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Stroke-associated pneumonia with low PaO₂/FiO₂ ratio in acute large vessel occlusion after endovascular therapy: risk factors and prognosis

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Background: Stroke-associated pneumonia (SAP) often occurs after ischemic stroke. A deterioration in SAP manifests itself in a decreased partial pressure oxygen (PaO₂)/fraction of inspired oxygen (FiO₂) ratio, indicating gas exchange dysfunction. We aimed to investigate independent predictors and outcomes of SAP with low PaO₂/FiO₂ ratio among patients with acute large vessel occlusion (ALVO) undergoing endovascular therapy.

Methods: We retrospectively analyzed the prospective data of consecutive adult post-interventional patients with ALVO admitted to neuro-intensive care units in Wuhan No. 1 Hospital from December 2020 to December 2022. Patients developing SAP without coronavirus disease 2019 were included in this study and divided into two subgroups: PaO₂/FiO₂ ratio > 240 and ≤ 240. The primary outcome was favorable neuro-function at 90 days (modified Rankin Scale score of 0–2). Secondary outcomes included hospitalization days, occurrence of symptomatic intracerebral hemorrhage, and 90-day mortality. The independent risk factors and prognosis for SAP with PaO₂/FiO₂ ratio ≤ 240 were identified by logistic regression analyses.

Results: A total of 159 subjects developing SAP were included in this study: 53 with PaO₂/FiO₂ ratio > 240 and 106 with ratio ≤ 240. Compared to subjects with PaO₂/FiO₂ ratio > 240, those with PaO₂/FiO₂ ratio ≤ 240 had older ages, higher baseline National Institutes of Health Stroke Scales scores, larger proportions of baseline Glasgow Coma Scale (GCS) score of 3–8 and grade of kobuta water swallow test ≥ 3, higher white blood cell (WBC) counts (all *p* values < 0.05). The independent predictors for SAP with PaO₂/FiO₂ ratio ≤ 240 included ages (adjusted odds ratio [OR], 1.043; 95% confidential interval [CI], 1.011–1.077; *p* = 0.009), baseline GCS scores of 3–8 (adjusted OR, 2.802; 95% CI, 1.214–6.465; *p* = 0.016), and ln-transformed WBC counts after SAP diagnosis (adjusted OR, 3.977; 95% CI, 1.226–12.896; *p* = 0.021). SAP with PaO₂/FiO₂ ratio ≤ 240 was robustly associated with longer hospitalization days (adjusted OR, 1.074; 95% CI, 1.01–1.143; *p* = 0.024).

Conclusion: SAP with PaO₂/FiO₂ ratio ≤ 240 is shown in significant relevance to the prolonged in-hospital stays among post-interventional patients. Older ages, baseline GCS scores of 3–8, and higher WBC counts after SAP diagnosis can independently predict the occurrence of SAP with a lower PaO₂/FiO₂ ratio. Further validation studies are needed.

KEYWORDS

stroke-associated pneumonia, $\text{PaO}_2/\text{FiO}_2$ ratio, ischemic stroke, endovascular therapy, risk factor, prognosis

Introduction

Acute ischemic stroke (AIS) attributed to large vessel occlusion (LVO) burdens the global public health and economy (1). Although endovascular therapy (EVT) effectively reduces disability and death of patients with LVO (2), the occurrence of post-stroke complications due to infection can largely worsen clinical outcomes (3–5). Of note, stroke-associated pneumonia (SAP) has been the most common post-stroke infection (6, 7). The incidence of SAP varies from 8.5 to 14.3%, and rises to 28% in intensive care unit (6, 7).

The progression of SAP is featured as the obstacle to gas exchange. The partial pressure oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ratio is commonly employed to assess the severity of gas exchange (8). A significantly lower $\text{PaO}_2/\text{FiO}_2$ ratio was identified in association with poor prognosis among patients with lung diseases (e.g., bacterial and viral pneumonia) (9–11). As yet little is known of the clinical impact of SAP with decreased $\text{PaO}_2/\text{FiO}_2$ ratio on post-interventional patients.

In this study, we aimed to explore independent risk factors and prognosis for SAP with low $\text{PaO}_2/\text{FiO}_2$ ratio among acute stroke patients with LVO after EVT.

