249.50)	199.00(165.00,239.88)	**0.032**
Platelet count day1	201.00(168.50,242.00)	210.00(178.00,248.00)	196.00(160.00,234.00)	**0.014**
Platelet count day3	200.70(167.00,249.00)	213.65 (180.31, 260.50)	189.00(154.25.238.75)	**<.001**
Total Protein	71.42(68.00,74.97)	71.42 (68.12, 74.45)	71.42(67.90,75.20)	0.744
Albumin	39.63 (37.60,42.00)	39.70(37.96,42.00)	39.63 (37.14,42.00)	0.312
Triglycerides	1.35 (0.89, 1.71)	1.38 (0.99, 1.80)	1.33 (0.85, 1.66)	0.121
Total Cholesterol	4.72 (3.97, 5.35)	4.72 (3.96, 5.48)	4.72 (3.98, 5.25)	0.347
HDLC	1.17 (1.00, 1.35)	1.15 (1.00, 1.28)	1.19 (1.00,1.38)	0.510
LDLC	3.09 (2.54, 3.61)	3.09 (2.57, 3.67)	3.09 (2.50,3.47)	0.220
Creatinine	77.55(62.30,89.02)	76.70 (62.35, 88.70)	78.00(62.25,89.10)	0.559
Uric Acid	403.70(326.00,449.00)	407.50(325.25.452.00)	402.75 (334.25.442.50)	0.889
SII day0	801.00(467.70,1451.32)	685.66(383.83,1112.01)	968.64 (531.17.1735.55)	**<.001**
SII day1	1903.14(1243.01,2988.81)	1520.98 (969.29,2094.43)	2294.15 (1537.52,3525.99)	**<.001**
SII day3	1573.97 (979.86.2366.09)	1043.81 (680.77, 1496.19)	2009.58 (1456.36, 3111.40)	**<.001**
SIRI day0	1.68 (1.01,3.09)	1.43 (0.82. 2.35)	1.94 (1.18,3.79)	**<.001**
SIRI day1	5.50(3.32,8.77)	3.79 (2.53, 5.94)	6.85 (4.40,10.53)	**<.001**
SIRI day3	5.42 (2.75,9.49)	2.84 (1.52, 4.54)	7.55 (4.90,11.90)	**<.001**

Bold P-values indicate statistical significance (P < 0.05). **Subscript explanations:** d0, indicating data collected upon admission. d1, Day 1 post-procedure. d3, Day 3 post-procedure. **Abbreviations:** WBC, white blood cell count; HDLC, High-Density Lipoprotein Cholesterol; LDLC, Low-Density Lipoprotein Cholesterol; SII , Systemic Immune-Inflammation Index, SIRI, Systemic Inflammation Response Index.

specificity: 0.75] significantly better than that on Day 1 and Day 0. The optimal cut-off value for SIRI on Day 3 was 5.023.

Logistic regression models of SII and SIRI with poor outcome in patients

To further explore the association between SII and SIRI at different time points and patients' 90-day functional outcomes, we constructed a series of multivariate logistic regression models (Table 4). These models progressively adjusted for potential confounding factors to assess the independent predictive value of SII and SIRI. In the unadjusted crude model, SII and SIRI were significantly associated with poor outcomes at 90 days at all time points (all P < 0.001). After further adjusting for age, dyslipidemia, and atrial fibrillation (model 1), this association

