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Original Article

Prognostic evaluation of ischemic stroke complicated by pulmonary infection using SII and CALLY indices

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Abstract: Objective: To evaluate the prognostic value of the systemic immune-inflammation index (SII) and the CRP-Albumin-Lymphocyte (CALLY) index in ischemic stroke (IS) patients complicated by pulmonary infection (PI). Methods: We retrospectively analyzed clinical data from 122 IS patients with PI (observation group) and 100 IS patients without PI (control group) at the First Hospital of Hunan University of Chinese Medicine, from April 2022 to September 2024. All patients in the observation group were followed up for 6 months. Prognosis was assessed using the modified Rankin Scale (mRS). Results: The observation group had higher platelet, neutrophil, C-reactive protein, and SII levels, and lower lymphocyte, albumin, and CALLY levels compared to the control group (all $P<0.05$). Multivariate analysis identified these indices as independent predictors of prognosis (all $P<0.05$). Patients with poor prognosis exhibited elevated SII and reduced CALLY levels (both $P<0.05$). SII was positively correlated with mRS ($r=0.885$), while CALLY was negatively correlated ($r=-0.834$) ($P<0.001$). The area under the curve for predicting poor prognosis was 0.831 for SII, 0.877 for CALLY, and 0.905 for the combined indices. Conclusion: SII and CALLY indices are valuable for predicting the prognosis of IS with PI, and their combined use enhances predictive accuracy.

Keywords: Ischemic stroke, pulmonary infection, systemic immune inflammation index, CRP-Albumin-Lymphocyte index, relevance, prognosis

Introduction

Ischemic stroke (IS) remains a leading cause of global mortality and long-term disability, with its incidence and recurrence rates continuing to rise [1, 2]. Pulmonary infection (PI) is one of the most common complications in stroke patients and significantly worsens prognosis [3, 4]. The pathogenesis of post-stroke pulmonary infection is complex, closely linked to stroke-induced immunosuppression, and influenced by factors such as malnutrition, altered consciousness, and swallowing dysfunction [5, 6]. Therefore, accurately identifying high-risk patients early and predicting poor prognosis remains a key challenge.

The systemic immune-inflammation index (SII), derived from neutrophil (NEU), lymphocyte (LYM), and platelet (PLT) counts, is a reliable indicator of systemic immune and inflammatory responses [7, 8]. Previous studies have demonstrated the prognostic value of the SII index in diseases such as cancer, cardiovascular diseases, and infections [9, 10]. The CRP-Albumin-Lymphocyte (CALLY) index, which combines C-reactive protein (CRP), albumin (ALB), and LYM, serves as an effective tool for assessing the status of critically ill patients [11, 12].

Patients with IS complicated by PI often exhibit increased inflammation, weakened immune function, and poor nutritional status, supporting the theoretical application of the SII and CALLY indices [13, 14]. However, research on the use of these indices to predict the prognosis of such patients remains limited, and further investigation is needed to establish their clinical value and applicability. In this study, we retrospectively analyzed clinical data from IS patients with PI to assess the prognostic value of the SII and CALLY indices and explore

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their correlation with poor outcome, providing a basis for timely intervention and effective patient management.

Materials and methods

Patients

This study retrospectively examined the medical records of 122 patients with IS complicated by PI, and 100 IS patients without PI treated at the First Hospital of Hunan University of Chinese Medicine from April 2022 to September 2024. Subjects were enrolled based on rigorous inclusion and exclusion criteria. This study was approved by the Ethics Committee of the First Hospital of Hunan University of Chinese Medicine, and was conducted in accordance with ethical guidelines for research involving human participants.

Inclusion criteria: patients in both groups were diagnosed with IS confirmed by cranial MRI or CT [15]; those in the observation group met the diagnostic criteria for PI during hospitalization [16]; and all had complete clinical data.

Exclusion criteria: patients with hemorrhagic stroke or other encephalopathies; those with severe systemic inflammatory diseases, malignancies, or significant liver and kidney dysfunction; recent use of immunosuppressants or glucocorticoids; and patients lost to follow-up.

Patients with IS complicated by PI were assigned to the observation group, and those with IS alone were placed in the control group.

Research methods

The general data, including gender and age, of all patients were retrospectively analyzed. All patients underwent standardized blood testing upon admission, and all hematologic data were obtained from the first laboratory examination after admission. The tested data included PLT, NEU, LYM, CRP, and ALB. Venous blood samples were collected within 24 hours of admission under fasting conditions and analyzed using an automated hematology analyzer (Sysmex XN-9000; Sysmex Corporation, Kobe, Japan) for blood cell counts, and a biochemical analyzer (Beckman Coulter AU5800; Beckman Coulter, Inc.) for CRP and ALB measurements.

The SII was calculated as: SII = PLT×NEU/LYM [17]. The CALLY index was calculated as: CALLY = ALB×LYM/(CRP×10) [18].