Methods

This was a retrospective study of prospectively collected data from a monocentric EVT cohort of patients with LVO admitted to neuro-intensive care units in Wuhan No. 1 Hospital between December 2020 and December 2022. The Ethics Committees of Wuhan No. 1 Hospital approved this study with patient informed consent waived (No. 2022.025), and the study followed the 1975 Declaration of Helsinki (as revised in Edinburgh 2000).

Study population

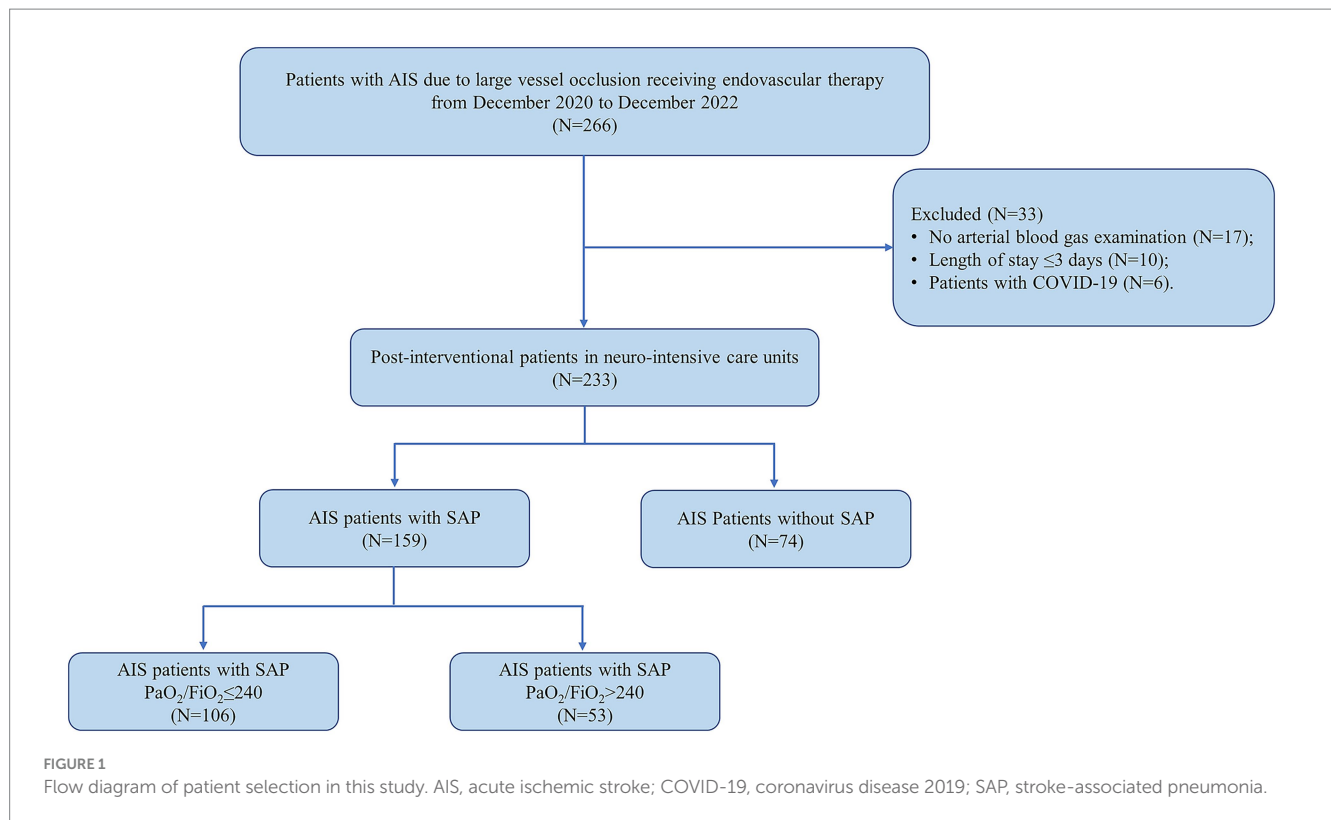
In this study, post-interventional patients with SAP were included. The inclusion criteria for this study were as follows: (1) aged over 18 years old; (2) diagnosed as AIS due to LVO via angiographic modalities; (3) had a premorbid modified Rankin Scale (mRS) scored <2 ; (4) performed emergency EVT; (5) suffered from SAP in the first 7 days post-stroke according to the modified criteria from the Centers for Disease Control and Prevention (CDC) (The detailed diagnostic description was shown in [Supplementary Table 1.](#)) (12). The exclusion criteria included: (1) diagnosed as pneumonia before the date of new-onset stroke; (2) any contraindication to EVT; (3) diagnosed as coronavirus disease 2019 (COVID-19), based on lung computed tomography and nasopharyngeal swab; (4) any important data missing (e.g., no arterial blood gas examination); (5) length of hospitalization stay ≤ 3 days; (6) any history of immune dysfunction, malignant tumors, sepsis or other diseases that might lead to death in 3 months. The flow chart for the subject selection was presented in [Figure 1](#).