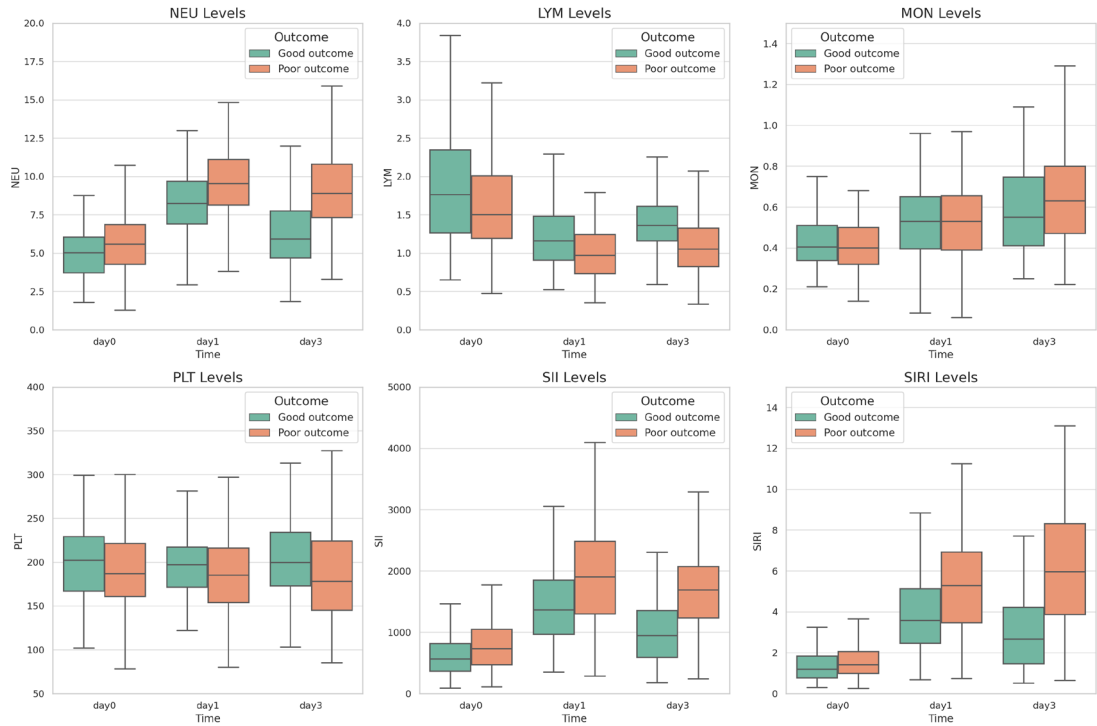

Figure 1. Temporal dynamics of biomarker levels in relation to patient outcomes.

persisted, and the effect size remained essentially unchanged. In model 2, we additionally included clinical characteristics such as baseline NIHSS score, GCS score, and the number of mechanical thrombectomy attempts. The results showed that the association between SII and SIRI and poor outcomes remained significant (all $P < 0.001$).

In the final model (model 3), we further adjusted for laboratory indicators at admission, including white blood cell count, lymphocyte count, neutrophil count, red blood cell count, and platelet count. The results indicated that the association between SII and SIRI at admission (Day 0) and poor outcomes at 90 days became non-significant. However, SII and SIRI on the first and third days after the procedure still maintained significant predictive value. In particular, SIRI on the third day showed the strongest independent predictive ability (OR 1.35, 95% CI 1.24-1.47, $P < 0.001$).

Linear trend analysis of SII and SIRI

Spearman correlation analysis revealed significant correlations between SII and SIRI at different time points and 90-day mRS scores (Figure 3). Notably,

Table 3: Comparison of laboratory parameters at different time points between good and poor outcome groups

Outcome and Parameter	AUC (95% CI)	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Cut-off Value
SII day0	0.62 (0.56-0.67)	0.55 (0.50-0.60)	0.81 (0.75-087)	0.38 (0.32-0.44)	1181.597
SII day1	0.70 (0.65-0.75)	0.67 (0.63-0.72)	0.67 (0.63-0.72)	0.70 (0.65-0.76)	1723.949
SII day3	0.80 (0.76-0.84)	0.74 (0.70-0.79)	0.77 (0.70-0.83)	0.73 (0.67-0.78)	1508.035
SIRI day0	0.63 (0.57-0.68)	0.63 (0.58-0.68)	0.46 (0.38-0.53)	0.74 (0.69-0.79)	1.244
SIRI day1	0.73 (0.68-0.78)	0.69 (0.64-0.73)	0.72 (0.65-0.79)	0.66 (0.60-0.72)	5.404
SIRI day3	0.82 (0.78-0.86)	0.77 (0.72-0.81)	0.80 (0.74-0.86)	0.75 (0.69-0.80)	5.023