All patients in the observation group underwent a 6-month follow-up. Prognosis was evaluated using the modified Rankin Scale (mRS) [19], where higher scores corresponded to greater disability. Patients scoring between 0 and 2 were classified into the good prognosis group (n=82), while those with scores from 3 to 6 were assigned to the poor prognosis group (n=40).

Statistical methods

Statistical analyses were performed using SPSS 22.0, while GraphPad Prism 8 was used for data visualization. Categorical variables were presented as rates (%) and compared between groups using the chi-square test. Continuous variables were expressed as means ± standard deviation and were analyzed with t-tests for pairwise comparisons. Multivariate analysis was conducted by logistic regression. Pearson correlation was employed to evaluate associations among variables. ROC curve analysis assessed the prognostic performance of the SII and CALLY indices in patients with IS complicated by PI. A *P*-value less than 0.05 was considered significant.

Results

Comparison of general data

There were no significant differences in general data between the two groups (all P>0.05), as shown in **Table 1**.

Comparison of hematologic data

The observation group exhibited significantly higher levels of PLT, NEU, and CRP compared to the control group, while LYM and ALB levels were notably lower in the observation group (all P<0.05), as shown in **Figure 1**.

Comparison of SII and CALLY indices

The observation group had a significantly higher SII and a lower CALLY compared to the control group (both P<0.05), as shown in **Figure 2**.

Table 1. Comparison of general data of patients between the two groups

Clinical information	Control group (n=100)	Observation group (n=122)	t/χ^2	P
Age (years)	54.93±5.26	55.62±5.47	0.951	0.343
Sex (male/female)	56/44	60/62	1.024	0.311
Body mass index (kg/m^2)	25.34±2.96	25.15±3.08	0.465	0.642
History of hypertension [n (%)]	52 (52.00)	68 (55.74)	0.309	0.578
History of diabetes [n (%)]	28 (28.00)	38 (31.15)	0.201	0.610
History of hyperlipidaemia [n (%)]	15 (15.00)	24 (19.67)	0.828	0.363
Smoking history [n (%)]	53 (53.00)	70 (57.38)	0.426	0.514
Drinking history [n (%)]	58 (58.00)	65 (53.28)	0.496	0.481
Dysphagia [n (%)]	32 (32.00)	44 (36.07)	0.404	0.525
Hospitalization (days)	11.92±1.46	12.25±1.38	1.727	0.086

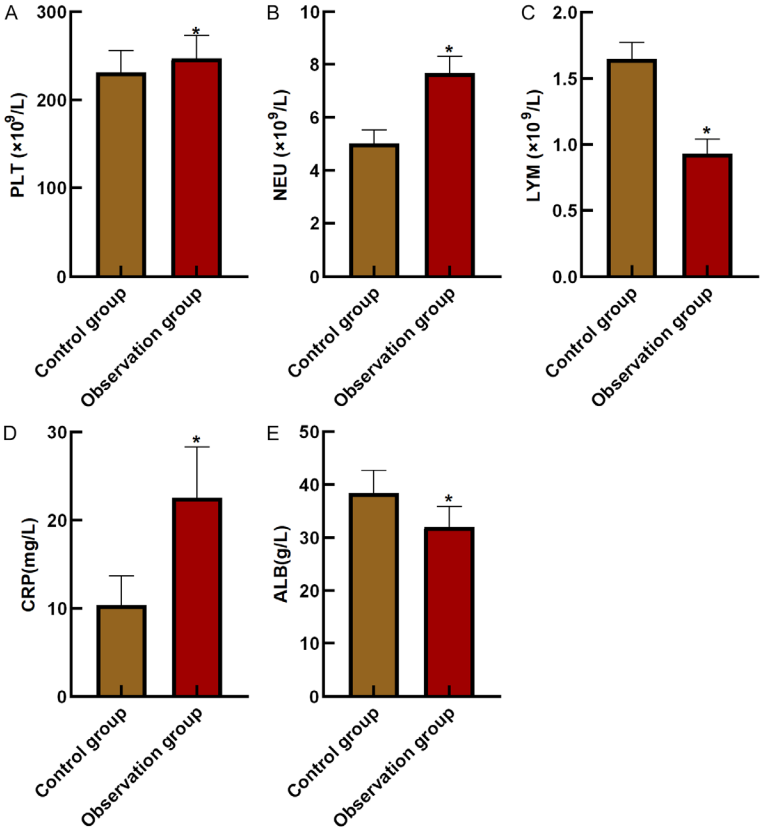

Figure 1. Comparison of hematologic data. A. Comparison of PLT between two groups; B. Comparison of NEU between two groups; C. Comparison of LYM between two groups; D. Comparison of CRP between two groups; E. Comparison of ALB between two groups. Note: Compared with the control group, *P<0.05. PLT: Platelets; NEU: Neutrophils; LYM: Lymphocytes; CRP: C-reactive protein; ALB: Albumin.

