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Systemic inflammatory response index as a predictor of stroke-associated pneumonia in patients with acute ischemic stroke treated by thrombectomy: a retrospective study

Feng Zheng^{1,2*†}, Wen Gao^{1,2,3†}, Yinfeng Xiao^{2,4†}, Xiumei Guo^{1,2,3†}, Yu Xiong^{1,2}, Chunhui Chen^{1,2}, Hanlin Zheng^{1,2}, Zhigang Pan^{1,2}, Lingxing Wang^{2,3}, Shuni Zheng⁵, Chuhan Ke^{1,2}, Qiaoling Liu^{4*}, Aihua Liu^{6,7*}, Xinyue Huang^{1,2*} and Weipeng $Hu^{1,2^*}$

Abstract

Background The predictive value of systemic inflammatory response index (SIRI) for stroke-associated pneumonia (SAP) risk in patients with acute ischemic stroke (AIS) treated by thrombectomy remains unclear. This study aimed to investigate the predictive value of SIRI for SAP in patients with AIS treated by thrombectomy.

Methods We included AIS patients treated by thrombectomy between August 2018 and August 2022 at our institute. We used multivariate logistic regression to construct the prediction model and performed a receiver operating characteristic curve analysis to evaluate the ability of SIRI to predict SAP and constructed a calibration curve to evaluate the prediction accuracy of the model. We evaluated the clinical application value of the nomogram using decision curve analysis.

Results We included 84 eligible patients with AIS in the analysis, among which 56 (66.7%) had SAP. In the univariate analysis, there were significant differences in sex ($p=0.035$), National Institute of Health Stroke Scale score at admission≥20 (*p*=0.019) and SIRI (*p*<0.001). The results of multivariable logistic analysis showed that the risk of SAP increased with the SIRI value (OR=1.169, 95% CI=1.049–1.344, *p*=0.014). Age≥60 (OR=4.076, 95% CI=1.251–14.841,

† Feng Zheng, Wen Gao, Yinfeng Xiao and Xiumei Guo contributed equally to this work.

*Correspondence: Feng Zheng dr.feng.zheng@gmail.com Qiaoling Liu liuqiaoling592@163.com Aihua Liu liuaihuadoctor@ccmu.edu.cn Xinyue Huang 1303433529@qq.com Weipeng Hu neurosurgery_fyey@163.com

Full list of author information is available at the end of the article

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Background

Acute ischemic stroke (AIS) is a common cause of disability and death worldwide [[1,](#page-6-0) [2](#page-6-1)] and its two therapeutic options focus on reperfusion with intravenous thrombolysis and endovascular thrombectomy (EVT) [\[3](#page-6-2), [4](#page-6-3)]. Stroke-associated pneumonia (SAP) is a common medical complication of stroke, with an incidence of 7–38% in AIS patients occurring most frequently in the first seven days after a stroke, which may exacerbate the disease, prolong hospital stays, and increase social and economic burdens [[5](#page-6-4)[–7](#page-6-5)]. EVT is a common and effective method for the treatment of AIS. SAP remains a threat to AIS

p=0.024) was also statistically significant. A nomogram with SIRI showed good prediction accuracy for SAP in AIS patients treated by thrombectomy (C-index value=0.774).

Conclusions SIRI is an independent predictor for SAP in patients with AIS treated by thrombectomy. A high SIRI value may allow for the early identification of patients with AIS treated by thrombectomy at high risk for SAP.

Keywords Systemic inflammatory response index, Stroke-associated pneumonia, Predictor, Epidemiology

patients, even if they use EVT. Therefore, early identification of SAP is essential for the timely treatment of AIS after EVT [[8,](#page-6-6) [9](#page-6-7)].

