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Risk factors of stroke-associated pneumonia in patients with acute ischemic stroke treated by endovascular thrombectomy

Kangyue Lin¹, Xiaoqing Deng², Yumei Xiao¹, Zhiyong Yang¹, Zhiyi He¹, Xiangjun Li¹ and Wenwen Cheng^{3*}

Abstract

Background Although there are a variety of risk factors and predictive models for stroke-associated pneumonia (SAP) in patients with acute ischemic stroke (AIS), the risk factors and predictive value for SAP in patients with AIS treated by endovascular thrombectomy (EVT) remain unclear. This study aimed to investigate the occurrence of SAP in acute ischemic stroke patients treated with EVT and identify independent predictors of SAP.

Methods We enrolled patients with acute ischemic stroke who underwent endovascular thrombectomy (EVT) at the stroke center of Maoming People's Hospital between January 2021 and December 2023. The patients were categorized into the SAP group and Non-SAP group. Univariate analysis was performed to examine the correlation between each potential risk factor and SAP. Multivariate logistic regression analysis and receiver operating characteristic curve (ROC) were applied to identify independent predictors of SAP and evaluate their predictive value, respectively.

Results A total of 233 participants were included in this study. Among them, 131 (56.22%) patients were identified with SAP. The univariate analysis showed significant differences in the following variables between groups: admission National Institute of Health Stroke Scale score (NIHSS) (P=0.005), procedural time (P=0.000), dysphagia (P=0.004), white blood cell (WBC) (P=0.044), neutrophils (P=0.019), and neutrophil-lymphocyte ratio (NLR) (P=0.002). The multivariable logistic analysis identified the following independent predictors of SAP: admission NIHSS score [OR=1.078, 95% CI=1.020–1.140, P=0.008], procedural time [OR=1.023, 95% CI=1.014–1.032, P=0.000], NLR [OR=1.152, 95% CI=1.005–1.320, P=0.042], and dysphagia [OR=0.340, 95% CI=0.151–0.767, P=0.009]. Furthermore, the receiver operating characteristic (ROC) curve analysis demonstrated that procedural time had the best predictive performance for SAP in AIS patients undergoing EVT.

Conclusion Admission NIHSS score, procedural time, NLR, and dysphagia were associated with SAP in patients with AIS treated with EVT and can be an independent predictor for SAP.

Keywords Stroke-associated pneumonia, Acute ischemic stroke, Endovascular thrombectomy, Risk factors

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Introduction

Acute ischemic stroke (AIS) is one of the main causes of mortality and disability worldwide [1, 2], and significantly increases the caregiving and economic burden. Endovascular thrombectomy (EVT) is one of the therapeutic options focused on reperfusion and has been proven effective for the treatment of AIS [3–5]. However, complications after thrombectomy often affect the clinical prognosis and increase the length and cost of hospitalization [6].

An increasing body of evidence identifies stroke-associated pneumonia (SAP) as a common and severe medical complication after acute ischemic stroke, and the prevalence rates vary between 3.2% and 56.6% [7–9]. Previous studies have demonstrated that SAP is associated with poorer clinical outcomes, prolonged hospital stays, and higher rates of severe disability [8, 10, 11]. Although EVT has become a standard treatment for AIS, SAP continues to pose a significant threat to these patients, with reported incidence rates of 13.3–19.6% in the post-EVT population [12, 13]. Consequently, early detection of SAP in AIS patients following EVT is clinically crucial, underscoring the need to identify reliable predictive risk factors.

Many risk factors such as age, atrial fibrillation, dysphagia, stroke severity, fibrinogen, serum calcium, and inflammatory biomarkers have been identified for SAP in patients with acute stroke already [14-19]. However, existing studies have predominantly focused on AIS patients not receiving EVT, leaving the risk factors for post-EVT SAP poorly characterized. To date, only two recent studies by Zheng et al. and Zhu et al. have specifically investigated independent predictors of SAP following endovascular thrombectomy. Zhu et al. expanded the investigation beyond conventional risk factors to include time intervals of EVT (onset-to-treatment time, puncture-to-reperfusion time, and onset-to-reperfusion time) and vascular recanalization status, and reported that failed recanalization significantly correlates with SAP development in post-thrombectomy AIS patients [19]. Zheng et al. identified the systemic inflammatory response index as an independent SAP predictor in this population [16]. Nevertheless, one of these two articles only focused on the relationship between a single inflammatory marker and SAP [16], while the other included rare inflammatory markers as risk factors [19]. Most importantly, both studies were constrained by relatively small sample sizes, potentially introducing selection bias. Therefore, the definitive risk factors and their predictive value for SAP in post-thrombectomy AIS patients remain to be fully elucidated.