Bold P-values indicate statistical significance ($P < 0.05$). **Subscript explanations:** day0, indicating data collected upon admission. day1, Day 1 post-procedure. day3, Day 3 post-procedure. **Abbreviations:** SII , Systemic Immune-Inflammation Index, SIRI, Systemic Inflammation Response Index.

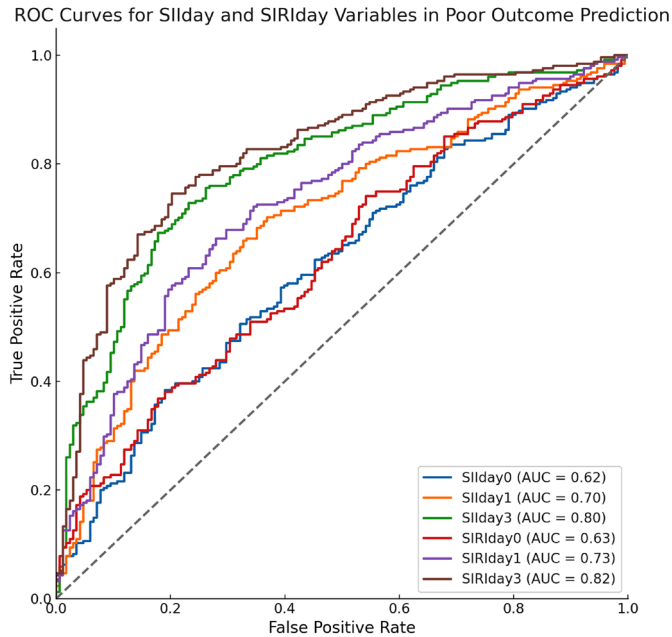

Figure 2. ROC curves for SII day and SIRI day variables in poor outcome prediction.

SII day 3 and SIRI day 3 showed the strongest correlations with mRS scores (SII: r = 0.56, P<0.001; SIRI: r=0.57, P<0.001). To quantify the relationship between SII and SIRI and mRS scores, we constructed a series of multivariate linear regression models (Table 5). In the unadjusted crude model, SII and SIRI were significantly positively correlated with mRS scores at all time points (all P < 0.001). This association remained stable after adjusting for age, dyslipidemia, and atrial fibrillation (model 1). After further including clinical characteristics (including the number of mechanical thrombectomy attempts, baseline NIHSS score, and GCS score) (model 2), the association between SII and SIRI and mRS scores remained significant (all P < 0.001).

In the final model (model 3), we additionally adjusted for laboratory indicators at admission. The results showed that the association between SII and SIRI at admission and mRS scores became non-significant. However, SII and SIRI on the first and third days after the procedure still maintained a significant association with mRS scores. In particular, SIRI on the third day showed the strongest independent association (β = 0.09, 95% CI: 0.07-0.11, P < 0.001).

Table 4: Logistic regression models assessing the association of SII and SIRI with poor outcome in patients

Variables	Crude Model		Model 1		Model 2		Model 3	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
SII day0	1.01(1.01~1.01)	**<.001**	1.01(1.01~1.01)	**<.001**	1.01(1.01~1.01)	**<.001**	1.00(1.00~1.00)	0.543
SII day1	1.01(1.01~1.01)	**<.001**	1.01(1.01~1.01)	**<.001**	1.01(1.01~1.01)	**<.001**	1.01(1.01~1.01)	**<.001**
SII day3	1.01(1.01~1.01)	**<.001**	1.01(1.01~1.01)	**<.001**	1.01(1.01~1.01)	**<.001**	1.01(1.01~1.01)	**<.001**
SIRI day0	1.22(1.11~1.35)	**<.001**	1.27 (1.14~1.41)	**<.001**	1.25 (1.12~1.39)	**<.001**	1.13 (0.95~1.34)	**0.183**
SIRI day1	1.21(1.14~1.29)	**<.001**	1.22(1.15~1.30)	**<.001**	1.20(1.12~1.27)	**<.001**	1.18 (1.11 ~ 1.26)	**<.001**
SIRI day3	1.36 (1.26~1.46)	**<.001**	1.36 (1.26~1.47)	**<.001**	1.33 (1.23~1.44)	**<.001**	1.35 (1.24~1.47)	**<.001**