Prognosis of patients with IS complicated by PI

The prognosis of patients was evaluated according to the mRS score. Among the patients, 82 had a good prognosis (67.21%), and 40 had a poor prognosis (32.79%).

Comparison of hematological data in patients with varying prognoses

Compared to the good prognosis group, the poor prognosis group exhibited elevated levels of PLT, NEU, and CRP, and decreased levels of LYM and ALB (all P<0.05), as shown in **Figure 3**.

Comparison of SII and CALLY indices in patients with different prognosis

The poor prognosis group showed a significantly higher SII index and a lower CALLY index compared to the good prognosis group (both P< 0.05), as shown in **Figure 4**.

Multiple factor logistic regression analysis of IS complicated by PI

Multivariate analysis revealed that PLT, NEU, LYM, CRP, ALB, SII index, and CALLY index were independent factors affecting PI in patients with IS (all P<0.05), as shown in **Table 2**.

Association of SII and CALLY indices with mRS scores

In patients with IS complicated by PI, the SII index showed a positive correlation with the mRS score (r=0.885, P<0.001), whereas the CALLY index was negatively correlated with the

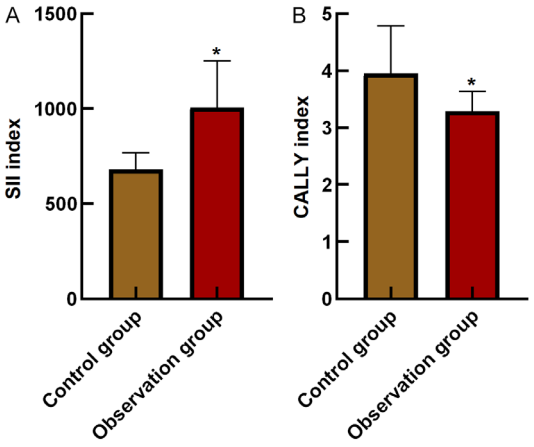

Figure 2. Comparison of SII and CALLY index across the two groups. A. Comparison of SII index between two groups; B. Comparison of CALLY index between two groups. Note: Compared to the control group, *P<0.05. SII: Systemic immune-inflammation; CALLY: CRP-Albumin-Lymphocyte.

mRS score (r=-0.834, P<0.001), as shown in **Figure 5**.

Prognostic significance of each index in IS patients complicated by PI

ROC curve analysis showed the following AUC values for predicting the prognosis of IS complicated with PI:

The AUC for PLT was 0.645 (95% CI: 0.538-0.751), with an optimal cutoff value of 265.00, Jordan index of 0.316, sensitivity of 47.5%, and specificity of 84.1%.

The AUC for NEU was 0.782 (95% CI: 0.694-0.869), with an optimal cutoff value of 6.72, Jordan index of 0.528, sensitivity of 67.5%, and specificity of 85.3%.

The AUC for LYM was 0.761 (95% CI: 0.669-0.853), with an optimal cutoff value of 1.18, Jordan index of 0.468, sensitivity of 72.5%, and specificity of 74.3%.

The AUC for CRP was 0.721 (95% CI: 0.621-0.822), with an optimal cutoff value of 24.86, Jordan index of 0.433, sensitivity of 64.1%, and specificity of 79.2%.

The AUC for ALB was 0.707 (95% CI: 0.609-0.805), with an optimal cutoff value of 35.55, Jordan index of 0.344, sensitivity of 62.5%, and specificity of 71.9%.

The AUC for the SII index was 0.831 (95% CI: 0.745-0.916), with an optimal cutoff value of 1111.00, Youden index of 0.677, sensitivity of 77.5%, and specificity of 90.2%.

The AUC for the CALLY index was 0.877 (95% CI: 0.813-0.941), with an optimal cutoff value of 2.96, Youden index of 0.716, sensitivity of 87.5%, and specificity of 84.1%.

When combining both indices, the AUC improved to 0.905 (95% CI: 0.843-0.968), with a Youden index of 0.776, sensitivity of 82.5%, and specificity of 95.1%, as shown in **Table 3** and **Figure 6**.

Typical case

A 63-year-old male patient was admitted to the emergency department with the chief complaint of "sudden-onset dizziness and unsteady gait for approximately 40 hours". He was initially diagnosed with "acute cerebrovascular disease: cerebral infarction?". Upon admission, the patient was conscious and in fair condition. He complained of dizziness without evident vertigo, mild headache, weakness in both lower limbs with inability to walk, limb numbness, nausea, and vomiting. He exhibited a broad-based gait with leftward deviation upon standing. Dysarthria and slurred speech were present, and he was unable to open his mouth. The patient had excessive sputum production but no facial asymmetry, tinnitus, or hearing loss. He was on a liquid diet and experienced choking when drinking quickly. Sleep was adequate, urination was normal, and defecation had not occurred in two days. No significant weight changes were noted over the past three months. Neurological examination revealed a clear mental status and cooperative behavior. He was oriented, with intact memory, calculation, and orientation abilities. Pupils were equal, round, and reactive to light (3 mm in diameter). Eye movements were intact, though horizontal nystagmus of the left eye was observed. Bilateral forehead wrinkles and nasolabial folds were symmetrical. Muscle strength was grade 5 in both upper limbs and grade 5- in both lower limbs. Muscle tone was normal in all limbs. Sensation was intact, and tendon reflexes were brisk (++), with no pathological reflexes. The patient was unable to cooperate with tandem gait and Romberg testing. Finger-to-nose and heel-knee-shin tests on the left side were inac-