In this study, we aimed to investigate the occurrence of SAP in acute ischemic stroke patients treated with EVT and identify independent predictors of SAP. These findings may facilitate early recognition and targeted intervention for high-risk patients.

Methods

Research participants

Patients with AIS treated by EVT at the stroke center of Maoming People's Hospital within 12 h of symptom onset were recruited between January 2021 and December 2023. The inclusion criteria were as follows: (1) aged over 18 years; (2) diagnosed with acute ischemic stroke by cerebral computed tomographic angiography, magnetic resonance angiography, or digital subtraction angiography; (3) treated by endovascular thrombectomy within 12 h of symptom onset; (4) blood parameters were measured within 24 h after admission. Participants were excluded based on the following criteria: (1) active infection (symptoms of respiratory infections, such as cough, expectoration, nasal congestion, runny nose, and dyspnea) or pyrexia within two weeks of admission; (2) existence of pneumonia at the time of admission; (3) History of blood disorders, malignant tumors, or current immunosuppressive therapy; (4) incomplete blood parameter data; (5) failed recanalization (eTICI < 2b50). The present study was approved by the Medical Ethics Committee of Maoming People's Hospital and was based on the Helsinki Declaration and TRIPOD reporting guidelines [20]. Since the study was retrospective and all data were pseudonymous, the patient informed consent was waived.

Diagnosis of SAP

The observed outcome of this study was SAP which occurred within the first 7 days after stroke onset. Diagnosis of SAP was according to the modified Centers for Disease Control and Prevention criteria, based on clinical and laboratory indicators of respiratory infection, and was confirmed by chest X-ray or CT [21]. The diagnosis of SAP met criteria as follows: at least 1 of the following: (1) fever (>38 $^{\circ}$ C) with no other recognized cause; (2) Leukopenia (<4000 WBC/mm³) or leukocytosis (>12000 WBC/mm³); (3) For adults \geq 70 y old, altered mental status with no other recognized cause; and at least 2 of the following: (1) new onset of purulent sputum, or change in character of sputum over a 24 h period, or increased respiratory secretions, or increased suctioning requirements; (2) new onset or worsening cough, or dyspnea, or tachypnea (respiratory rate > 25/min); (3) Rales, crackles, or bronchial breath sounds; (4) worsening gas exchange (e.g., O^2 desaturation [eg, PaO_2 /Fi $O_2 \le 240$], increased oxygen requirements); and chest X-ray or CT with at least 1 of the following: new or progressive and persistent infiltrate, consolidation, or cavitation.

Data collection

Demographic, clinical parameters, and laboratory parameters of each patient were collected from the medical record system of our hospital. Demographic and clinical parameters including age, sex, comorbidities (hypertension, diabetes, atrial fibrillation), admission NIHSS score, procedural time (PT, time from groin puncture to reperfusion), occlusion site (anterior circulation, posterior circulation), and dysphagia (assessed by Kubota Water Swallowing Test). Swallowing function was evaluated by the Kubota Water Swallowing Test within the first day after admission, and dysphagia was identified when the test was graded at level 4 or above. Laboratory parameters included white blood cell (WBC), neutrophils, lymphocyte, and eosinophils count, as well as NLR, fibrinogen, and serum calcium levels. Fasting blood was collected from all patients within 24 h of admission.

Statistical analysis

Continuous variables were expressed as mean \pm standard deviation or median and interquartile range (IQR) based on the distribution of data and analyzed by t-test or Mann–Whitney U-test. Categorical variables are expressed as constituent ratios and analyzed by chisquare test or Fisher exact test. Binary logistic regression analysis was adopted to determine predictors of SAP. We performed univariate analysis for each variable, and those P < 0.1 in univariate analyses were selected for inclusion

 Table 1
 Baseline characteristics of the patients with and without SAP

in multivariate logistic regression analysis. Based on previous literature [16, 22], age may also be risk factors for SAP, thus this variable was included in multivariate logistic regression analysis whether statistically significant or not in the univariate analyses. Moreover, the receiver operator characteristic (ROC) curve was used to evaluate the predicted ability of factors for the risk of SAP and determine the best cutoff values for each potential factor. All statistical tests were two-sided, and values of P < 0.05were considered statistically significant. All data were analyzed using the SPSS 22.0 software.