Recently, increasing evidence has shown that inflammatory biomarkers, such as neutrophil-to-lymphocyte ratio, systemic immune-inflammation index and plateletto-lymphocyte ratio, are associated with SAP [[10](#page-6-8)[–13](#page-6-9)]. While these biomarkers have shown promise, the systemic inflammatory response index (SIRI) offers a unique advantage. The systemic inflammatory response index (SIRI), calculated based on the number of inflammatory cells in the peripheral blood, can comprehensively reflect the balance between the inflammatory response and immune status [\[14,](#page-6-10) [15\]](#page-6-11). SIRI has a good predictive value for the prognosis of some brain tumors [\[16](#page-6-12)] and aneurysmal subarachnoid hemorrhage [[17,](#page-6-13) [18](#page-6-14)]. In addition, SIRI can also predict SAP in AIS patients treated conservatively [[15](#page-6-11)]. However, the predictive value of SIRI for SAP risk in patients with AIS treated by thrombectomy remains unclear. Therefore, this study aimed to investigate the relationship between SIRI and SAP in AIS patients treated by thrombectomy. This would help in the early identification of high-risk patients and ensure that early intervention is implemented to improve prognosis.

Methods

Patient selection

We included consecutive AIS patients who underwent thrombectomy at the Second Affiliated Hospital of Fujian Medical University within 6 h of symptom onset between August 2018 and August 2022. The inclusion criteria were: (1) patients diagnosed with ischemic stroke by digital subtraction angiography or cerebral computed tomographic angiography and who underwent thrombectomy within 6 h of symptom onset; (2) patients aged \geq 18 years; and (3) patients with blood parameters measured within one day after admission, including count of lymphocyte, neutrophil and monocyte. The exclusion criteria were: (1) presence of other diseases, including hematologic disorders, malignant tumors, use of immunosuppressive drugs, active infections within two weeks before admission, and those diagnosed with pulmonary infections at the time of admission, and (2) missing blood parameter data.

This study is based on the current version of the Helsinki Declaration and TRIPODreporting guidelines [[19\]](#page-6-15), and all procedures were carried out in accordance with relevant guidelines and regulations. This study was approved the medical ethics committee of the Second Affiliated Hospital of Fujian Medical University, China (Ethical approval no. 533/2022). All procedures conducted in studies involving human participants complied with the ethical standards of the Institutional Research Committee. Since data were evaluated retrospectively, pseudonymously, and was solely obtained for treatment purposes, a requirement of informed consent was waived by the Ethics Committee of the Second Affiliated Hospital of Fujian Medical University, China (Ethical approval no. 533/2022).

Parameter acquisition

We collected demographic and clinical characteristics from the medical record database of our institute. The SIRI was calculated as follows: SIRI = (neutrophil count \times monocyte count) / lymphocyte count [\[15](#page-6-11)]. According to previous research [\[20](#page-6-16), [21\]](#page-7-0), patients' fasting blood was collected within the first day of admission, and their blood parameters were measured, including white blood cell, platelet, neutrophil, hemoglobin, lymphocyte, red blood cell, and monocyte counts. The National Institute of Health Stroke Scale (NIHSS) and Glasgow Coma Scale (GCS) scores were evaluated by trained neurologists upon admission.

Outcome measure

The outcome of this study was SAP, which occurred most frequently in the first seven days after a stroke. According to the modified Centers for Disease Control and Prevention criteria, the medical diagnosis of SAP is based on radiographic images, clinical signs, and laboratory parameters of pulmonary infection [[22\]](#page-7-1).

Statistical analyses

We used the statistical package for the social sciences software (26th edition, IBMRSPSS R, Chicago, Illinois) for analyses. Continuous variables with normal distribution were expressed as mean±standard deviation, while other variables were expressed as the median and interquartile range (IQR). We compared nominal variables using a Pearson's chi-square test or Fisher's exact test, and continuous variables based on data distribution using the Mann-Whitney U test. Logistic regression

analysis was used to determine predictors of postoperative pneumonia after undergoing thrombectomy. We performed univariate logistic regression for each variable. Variables with *p*<0.2 in univariate analyses were used as input data for the multivariate logistic regression model. We used receiver operating characteristic (ROC) curve analyses to determine the area under the curve (AUC) values. Sensitivity, specificity, and the optimal test cut-off points were determined by calculating the Youden index (sensitivity $+$ [1-specificity]). In addition, the nomogram was formulated based on these predictors in the multivariate analysis using the package "rms" in R (version 3.5.2). The consistency index (equivalent to the AUC value, expressed as the c index) reflects the ability of the SIRI multivariate model to distinguish patients with or without pneumonia. A calibration curve was constructed to evaluate the model's prediction accuracy by comparing the prediction probability with the observation probability. The calibration curve was considered appropriate if the point on the calibration plot was close to a 45 ° diagonal. We used decision curve analysis to quantify the net benefits under different thresholds to evaluate the clinical effectiveness of the SAP nomogram in a cohort of patients with AIS treated by thrombectomy. Unless otherwise stated, *p*<0.05 was considered statistically significant.