Table 2. Multiple factor logistic regression analysis of IS complicated by PI

Factor	B	SE	Wald	Sig.	Exp (B)	95% CI
PLT	0.004	0.015	7.55	0.001	1.004	0.999-1.009
NEU	0.213	0.069	9.57	0.002	1.238	1.082-1.416
LYM	-0.310	0.127	6.03	0.015	0.734	0.572-0.942
CRP	0.042	0.015	7.55	0.006	1.043	1.012-1.076
ALB	-0.127	0.049	6.78	0.009	0.881	0.800-0.970
SII index	0.001	0.001	4.70	0.030	1.001	1.000-1.002
CALLY index	-0.434	0.165	7.01	0.008	0.648	0.472-0.890

Note: PLT: Platelets; NEU: Neutrophils; LYM: Lymphocytes; CRP: C-reactive protein; ALB: Albumin; SII: Systemic immune-inflammation; CALLY: CRP-Albumin-Lymphocyte.

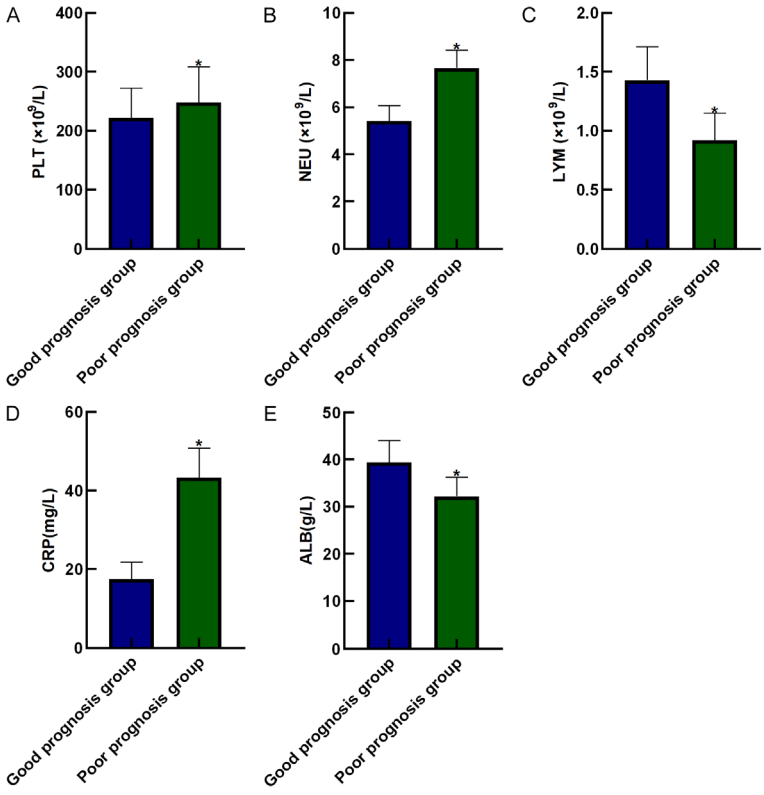

Figure 3. Comparison of hematologic data in patients with varying prognoses. A. Comparison of PLT with different prognosis; B. Comparison of NEU with different prognosis; C. Comparison of LYM with different prognosis; D. Comparison of CRP with different prognosis; E. Comparison of ALB with different prognosis. Note: Compared tp the group with good prognosis, *P<0.05. PLT: Platelets; NEU: Neutrophils; LYM: Lymphocytes; CRP: C-reactive protein; ALB: Albumin.

curate. NIHSS score: 3 (ataxia 2 + dysarthria 1); mRS score: 1; ADL score: 60; Kubota Water Swallowing Test: Grade 3.

At discharge, the patient's cough and sputum production had improved. Dizziness and headache were relieved, and bilateral lower limb weakness and numbness had improved. He could walk slowly with reduced leftward deviation and improved gait stability. However, dysarthria and slurred speech persisted. Swallowing difficulties remained, and he was maintained on nasogastric tube feeding with a liquid diet. No nausea, vomiting, facial asymmetry, tinnitus, or hearing loss were reported. Neurological status at discharge remained similar: alert and oriented, with mild dysarthria. Pupils were equal and reactive, with horizontal left eye nystagmus. Symmetrical facial features and muscle strength (upper limbs: grade 5; lower limbs: grade 5-) were maintained. Sensation and reflexes were unchanged. Finger-to-nose and heel-knee-shin tests on the left remained inaccurate. Head MRI and lung CT examination upon admission are shown in **Figures 7**, **8**.