Results

A total of 285 ischemic stroke patients treated with endovascular thrombectomy were screened in our center initially from January 2021 to December 2023. Patients with active infection or pyrexia within two weeks of admission (n = 20), presented community-acquired pneumonia on admission (n = 24), and incomplete blood parameter data (n = 8) were excluded. Finally, 233 patients were included in the study (mean age: 67.52 years; male sex: 147 (63.09%)). Among them, 131(56.2%) patients were diagnosed with stroke-associated pneumonia. The baseline characteristics of the patients with and without SAP are shown in Table 1. Patients with SAP group were significantly had higher admission NIHSS score [13 (10, 18) versus 11 (6, 15); P < 0.05] and rates of dysphagia [36 (27.48%) versus 12 (11.76); p < 0.05], longer procedural

Variables	Total (n = 233)	Non-SAP (<i>n</i> = 102)	SAP (n = 131)	Р
Demographics				
Age (years)	67.52±12.68	66.55 ± 11.80	68.27±12.68	0.197
Male (%)	147 (63.09)	64 (62.75)	83 (63.36)	0.923
Comorbidities (%)				
Hypertension	128 (54.94)	58 (56.86)	70 (53.44)	0.602
Diabetes	43(18.45)	23 (22.55)	20 (15.27)	0.155
Atrial fbrillation	66 (28.33)	25 (24.51)	41 (31.30)	0.254
Clinical parameters				
Admission NIHSS score	12 (8, 16)	11 (6, 15)	13 (10, 18)	0.004
Procedural time (min)	95 (65, 125)	80.5 (55, 101.75)	110 (77.5, 140)	0.000
Dysphagia (%)	48 (20.60)	12 (11.76)	36 (27.48)	0.003
Occlusion site (%)				0.060
Anterior circulation	204 (87.55)	94 (92.16)	110 (83.97)	
Posterior circulation	29 (12.45)	8 (7.84)	21 (16.03)	
Laboratory parameters				
WBC (×10 ⁹ /L)	9.7 (7.68, 11.36)	9.06 (7.07, 10.91)	10.21 (8.08, 11.72)	0.007
Neutrophils (×10 ⁹ /L)	7.56 (5.47, 9.44)	7.07 (5.12, 9.06)	8.12 (6.06, 9.97)	0.002
Lymphocyte (×10 ⁹ /L)	1.24 (0.90, 1.70)	1.33 (1.02, 1.79)	1.21 (0.83, 1.61)	0.036
Eosinophils (×10 ⁹ /L)	0.05 (0.02, 0.13)	0.08 (0.02, 0.12)	0.03 (0.01, 0.10)	0.007
NLR (%)	6.23 (3.65, 10.02)	5.31 (2.86, 7.76)	6.91 (4.01, 11.25)	0.011
Fibrinogen (g/L)	3 (2.63, 3.61)	3.02 (2.64, 3.61)	3 (2.62, 3.60)	0.845
Serum calcium (mmol/L)	2.26±0.13	2.27±0.14	2.26 ± 0.13	0.420

*SAP: stroke-associated pneumonia; WBC: white blood cell; NLR: neutrophil-lymphocyte ratio

time [110 (77.5, 140) versus 80.5 (55, 101.75); P < 0.05], higher WBC [10.21 (8.08, 11.72) versus 9.06 (7.07, 10.91); P < 0.05], neutrophil [8.12 (6.06, 9.97) versus 7.07 (5.12, 9.06); P < 0.05], NLR [6.91 (4.01, 11.25) versus 5.31 (2.86, 7.76); P < 0.05] counts and lower lymphocyte [1.21 (0.83, 1.61) versus 1.33 (1.02, 1.79); P < 0.05], eosinophils [0.03 (0.01, 0.10) versus 0.08 (0.02, 0.12); P < 0.05] counts compared to non-SAP group (P < 0.05) (Table 1). There were no significant differences in variables of age, male, comorbidities, occlusion site, fibrinogen, and serum calcium between these two groups.