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; SII , Systemic Immune-Inflammation Index, SIRI, Systemic Inflammation Response Index; **Note:** Crude Model: Unadjusted. Model 1: Adjusted for age, dyslipidemia, and atrial fibrillation. Model 2: Adjusted for variables in Model 1 plus number of thrombectomy attempts, Baseline NIHSS, and Baseline GCS. Model 3: Adjusted for variables in Model 2 plus admission white blood cell count, lymphocyte count, neutrophil count, red blood cell count and platelet count.

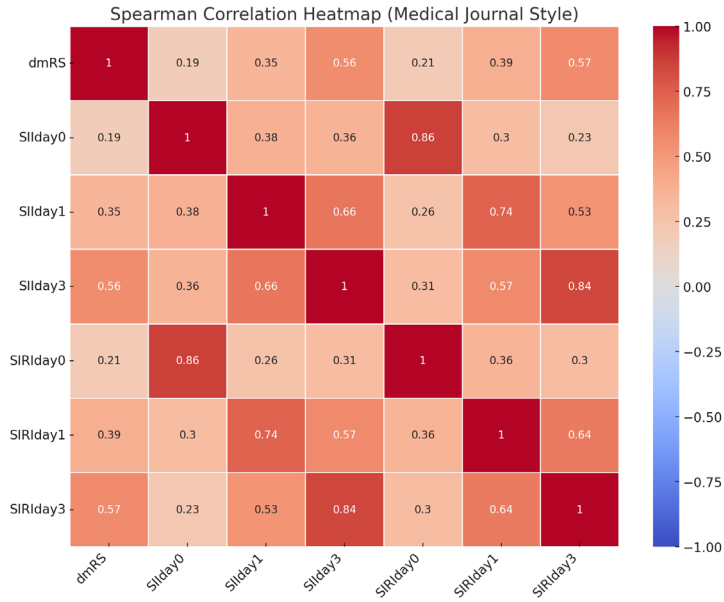

Figure 3. Spearman correlation heatmap (Medical journal style)

DISCUSSION

This retrospective cohort study systematically evaluated the dynamic changes of SII and SIRI after MT treatment and their predictive value for functional outcomes in AIS patients. Our key findings include: First, peripheral blood inflammatory markers exhibited significant dynamic change patterns after MT. Both groups of patients had SII and SIRI reaching peak values on the first day after the procedure and subsequently decreasing, but the poor outcome group still maintained relatively high levels on the third day. Notably, the poor outcome group also showed persistently elevated neutrophil counts and more pronounced decreases in lymphocyte and platelet counts, which may reflect a sustained inflammatory state and potential immune dysfunction. Second, we found that SII and SIRI measured on the third day after the procedure had the strongest predictive ability for poor functional outcomes at 90 days, significantly better than the values measured at admission and on the first day after the procedure. Moreover, SII and SIRI on the third day after the procedure were significantly positively correlated with 90-day mRS scores, further supporting the potential of these inflammatory markers as independent prognostic factors.