Discussion

In IS patients, PI is a common and serious complication that can significantly prolong hospitalization, increase medical costs, and even worsen neurological deficits, ultimately affecting long-term prognosis [20, 21]. Early identification of high-risk patients with poor prognosis is crucial. However, traditional evaluation methods (such as basic laboratory tests or imaging) have limitations, including low sensitivity and long evaluation periods [22, 23]. Therefore, identifying simple, sensitive, and reproducible serum biomarkers is essential to guide clinical decision-making.

Inflammatory response plays a key role in the pathogenesis of both IS and PI. The SII, a com-

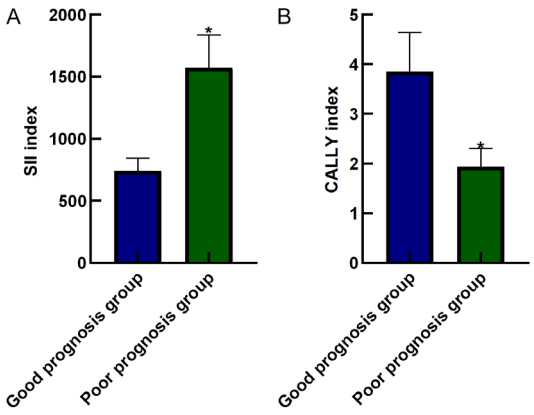

Figure 4. Comparison of SII index and CALLY index among patients with different prognosis. A. Comparison of SII index of different prognosis; B. Comparison of CALLY index of different prognosis. Note: Compared to the group with good prognosis, *P<0.05. SII: Systemic immune-inflammation; CALLY: CRP-Albumin-Lymphocyte.

prehensive inflammatory marker constructed from PLT, NEU and LYM counts, reflects the immune and inflammatory status of the body and has been shown to have good predictive value for various diseases [24, 25]. Similarly, the CALLY index, which combines CRP, ALB, and LYM, provides insight into the body's inflammation and nutritional status and is widely used for prognostic evaluation in diseases such as cancer and severe infections [26, 27].

The study findings revealed that the observation group had elevated levels of PLT, NEU, CRP, and SII compared to the control group, while LYM, ALB, and CALLY levels were reduced in the observation group. The SII index, as a composite marker combining PLT, NEU, and LYM, has been shown by Hou et al. [28] to possess high sensitivity and specificity in predicting the prognosis of IS patients, which aligns with the findings of this study. The reductions in ALB and the CALLY index reflect a deterioration in nutritional and immune status. The CALLY index, which integrates inflammation, nutrition, and immune function, has been supported by Pan et al. [29] as an effective prognostic tool in neurological diseases.

The likely underlying mechanism was analyzed as follows. PI induces a strong inflammatory response, promoting the release of neutrophils into the bloodstream to combat pathogens, which contributes to an increase in the SII. PLT are involved not only in hemostasis but also in cytokine release and leukocyte adhesion during inflammation. Infected states lead to PLT activation, reflecting enhanced inflammation and vascular endothelial reactions. The sympathetic nervous system and stress response activated after IS inhibit lymphocyte production and induce apoptosis, contributing to the rise in SII. CRP, a classical marker of acute inflammation, is synthesized in large quantities by the liver during infection, rapidly increasing in response to inflammation, which contributes to the decline of the CALLY index. In infectious and inflammatory states, the liver prioritizes the synthesis of acute-phase proteins, inhibiting ALB synthesis. Furthermore, IS patients often suffer from inadequate nutritional intake and metabolic disorders, which further reduce ALB levels. The decrease in LYM reflects immune system suppression, which is related to the activation of the neural immune axis and stress response following IS, and is a key factor contributing to the decline in the CALLY index [30, 31].

Additionally, the study showed that patients in the poor prognosis group had higher levels of PLT, NEU, CRP, and SII, while their LYM, ALB, and CALLY levels were lower, indicating that these patients had significantly enhanced systemic inflammatory responses and poorer nutritional status.

This study found that in IS patients with PI, the SII index was positively correlated with the mRS score, whereas the CALLY index showed a negative correlation with the mRS score. This suggested that as the SII index increases and the CALLY index decreases, the prognosis of patients with IS complicated by PI worsens. The SII index comprehensively reflects the intensity and immune status of inflammation. Patients with a larger stroke area and more severe infection often experience a more significant increase in SII, which leads to difficulties in recovery and a higher disability rate, resulting in a poor prognosis as reflected by the mRS score. Additionally, activated PLT promotes the release of inflammatory factors and thrombosis, which may exacerbate brain ischemia and dysfunction, further increasing the mRS score.