The univariate logistic regression analyses were used to identify the factors associated with the incidence of SAP. Our univariate analysis revealed that admission NIHSS score [OR = 1.067, 95% CI = 1.020-1.117, P = 0.005], procedural time [OR = 1.018, 95% CI = 1.011-1.026, P = 0.000], dysphagia [OR = 0.352, 95% CI = 0.172-0.719, P = 0.004], WBC [OR = 1.094, 95% CI = 1.002-1.193, P = 0.044], neutrophils [OR = 1.109, 95% CI = 1.017-1.209, P=0.019], and NLR [OR=1.094, 95% CI=1.033-1.159, P = 0.002] were correlated with the incidence of SAP (P-value < 0.05). After adjusting for age, admission NIHSS score, procedural time, dysphagia, WBC, neutrophils, lymphocyte, eosinophils, and NLR, the independent predictors of SAP were admission NIHSS score [OR = 1.078, 95% CI = 1.020-1.140, P = 0.008], procedural time [OR = 1.023, 95% CI = 1.014–1.032, P=0.000], NLR [OR=1.152, 95% CI=1.005-1.320, P=0.042], and dysphagia [OR = 0.340, 95% CI = 0.151-0.767, P = 0.009] (Table 2).

The result of the ROC curve was shown in Fig. 1. The ROC curve provided sensitivity, specificity, and best cutoff point for admission NIHSS score (sensitivity = 76.3%, specificity = 44.1%, best cutoff point = 9.5, patients with a NIHSS score>9.5 were more likely to develop pneumonia), procedural time (sensitivity = 52.7%)specificity = 81.4%, best cutoff point = 107 min), NLR (sensitivity = 42.0%)specificity = 77.5%, best cutoff point = 8.12), and dysphagia (sensitivity = 42.0%, specificity = 77.5%, best cutoff point = 8.12). Through the ROC curve of the multivariate model, both procedural time (AUC = 0.700, 95% CI = 0.634–0.767), admission NIHSS score (AUC = 0.608, 95% CI = 0.535–0.682), and NLR (AUC = 0.610, 95% CI = 0.538–0.682) could predict SAP in patients with AIS treated by EVT, while the predictive power of the latter two is relatively weak.

Discussion

The purpose of this study was to explore the independent predictors of SAP in acute ischemic stroke patients who underwent EVT. Our findings demonstrated a 56.22% incidence of SAP, which was significantly associated with higher baseline NIH Stroke Scale (NIHSS) scores, prolonged procedural time, elevated neutrophil-to-lymphocyte ratio (NLR), and increased prevalence of dysphagia.

The NIHSS score was an important indicator of stroke severity, and the higher the score, the more severe the disease. The results of our study demonstrated that higher admission NIHSS score was significantly correlation with SAP. This is consistent with previous studies [23, 24]. A cross-sectional study conducted by Li et al. on SAP with acute stroke revealed that the NIHSS score was one of the risk factors for SAP, and a higher NIHSS score was associated with SAP in patients with acute stroke [23]. Shi et al. enrolled acute ischemic stroke after rt-PA treatment and also showed that patients with SAP were correlated with higher levels of initial NIHSS score [24]. Similar results were reported in studies on stroke-associated infection [14]. Chen et al. reported that patients with stroke-associated infection suffered from relatively severe neurological deficits, in another word, admission NIHSS score was a standalone risk factor for stroke-associated infection [14]. The above results strongly suggested that admission NIHSS score can be used to predict the occurrence of SAP in acute stroke. Our results also support this view, and due to the participants included in this study, the application of SAP predictions was extended to acute ischemic stroke patients treated with EVT. In contrast, a recent study involving AIS patients undergoing thrombectomy reported no significant association

Table 2 Multivariable logistic regression of the independent predicting factors of SAP in AIS patients after EVT

Variables	Univariate analysis			Multivariate analysis		
	P-value	OR	95% CI	P-value	OR	95% CI
Age	0.305	1.011	0.990-1.032	0.283	1.015	0.988-1.042
Admission NIHSS score	0.005	1.067	1.020-1.117	0.008	1.078	1.020-1.140
Procedural time	0.000	1.018	1.011-1.026	0.000	1.023	1.014-1.032
Dysphagia	0.004	0.352	0.172-0.719	0.009	0.340	0.151-0.767
WBC	0.044	1.094	1.002-1.193	0.444	1.393	0.596-3.258
Neutrophils	0.019	1.109	1.017-1.209	0.373	0.669	0.277-1.620
Lymphocyte	0.060	0.678	0.452-1.016	0.945	1.044	0.310-3.514
Eosinophils	0.079	0.121	0.011-1.282	0.204	0.122	0.005-3.128
NLR	0.002	1.094	1.033-1.159	0.042	1.152	1.005-1.320

*SAP: stroke-associated pneumonia; AIS: acute ischemic stroke; EVT: endovascular thrombectomy; WBC: white blood cell; NLR: neutrophil-lymphocyte ratio