Results

Of all the patients with AIS screened at our institute between August 2018 and August 2022, 112 were admitted within 6 h of symptom onset and treated by thrombectomy. Patients with missing blood cell count data $(n=1)$, malignant tumors $(n=2)$, and active infection within two weeks of admission (*n*=25) were excluded. Finally, 84 qualified patients were included in the study (mean age: 64.36 years; female sex: 29 (34.5%)). Fiftysix (66.7%) of the patients with AIS also had SAP. The baseline characteristics of the patients with and without SAP are shown in Table [1](#page-3-0). Patients with SAP were older, their NIHSS score at admission was higher, their GCS score at admission was lower, more were male, more had hypertension and more required mechanical ventilation. The incidence of NIHSS≥20 and GCS score (3–8) at admission were higher in patients with SAP than those in patients without SAP. Leukocyte, neutrophil, and monocyte counts were higher, and lymphocyte counts were lower in patients with SAP than in those without SAP. The median SIRI value was 7.79 [4.42–14.88] in patients with SAP, which was significantly higher than that in patients without SAP at 2.54 [1.84–6.94] (*p*<0.05) (Table [1](#page-3-0)).

We used multivariate logistic regression analyses to determine the factors suitable for predicting SAP. After further adjusting for confounding factors, the results of multivariate analysis showed that the risk of SAP increased with the SIRI value (OR=1.169, 95%) CI=1.049–1.344, $p=0.014$). In addition, significant differences were observed in age (OR=4.076, 95% CI=1.251– 14.841, *p*=0.024) (Table [2](#page-4-0)).

Based on two identified variables (age≥60 and SIRI value), we used multivariate logistic regression to construct a predictive model which was shown as a nomogram (Fig. [1](#page-4-1)). We subsequently analyzed the ROC curve to determine the ability of SIRI values to predict SAP in patients with AIS treated by thrombectomy (Fig. [2](#page-5-0)). Through the ROC curve of the multivariate model, SIRI could predict SAP in patients with AIS treated by thrombectomy (AUC=0.774, 95% CI=0.666–0.881). The optimal critical value of SIRI was 3.617; that is, patients with a score>3.617 were more likely to develop pneumonia (Youden index=0.464, sensitivity=82.1%, specificity=64.3%). The calibration curve was used to assess the risk of SAP in patients with AIS treated by thrombectomy, with good consistency throughout the cohort, and the data points were close to the 45° diagonal (Fig. [3](#page-5-1)). The clinical application value of the nomogram was evaluated using the decision curve analysis. According to the deci-sion curve (Fig. [4\)](#page-5-2), within the threshold interval of $0-1$, SAP prediction using this model is more profitable.

Discussion

Acute ischemic stroke (AIS) is a common cause of disability and death worldwide, especially in cases of large vascular occlusions requiring thrombectomy [\[1](#page-6-0), [2](#page-6-1)] SAP worsens stroke outcomes, lengthens hospitalization, and increases the occurrence of severe disabilities and mortality [\[5–](#page-6-4)[7\]](#page-6-5). Therefore, early identification of effective predictors of SAP is critical for timely treatment. To the best of our knowledge, this is the first study to determine the prognostic role of SIRI in the occurrence and progression of SAP in patients with AIS treated by thrombectomy.