The CALLY index integrates immune function, nutritional status, and inflammation levels. A high CALLY index indicates low inflammation,

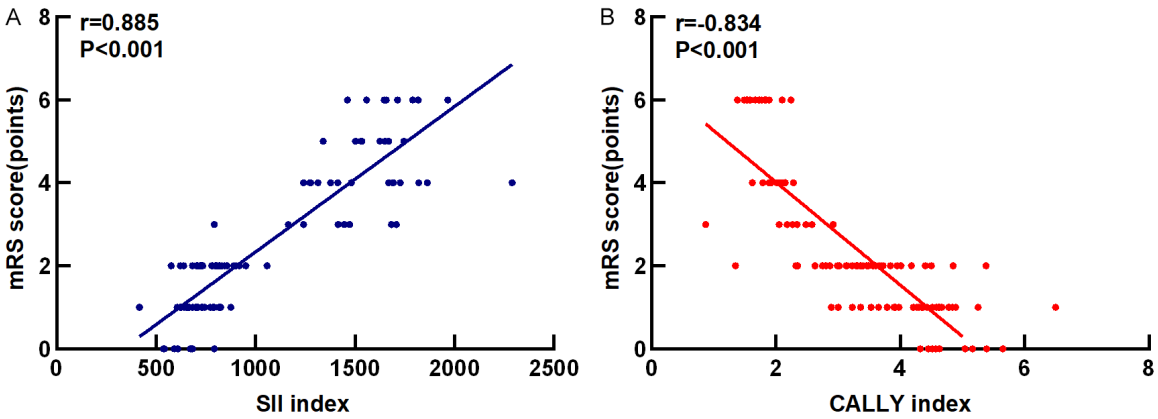

Figure 5. Association of SII and CALLY indices with mRS scores. A. Correlation between SII index and prognosis of patients; B. Correlation between CALLY index and prognosis of patients. Note: SII: Systemic immune-inflammation; CALLY: CRP-Albumin-Lymphocyte; mRS: modified Rankin Scale.

Table 3. Prognostic significance of each index on IS and patients complicated by PI

Predictive index	AUC	95% CI	Youden index	Sensitivity (%)	Specificity (%)	Cut-off value
PLT	0.645	0.538-0.751	0.316	47.50	84.10	265.00
NEU	0.782	0.694-0.869	0.528	67.50	85.30	6.72
LYM	0.761	0.669-0.853	0.468	72.50	74.30	1.18
CRP	0.721	0.621-0.822	0.433	64.10	79.20	24.86
ALB	0.707	0.609-0.805	0.344	62.50	71.90	35.55
SII index	0.831	0.745-0.916	0.677	77.50	90.20	1111.00
CALLY index	0.877	0.813-0.941	0.716	87.50	84.10	2.96
SII combined with CALLY prediction	0.905	0.843-0.968	0.776	82.50	95.10	-

Note: PLT: Platelets; NEU: Neutrophils; LYM: Lymphocytes; CRP: C-reactive protein; ALB: Albumin; SII: Systemic immune-inflammation; CALLY: CRP-Albumin-Lymphocyte; AUC: Area under curve.

good nutrition, and strong immunity, which helps effectively eliminate infections. Moreover, good nutrition and immune status contribute to infection control and neurological functional recovery. As a result, patients with high CALLY values tend to have a lower mRS score and better prognosis [32, 33].

The ROC curve analysis in this study demonstrated that the AUC for PLT, NEU, LYM, CRP, and ALB in predicting the prognosis of IS patients complicated by PI were 0.645, 0.782, 0.761, 0.721, and 0.707, respectively. The AUC for the SII and CALLY indices were 0.831 and 0.877, respectively, and when combined, the AUC increased to 0.905. These results suggest that the combined use of the two indices for prognosis prediction was significantly more accurate than using either index alone. Our findings align with previous studies [34], which reported that the SII index, integrating PLT, NEU, and LYM, serves as a robust marker of the host's inflammatory and immune response and has strong prognostic value in IS and related complications. Elevated SII reflects excessive inflammatory activation mediated by NEU and PLT, as well as impaired immune surveillance due to LYM, which together promote secondary brain injury and increase susceptibility to PI [35].

Mechanistically, combining SII and CALLY captures a broader spectrum of pathophysiologic changes: SII emphasizes the balance between innate and adaptive immunity, while CALLY incorporates systemic inflammation and nutritional status. This dual-index approach allows for better risk stratification by integrating multiple dimensions of the patient's systemic response to ischemic injury and infection, which explains its higher predictive accuracy in our cohort.