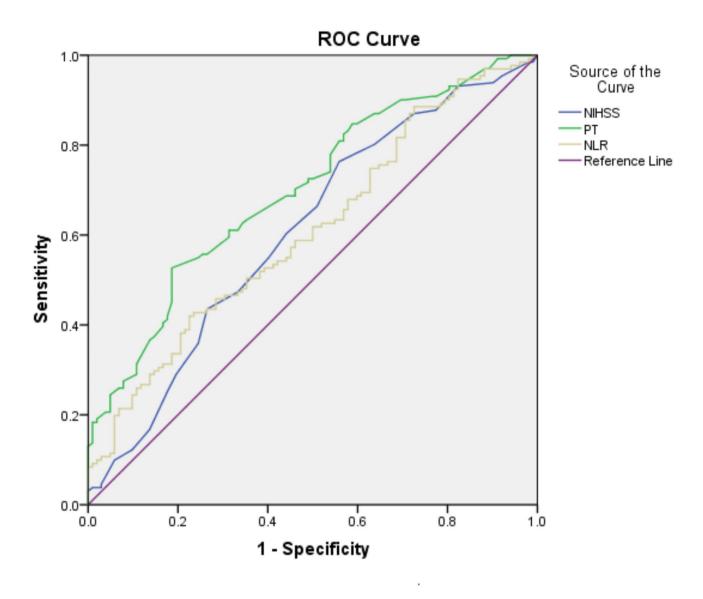


Fig. 1 Receiver operating characteristic (ROC) curve for diagnostic value of SAP. SAP: stroke-associated pneumonia; PT: procedural time; NLR: neutrophillymphocyte ratio

between admission NIHSS scores and SAP risk [16], suggesting that NIHSS may not serve as an independent predictor for SAP in AIS who treated with EVT. However, the limited sample size in that study potentially compromises the reliability of its findings. When synthesizing our current results with existing evidence, we postulate that higher admission NIHSS scores likely represent an independent risk factor for SAP development in patients with AIS after EVT.

Some literature has suggested that the procedure time of EVT might be related to prognosis in stroke patients [25–27]. The longer the procedure time for thrombectomy, the higher the probability of failed recanalization, resulting in worse clinical outcomes. Failed recanalization following EVT might be associated with increased SAP risk [19]. On the one hand, patients with failed

recanalization had more dysphagia rates, which was correlated with SAP occurrence intensely. On the other hand, the use and duration of mechanical ventilation was might greater in patients with failed recanalization thus increasing the risk of SAP. However, few studies focused on the relationship between the procedural time of EVT and the incidence of SAP directly. As far as we know, only one study with a small sample of patients with acute anterior large artery occlusion stroke who underwent EVT had explored this issue initially [19]. In their study, time intervals of EVT included time from onset to treatment, time from groin puncture to reperfusion, and time from onset to reperfusion, and the results suggested none of the three time intervals were significantly associated with the occurrence of SAP [19]. This is not in line with our findings. Our results revealed that procedural time

was significantly higher in SAP patients with AIS treated by EVT than in non-SAP patients, suggesting that procedural time might be an independent predictor of SAP in patients with AIS treated by thrombectomy. The difference between this study and previous study may be due to the different sample sizes, and further related studies with larger sample sizes are needed to clarify this issue in the future.

Previous studies have proved that NLR could reflect systemic inflammation [28, 29], and as an inflammatory biomarker, it may have shown promise in predicting SPA [16, 28]. Increasing evidence has demonstrated that NLR was associated with the occurrence of SAP in patients with acute ischemic stroke [19, 30]. For example, a largescale study recruited acute ischemic stroke without EVT revealed that a higher NLR predicted SAP in patients with acute ischemic stroke, and they claimed that NLR might help to identify high-risk for SAP in AIS patients to begin intervention in time [30]. Moreover, Zhu et al. suggested that even in AIS patients who underwent EVT, higher NLR was also significantly associated with SAP, and could independently predict SAP after EVT [19]. Our results also showed higher NLR was significantly association with SAP, and indicated that NLR was an independent predictor for SAP in AIS patients with EVT. The most possible explanation for this result was that the severity of the stroke may be the link between NLR and SAP. A close relationship has been found between NLR and severe large-area stroke [31, 32]. In our cohort, patients who developed SAP exhibited significantly higher NLR and more severe baseline neurological deficits as reflected by elevated admission NIHSS scores. Previous studies have established that both stroke severity and large infarct volume constitute significant risk factors for SAP development [11, 33, 34]. These findings collectively suggest that NLR may serve as a potential biomarker for SAP susceptibility in patients with severe ischemic stroke.