Data collection and follow-up

We reviewed the entire clinical parameters of all subjects from in-hospital electronic medical records (e.g., case report forms, nursing records, laboratory and radiological examinations). Patient clinical information on demographic features, past history, admission and hospitalization evaluations, stroke etiology, occlusion site, endovascular and medical therapy were collected. The worst laboratory results, including the PO_2/FiO_2 ratio in the most severe condition of arterial blood gas analyses and the worst white blood cell (WBC) counts, were recorded after the diagnosis of SAP. Follow-up assessments were conducted at 90 days after stroke onset via either outpatient clinics or telephone. The 90-day mRS scores were used to evaluate patient neuro-functional prognosis: a favorable function was defined as 0 to 2; death as 6. The primary outcome was favorable neuro-function at 90 days (mRS score of 0–2). Secondary outcomes included hospitalization days, in-hospital occurrence of symptomatic intracerebral hemorrhage (sICH), and 90-day all-cause mortality. sICH was diagnosed during hospitalization in line with the European Cooperative Acute Stroke Study criteria (13). The above diagnosis, disease severity and outcome evaluations were independently performed by two experienced physicians (ZB.G. and Y.Y.) in a blinded manner. In the event of any disagreement, a third physician (WH.L.) participated in discussion and made consensus.

Statistical analysis

Statistical analyses were conducted by SPSS version 26.0 (IBM Corp., NY, United States) and GraphPad Prism version 9.0 (GraphPad Software Inc., CA, United States). Continuous variables were expressed as medians [interquartile range (IQR)], and categorical variables as numbers (percentages). According to the modified diagnostic criteria from CDC, $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 240 is used as one of determinants of SAP and indicates worsened gas exchange (12), and thus $\text{PaO}_2/\text{FiO}_2$ ratio of 240 was chosen as a cut-off value in this study. The baseline clinical characteristics, therapeutic and prognostic metrics of patients with SAP were compared between $\text{PaO}_2/\text{FiO}_2$ ratio > 240 and ≤ 240 by Mann–Whitney U test, chi-square test, or Fisher's exact test, where appropriate. Multivariate logistic regression models adjusted for variables with p value less than 0.05 were used to investigate the independent effect of SAP with $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 240 on patient prognosis, and to further estimate independent risk factors for SAP with $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 240 . Logarithmic transformation (\ln) was applied to WBC count to improve model fit in regression analyses via smoothing data. The diagnostic accuracy of potential predictors for SAP with $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 240 was assessed by receiver operating characteristic (ROC) curve and area under ROC curve (AUC). Model calibration was evaluated via the Hosmer–Lemeshow goodness-of-fit test. A two-tailed p value < 0.05 was regarded as statistically significant.



Results

Comparisons of baseline clinical data of SAP between PaO₂/FiO₂ ratio > 240 and ≤ 240

One hundred and fifty-nine post-interventional patients suffering from SAP (median ages, 69.0 [59.0–76.0] years old; male, 67.3%) were included in this study: 53 with PaO₂/FiO₂ > 240 and 106 with PaO₂/FiO₂ ratio ≤ 240.

The comparisons of patient baseline clinical characters and therapeutic metrics between the two groups were listed in Table 1. Compared to subjects with PaO₂/FiO₂ ratio > 240, those with PaO₂/FiO₂ ratio ≤ 240 had older ages (70.5 [63.0–78.0] vs. 65.0 [54.5–73.0] years old, $p = 0.003$), higher baseline National Institutes of Health Stroke Scales (NIHSS) scores (16 [10–21] vs. 12 [8–17], $p = 0.005$), as well as larger proportions of baseline Glasgow Coma Scale (GCS) scores of 3–8 (50.9% vs. 20.8%, $p < 0.001$) and baseline grade of kobuta water swallow test ≥ 3 (87.7% vs. 67.9%, $p = 0.003$). Besides, subjects with PaO₂/FiO₂ ratio ≤ 240 were more likely to have larger WBC counts (12.56 [10.64–15.83] vs. 11.36 [9.69–13.58], $p = 0.027$), after diagnosed as SAP. Yet, no statistical differences were found in other clinical features between the two subgroups (all p values > 0.05).