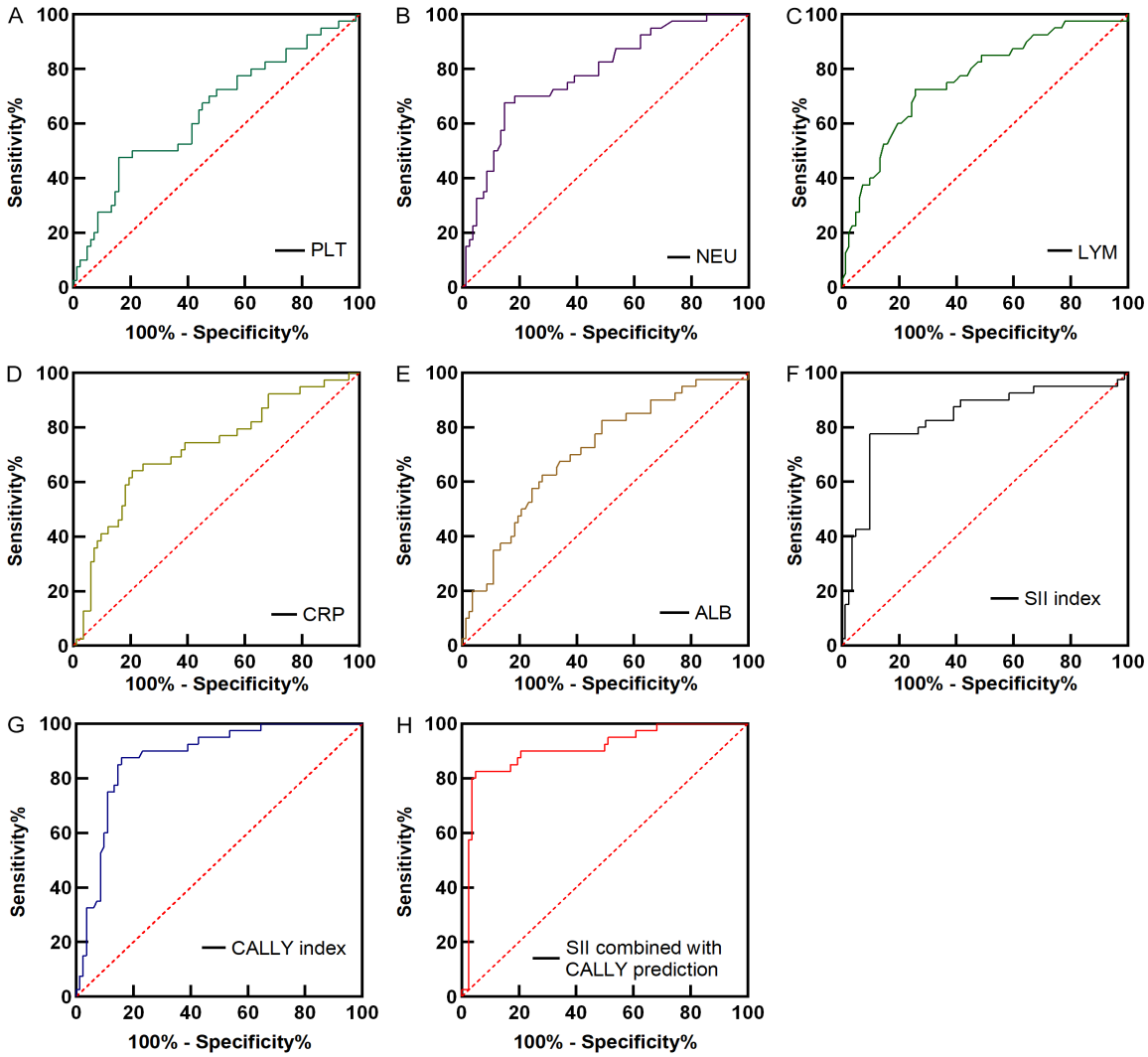

Figure 6. Prognostic significance of each index on IS and patients complicated by PI. A. Prognostic value of PLT in patients; B. Prognostic value of NEU in patients; C. Prognostic value of LYM in patients; D. Prognostic value of CRP in patients; E. Prognostic value of ALB in patients; F. Evaluation value of SII index on prognosis of patients; G. Evaluation value of CALLY index on prognosis of patients; H. Evaluation value of SII combined to CALLY prediction for prognosis of patients. Note: PLT: Platelets; NEU: Neutrophils; LYM: Lymphocytes; CRP: C-reactive protein; ALB: Albumin; SII: Systemic immune-inflammation; CALLY: CRP-Albumin-Lymphocyte.

In typical cases, patients often present with high-risk factors such as dysphagia and airway secretion retention upon admission. However, by combining SII and CALLY indices early on, clinicians can identify the high-risk state of pulmonary infection and implement targeted interventions such as intensive airway management, swallowing rehabilitation, and preventive anti-infection measures. This approach is expected to reduce the incidence and severity of infection. Although the patient presented in this study developed aspiration pneumonia on the third day of hospitalization, early identification and timely intervention led to significant clinical improvement, demonstrating the practical value of these findings for clinical management. Therefore, the combined use of SII and CALLY indices is a useful tool for clinicians to accurately stratify risks in the early stages of IS and to take targeted preventive measures, ultimately improving patient prognosis.