Dysphagia was common in stroke patients and increased the risk of aspiration. Studies have shown that acute stroke patients with dysphagia were more than three times at risk of developing SAP than those without dysphagia [35]. Early dysphagia screening and specialist swallow assessment might reduce the risk of SAP [17, 36]. In this study, the rate of dysphagia occurred in the SAP group was significantly higher than non-SAP group, further multivariate regression analysis also showed a significant correlation between dysphagia and the incidence of SAP, which indicated that dysphagia could be identified as a predictor of SAP in AIS patients with EVT. Our findings are consistent with previous reports [19, 23]. Existing evidence consistently demonstrates that dysphagia serves as a significant predictor of SAP in AIS patients, regardless of treatment modality (conservative management, thrombolytic therapy, or endovascular thrombectomy) [19, 24].

Our study did not identify age or atrial fibrillation as significant predictors of SAP, which contrasts with previous reports [8, 23, 37, 38]. Age and atrial fibrillation were not significantly different between SAP and non-SAP group in univariate analysis in this study. This finding aligns with several recent studies that similarly found no association between age/atrial fibrillation and SAP development [19, 23]. Specifically, Li et al.'s cross-sectional study of acute stroke patients found no correlation between atrial fibrillation and SAP risk [23]. Similarly, Zhu et al. applied patients in AIS with EVT reported that age and atrial fibrillation also failed to demonstrate predictive capability in the risk factor model [19]. Comparing the discrepancy of these studies, we postulate that these discrepant findings across studies may stem from variations in patient selection criteria and sample sizes.

The receiver operating characteristic (ROC) analysis demonstrated that procedural time achieved an area under the curve (AUC) of 0.7, indicating moderate discriminative capacity for SAP prediction. As a critical temporal parameter in endovascular thrombectomy for acute ischemic stroke, procedural duration exhibits a direct correlation with clinical outcomes, shorter procedures being associated with more favorable prognoses. Our analysis identified 107 min as the optimal procedural time cutoff, with longer durations significantly increasing SAP likelihood. In contrast, both NIHSS scores and NLR showed limited predictive value (AUC < 0.7). While we established cutoff values for these parameters, their clinical utility for risk stratification appears questionable given the suboptimal predictive performance.

Several limitations of this study should be mentioned. First, this was a single-center study. Although the sample size has increased compared to previous studies, it may still lead to selection bias. Second, we did not account for stress hyperglycemia - a known prognostic factor in EVT-treated AIS patients that may influence SAP risk. Additional unmeasured confounders included ventilation parameters, antibiotic exposure, and neuroanatomical stroke characteristics (particularly brainstem involvement). Third, although multiple regression analysis showed that a higher admission NIHSS score, longer procedural time, a higher neutrophil-lymphocyte ratio, and dysphagia were significantly correlated with SAP, only the AUC value of procedural time reached 0.7. Fourth, further analysis of the dynamic changes in NLR could not be performed in this study. Finally, due to the cross-sectional design of this study, we cannot establish a causal relationship. Therefore, the interpretation of our results should be approached with caution.

Conclusion

The current study reveals that higher admission NIHSS score, NLR, longer procedural time, and dysphagia were significantly associated with SAP in AIS patients with EVT. Among them, the procedure time of EVT has the highest predictive value for SAP. Taken together, these findings suggest that both admission NIHSS score, NLR, procedural time, and dysphagia could be effectively utilized as a screening tool for the early detection of SAP in AIS patients with EVT in clinical environments. However, further large-scale studies are needed to confirm these findings.

Abbreviations

SAP Stroke-associated pneumonia AIS Acute ischemic stroke EVT Endovascular thrombectomy ROC Receiver operating characteristic curve NIHSS National Institute of Health Stroke Scale WBC White blood cell PΤ Procedural time NLR Neutrophil-lymphocyte ratio

Author contributions

WWC take responsibility for the integrity of data and accuracy of its analysis. WWC and KYL contributed to the conception and design of the study and writing of the manuscript. XQD prepared the figures and tables. XQD, YMX, ZYY, ZYH, and XJL all contributed substantially to the data analysis.

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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 by the Medical Ethics Committee of Maoming People's Hospital. Since the study was retrospective and all data were pseudonymous, the patient informed consent was waived.

Competing interests

The authors declare no competing interests.

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