In this retrospective single-center study, we analyzed the data of 84 patients with AIS treated by thrombectomy, of which SAP occurred in 66.7%. We found that higher SIRI, the male sex, and age>60 years were risk factors for SAP [[23,](#page-7-2) [24\]](#page-7-3). In previous studies, a history of smoking, stroke severity, level of consciousness, high blood pressure, diabetes mellitus, and atrial fibrillation were deemed to be potential predictors of SAP, but similar results were not detected in the present study. This may be due to the relatively small sample size of our study. In addition, in previous reports, age was independent predictors of SAP in patients with AIS, with higher rates of SAP occurring and those aged>60 years. This is consistent with our findings. Furthermore, in our study, SIRI levels were significantly higher in SAP patients with AIS treated by thrombectomy than in non-SAP patients

Table 1 Comparison of baseline characteristics of AIS patients with and without SAP

AIS: acute ischemic stroke; GCS: Glasgow Coma Scale; NIHSS: National Institute of Health Stroke Scale; SAP: stroke-associated pneumonia; SIRI: systemic inflammatory response index

with AIS treated by thrombectomy (OR=1.171, 95% CI=1.034–1.325, $p=0.013$), indicating that SIRI might be an independent predictor of SAP in patients with AIS treated by thrombectomy. In addition, the optimal critical value of SIRI was 3.617, and prevention and treatment are recommended for patients with SIRI>3.617.

Nomograms are widely used to predict the possibility of clinical events by integrating various variables. In the present analysis, we constructed a reliable and convenient nomogram to predict SAP in patients with AIS treated by thrombectomy. By integrating demographic characteristics, clinical symptoms, and serum biological indicators, our study developed a nomogram using SIRI. This tool assigns points on a scale to each predictor value and the total points indicate a predicted risk of SAP in patients with AIS who underwent thrombectomy. Our findings suggest that the nomogram has high predictive accuracy and can assist clinicians in making timely decisions for the management of these patients.

The close relationship between SIRI and SAP may be due to stroke-induced immunosuppression. A prolonged excessive inflammatory response depletes the immune system, ultimately suppressing systemic immunity to protect the brain $[25]$ $[25]$. However, this makes the body

AIS: acute ischemic stroke; CI: confidence interval; GCS: Glasgow Coma Scale; NA: not applicable; NIHSS: National Institute of Health Stroke Scale; OR: odds ratio; SAP: stroke-associated pneumonia; SIRI: systemic inflammatory response index. Variables with p <0.20 in univariate analysis were included in multivariable logistic regression models for adjustment; **p*<0.05. Multivariable logistic regression was adjusted for age≥60 years, sex, hypertension, mechanical ventilation, admission NIHSS score≥20, GCS score at admission, occlussion site and SIRI

Fig. 1 Nomogram for predicting SAP in patients with AIS treated by thrombectomy. The risk nomogram is based on sex, age, and SIRI values. The total score of each variable corresponds to a probability of pneumonia. AIS: acute ischemic stroke; SAP: stroke-associated pneumonia; SIRI: systemic inflammatory response index

more vulnerable to pathogens, leading to stroke-induced immunosuppression syndrome (SIDS) and infections [\[25](#page-7-4), [26\]](#page-7-5). SIDS is associated with the activation of the sympathetic nervous system (SNS) [[27](#page-7-6)], parasympathetic nervous system (PNS) [\[28\]](#page-7-7), and hypothalamic-pituitaryadrenal (HPA) axis [\[29](#page-7-8)]. Stroke initially overstimulates

the SNS, releasing catecholamines (epinephrine, norepinephrine, and dopamine) into the bloodstream [\[30](#page-7-9)]. Persistent high catecholamine levels reduce circulating lymphocytes, weakening immune function and increasing SAP risk [[31\]](#page-7-10). Through the cholinergic anti-inflammatory pathway, the PNS releases acetylcholine to inhibit

Fig. 2 ROC curve of the multivariate SIRI regression model, representing prediction accuracy. ROC: receiver operating characteristic; SIRI: systemic inflammatory response index

Fig. 3 Calibration curve of nomogram predicting SAP in patients with AIS treated by thrombectomy. Note: The prediction of SAP is presented on the X-axis and the actual SAP is presented on the Y-axis. The thick dotted line symbolizes an excellent prediction with an ideal model. The solid line epitomizes the performance of our prediction mode, and the thin dotted line typifies the performance of our optimized model. When the thin dotted line is closer to the thick dotted line, the model is more accurate. When the c index is closer to 1, the accuracy of the nomogram for the risk of SAP in hospitalized patients is higher. AIS: acute ischemic stroke; SAP: stroke-associated pneumonia

peripheral inflammatory cytokines [[32\]](#page-7-11). Overstimulation of this pathway post-stroke can elevate pulmonary infection risk [[33\]](#page-7-12). In response to post-stroke inflammation, the hypothalamus activates the HPA axis, leading to