Compared to purely pharmacological treatment, AIS patients receiving MT treatment may experience a more intense inflammatory response. Previous studies have shown that although MT

Table 5: Liner trend analysis of SII and SIRI at different time points in relation to 90-day mRS in patients

Variables	Crude Model		Model 1		Model 2		Model 3	
	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*
SII day0	0.01 (0.01 ~ 0.01)	**<.001**	0.01 (0.01 ~0.01)	**<.001**	0.01 (0.01~0.01)	**<.001**	0.00 (-0.00~0.00)	0.617
SII day1	0.01 (0.01 ~ 0.01)	**<.001**	0.01 (0.01 ~ 0.01))	**<.001**	0.01 (0.01~0.01)	**<.001**	0.01 (0.01~0.01)	**<.001**
SII day3	0.01 (0.01 ~ 0.01)	**<.001**	0.01 (0.01 ~ 0.01)	**<.001**	0.01 (0.01~0.01)	**<.001**	0.01 (0.01~0.01)	**<.001**
SIRI day0	0.11 (0.05 ~ 0.16)	**<.001**	0.12 (0.07 ~ 0.17)	**<.001**	0.10 (0.05~0.15)	**<.001**	0.03 (-0.07~0.12)	0.576
SIRI day1	0.10 (0.07 ~ 0.12)	**<.001**	0.09 (0.07 ~ 0.12)	**<.001**	0.08 (0.05~0.10)	**<.001**	0.07 (0.04~0.10)	**<.001**
SIRI day3	0.11 (0.09 ~ 0.13)	**<.001**	0.11 (0.09 ~ 0.13)	**<.001**	0.10 (0.08~0.12)	**<.001**	0.09 (0.07~0.11)	**<.001**

Abbreviations: SII , Systemic Immune-Inflammation Index, SIRI, Systemic Inflammation Response Index.; β, Regression Coefficient. **Note:** Crude Model: Unadjusted. Model 1: Adjusted for age, dyslipidemia, and atrial fibrillation. Model 2: Adjusted for variables in Model 1 plus number of thrombectomy attempts, Baseline NIHSS, and Baseline GCS. Model 3: Adjusted for variables in Model 2 plus admission white blood cell count, lymphocyte count, neutrophil count, red blood cell count and platelet count.

treatment can effectively restore blood flow, it may also trigger reperfusion injury.[19] During the reperfusion process, ischemic-injured brain tissue releases large amounts of damage-associated molecular patterns, thereby activating innate and adaptive immune responses. This process involves various inflammatory cells, including neutrophils, monocytes, lymphocytes, platelets, as well as microglia and macrophages within the central nervous system. These cells infiltrate the damaged brain tissue and release multiple pro-inflammatory cytokines, such as tumor necrosis factor-α, interleukin-1β, and interleukin-6, which in turn trigger an inflammatory cascade.[20] Furthermore, the MT procedure itself may directly stimulate platelets and vascular endothelial cells through mechanical forces, further promoting the release of inflammatory mediators.[7-9] If this complex inflammatory response becomes uncontrolled, it may not only exacerbate local brain tissue damage but also lead to systemic complications, significantly affecting patient outcomes. Therefore, it is of great importance to thoroughly investigate the dynamic change patterns of the inflammatory response after MT and its relationship with clinical outcomes. This will not only help us better understand the pathophysiological processes of AIS but may also provide a theoretical basis for developing new immunomodulatory strategies to ultimately improve patients' long-term prognosis.