This study also has certain limitations. First, due to its retrospective design, there may have been selection bias, and the sample size was relatively small. Future research involving prospective, multicenter studies with larger

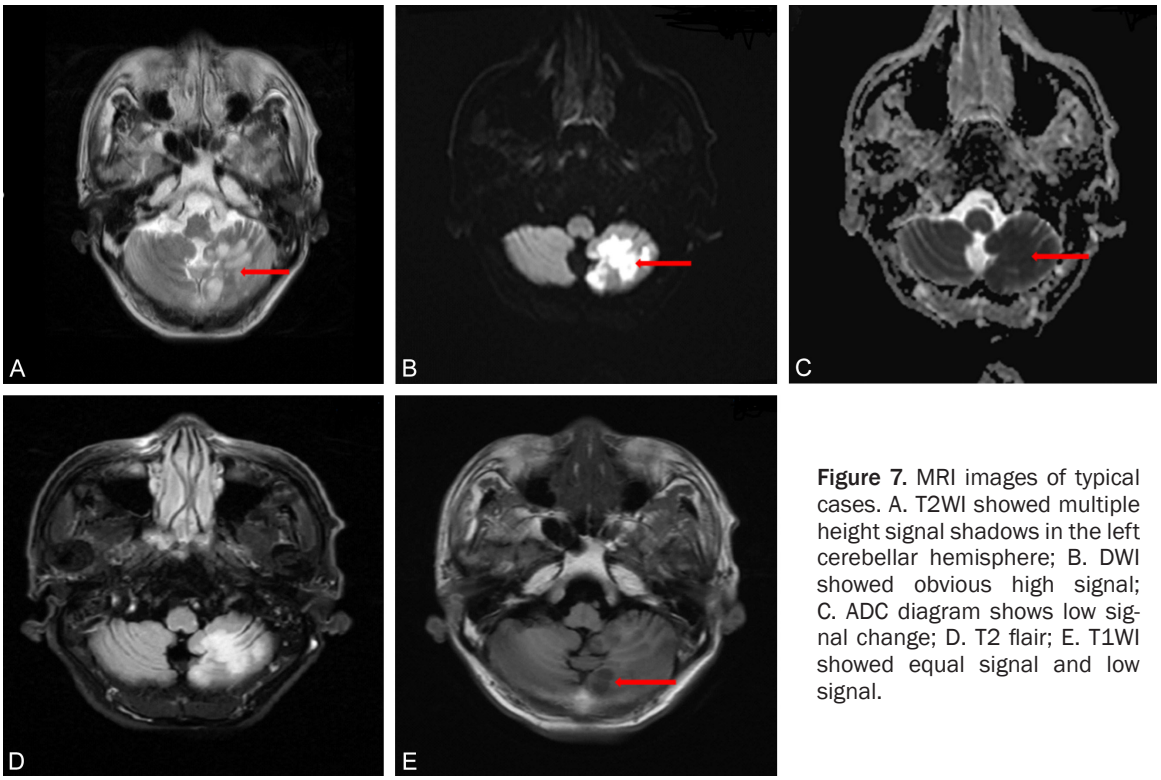

Figure 7. MRI images of typical cases. A. T2WI showed multiple height signal shadows in the left cerebellar hemisphere; B. DWI showed obvious high signal; C. ADC diagram shows low signal change; D. T2 flair; E. T1WI showed equal signal and low signal.

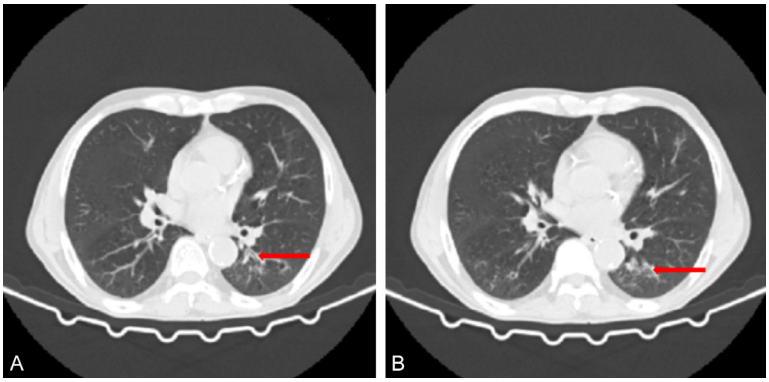

Figure 8. CT images of typical cases. The CT findings of lung are strip and patchy high density shadow and ground glass density shadow with blurred boundary.

cohorts is necessary to validate the generalizability and robustness of these findings. Additionally, some inflammatory and infectious markers were not included in the analysis, and without extended follow-up, the predictive values of SII and CALLY indices for long-term outcome remain uncertain. Therefore, multicenter, large-sample, and prospective studies are needed to further verify the stability and generalizability of the results.

In conclusion, IS patients with PI exhibit elevated SII index levels and reduced CALLY index levels. Both indices are significantly associated with patient prognosis, with higher SII and lower CALLY values corresponding to poorer outcome. The combined use of the SII and CALLY indices provides a valuable tool for accurately predicting prognosis in these patients.

Disclosure of conflict of interest

None.

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