Fig. 4 Decision curve analysis of a nomogram for assessing the risk of SAP in patients with AIS treated by thrombectomy. The Y-axis represents the net benefit. The grey line indicates all patients with pneumonia. The black line indicates no pneumonia. The red solid line indicates the risk of pneumonia in the prediction model. AIS: acute ischemic stroke; SAP: strokeassociated pneumonia

excessive glucocorticoid secretion [[34](#page-7-13), [35](#page-7-14)]. Furthermore, glucocorticoids have anti-inflammatory properties; however, their high levels further suppress immunity, increasing pneumonia risk [\[36](#page-7-15)].

This study had several limitations. First, because our study was conducted at a single center and was retrospective, the relatively small sample size might have compromised the power of the primary results. Second, this study used blood parameters on the first day after admission. Therefore, subsequent studies are required to explore the relationship between blood parameters of emergency admission and SAP. Third, whether thrombectomy may cause a systemic inflammatory response to mask the SIRI associated with SAP could not be determined in the present study; therefore, subsequent studies are required to investigate this detail. Finally, Further analysis of the dynamic changes in these inflammatory markers could not be achieved in the present study. Future studies are needed to determine whether changes in the SIRI over time are related to the occurrence of SAP in patients with AIS treated by thrombectomy.

Conclusions

SIRI is an independent predictor of SAP in patients with AIS treated by thrombectomy. A high SIRI value may contribute to the early identification of patients with AIS treated by thrombectomy at high risk for SAP. Future

studies with larger sample sizes are required to confirm these findings.

Abbreviations

- ROC Receiver operating characteristic
- SAP Stroke-associated pneumonia
- SIRI Systemic inflammatory response index

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Author contributions

Feng Zheng: Writing—original draft, review and editing. Wen Gao: Writing—original draft. Yinfeng Xiao: Writing—original draft. Xiumei Guo: Conceptualization. Yu Xiong: Conceptualization. Chunhui Chen: Conceptualization. Hanlin Zheng: Data curation. Zhigang Pan: Data curation. Shuni Zheng: Methodology. Chuhan Ke: Visualization. Qiaoling Liu: Writing review and editing. Aihua Liu: Writing—review and editing. Xinyue Huang: Writing—review and editing. Weipeng Hu: Writing—review and editing.

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Data availability

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

Declarations

Ethics approval and consent to participate

This study was approved the medical ethics committee of the Second Affiliated Hospital of Fujian Medical University, China (Ethical approval no. 533/2022).

Consent for publication

Since data were evaluated retrospectively, pseudonymously, and was solely obtained for treatment purposes, a requirement of informed consent was waived by the Ethics Committee of the Second Affiliated Hospital of Fujian Medical University, China (Ethical approval no. 533/2022).

Competing interests

The authors declare no competing interests.

Author details

¹ Department of Neurosurgery, the Second Affiliated Hospital, Fujian Medical University, No.34 North Zhongshan Road, Quanzhou 362000, Fujian Province, China

²Neuromedicine Center, the Second Affiliated Hospital, Fujian Medical University, No.34 North Zhongshan Road, Quanzhou 362000, Fujian Province, China

³Department of Neurology, the Second Affiliated Hospital, Fujian Medical University, No.34 North Zhongshan Road, Quanzhou 362000, Fujian Province, China

⁴Department of Clinical Laboratory, the Second Affiliated Hospital, Fujian Medical University, No.34 North Zhongshan Road, Quanzhou 362000, Fujian Province, China

5 Division of Public Management, the Second Affiliated Hospital, Fujian Medical University, No.34 North Zhongshan Road, Quanzhou 362000, Fujian Province, China

⁶Beijing Neurosurgical Institute, Beijing Tiantan Hospital, Capital Medical University, No. 119, South Fourth Ring West Road, Fengtai District, Beijing 100070, China

7 Department of Neurosurgery, Ningxia Hui Autonomous Region People's Hospital, Yinchuan 750000, China

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