In recent years, SII and SIRI have emerged as novel integrated inflammatory markers, demonstrating significant clinical value in the prognostic assessment of various diseases. These indices were initially used to evaluate prognosis in cancer patients and have subsequently shown remarkable significance in predicting outcomes in cardiovascular diseases, all-cause mortality, stroke, and other conditions.[10-14] SII and SIRI integrate information from multiple inflammatory cells, including neutrophils, lymphocytes, monocytes, and platelet counts, providing a more comprehensive reflection of the inflammatory state in patients' peripheral blood. These inflammatory cells participate in the pathological processes of brain injury through different mechanisms.[15,16] In the early stages of AIS, neutrophils are the first to accumulate in the infarct core and penumbra. Activated neutrophils release various cytokines, such as matrix metalloproteinase-9, chemokines, proteases, and reactive oxygen species, which exacerbate excitotoxicity and inflammatory cascades in neurons. Platelets interact with endothelial cells under high shear rate conditions, releasing proteins such as P-selectin, αIIbβ3, GPIbα, and ICAM-2.[21,22] These proteins bind to neutrophils, forming platelet-leukocyte aggregates that further aggravate vascular occlusion and ischemic injury.[23] Furthermore, substances released by platelet α-granules, such as fibrinogen, fibronectin, and platelet factor 4, promote platelet adhesion and aggregation, participating in the coagulation process and exacerbating thrombus formation.[24] The impact of lymphocytes on AIS varies depending on their subtype. CD4+, CD8+ T cells, and γδ T cells produce pro-inflammatory cytokines such as interferon-γ and interleukin-17, intensifying the inflammatory response and leading to neuronal death.[25] Conversely, regulatory T cells (Tregs) exert neuroprotective effects by secreting interleukin-10 (IL-10).[26] Monocytes, on the other hand, upregulate the expression of cytidine monophosphate kinase 2 (CMPK2), stimulating the production of oxidized mitochondrial DNA (Ox-mtDNA), which in turn activates the NLRP3 inflammasome in microglia and macrophages, further promoting neuroinflammation.[27]

Our study results provide clinical evidence for these mechanisms. At admission and on the first day after MT, the poor outcome group exhibited more pronounced elevations in neutrophils and reductions in lymphocytes and platelets. On the third day after MT, although both groups showed a decrease in neutrophil counts, the poor outcome group still maintained higher levels, and their lymphocyte count recovery was less robust. These findings reveal that sustained inflammatory responses may be one of the key factors leading to poor prognosis. Notably, the dynamics of inflammatory marker changes observed in our study highly align with the time course of neuroinflammatory cascades reported in previous literature. Typically, this response is initiated within hours after stroke, reaches its peak at 24-48 hours, and gradually subsides after 72 hours.[28-30] Our study (Figure 1) clearly demonstrates this dynamic process.

Our study has several notable strengths. First, to the best of our knowledge, this is the first study to systematically evaluate the relationship between SII and SIRI and functional outcomes in AIS patients after MT treatment. Second, by conducting multi-timepoint assessments at admission, day 1, and day 3 after MT, our study captured the dynamic changes in inflammatory markers, providing more comprehensive information than single-timepoint measurements. However, our study also has some limitations. First, this is a retrospective single-center study with a relatively

limited sample size. The generalizability of our findings needs to be validated in larger-scale, multicenter prospective cohorts. Second, our study only assessed short-term outcomes at 90 days. The impact of SII and SIRI on patients' long-term functional recovery and quality of life requires further investigation. Moreover, although we adjusted for multiple confounding factors, it is difficult to completely exclude the influence of residual confounding. Despite these limitations, our study provides important insights into understanding the dynamics of the inflammatory response and its impact on prognosis in AIS patients receiving MT treatment, paving the way for future research and clinical practice. Future studies should focus on the following aspects: further exploring the prognostic predictive value of SII and SIRI in different stroke subtypes and reperfusion treatment modalities, comparing them with other known prognostic markers such as NIHSS score and infarct volume, and establishing more comprehensive prognostic assessment models.

In conclusion, this study is the first to dynamically evaluate the application value of SII and SIRI in the prognostic assessment of AIS patients receiving MT treatment. We found that both SII and SIRI are independent predictors of 90-day functional outcomes in AIS patients, especially the measurements on the third day after the procedure, which have better predictive performance than those on the first day after the procedure and at admission. These findings provide new insights for early identification of high-risk patients and optimization of treatment strategies, potentially improving the long-term prognosis of AIS patients.

DISCLOSURE

Financial support: This work was supported by the Fujian Provincial Key Medical Discipline Construction Project (grant number 050172).

Conflicts of interest: None

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