Comparisons of clinical outcomes of SAP between PaO₂/FiO₂ ratio > 240 and ≤ 240

Figure 2 exhibited the distribution of the 90-day mRS scores between the two subgroups: 66.0% of subjects with PaO₂/FiO₂ ratio > 240 had favorable neuro-functional prognosis at 90 days (mRS 0–2),

while 32.1% of those with PaO₂/FiO₂ ratio ≤ 240 showed favorable 90-day neuro-function.

The comparisons of patient clinical outcomes between the two groups were displayed in Table 2. Subjects with PaO₂/FiO₂ ratio ≤ 240 were more possible to have a lower incidence of 90-day mRS of 0–2 (32.1% vs. 66.0%, $p < 0.001$), longer hospitalization days (13 [10–20] vs. 10 [7–13], $p < 0.001$), and a higher rate of all-cause death at 90 days (34.0% vs. 9.4%, $p = 0.001$). Yet, no statistical significance was found in the difference of sICH between the two groups ($p = 0.111$). In the multivariate analysis adjusted for ages, baseline NIHSS scores, baseline GCS scores of 3–8, baseline grade of kobuta water swallow test ≥ 3, and ln-transformed WBC counts after diagnosis of SAP, SAP with PaO₂/FiO₂ ratio ≤ 240 was revealed in strong association with longer hospitalization days (adjusted odds ratio [OR], 1.074; 95% confidential interval [CI], 1.01–1.143; $p = 0.024$).

Underlying risk factors for predicting SAP with PaO₂/FiO₂ ratio ≤ 240

Table 3 showed potential independent predictors for developing SAP with PaO₂/FiO₂ ratio ≤ 240. After adjusted for the confounders, the occurrence of SAP with PaO₂/FiO₂ ratio ≤ 240 was independently related to ages (adjusted OR, 1.043; 95% CI, 1.011–1.077; $p = 0.009$), baseline GCS scores of 3–8 (adjusted OR, 2.802; 95% CI, 1.214–6.465; $p = 0.016$), and ln-transformed WBC counts after diagnosis of SAP (adjusted OR, 3.977; 95% CI, 1.226–12.896; $p = 0.021$), rather than baseline NIHSS scores and grades of kobuta water swallow test ≥ 3.

Table 4 and Figure 3 detailed the predictive effect of combined indicators (ages, baseline GCS scores of 3–8, and ln-transformed WBC counts after diagnosis of SAP) on SAP with PaO₂/FiO₂ ratio ≤

TABLE 1 Baseline clinical features and treatment metrics of SAP patients with PaO₂/FiO₂ ratio ≤ 240 and >240.

Characteristics	Total (N = 159)	PaO ₂ /FiO ₂ ≤ 240 (N = 106)	PaO ₂ /FiO ₂ > 240 (N = 53)	p value
Demographic features				
Age, y, median (IQR)	69.0 (59.0–76.0)	70.5 (63.0–78.0)	65.0 (54.5–73.0)	0.003
Male, n (%)	107 (67.3%)	72 (67.9%)	35 (66.0%)	0.811
Medical history, n (%)				
Hypertension	103 (64.8%)	74 (69.8%)	29 (54.7%)	0.06
Hyperlipidemia	9 (5.7%)	6 (5.7%)	3 (5.7%)	1
Diabetes	42 (26.4%)	23 (21.7%)	19 (35.9%)	0.056
Atrial fibrillation	40 (25.2%)	29 (27.4%)	11 (20.8%)	0.366
Coronary heart disease	36 (22.6%)	23 (21.7%)	13 (24.5%)	0.688
Ischemic stroke	44 (27.7%)	30 (28.3%)	14 (26.4%)	0.802
Smoking	53 (33.3%)	33 (31.1%)	20 (37.7%)	0.405
Clinical assessments				
Baseline NHISS score, median (IQR)	15 (10–20)	16 (10–21)	12 (8–17)	0.005
Baseline GCS (3–8 scores), n (%)	65 (40.9%)	54 (50.9%)	11 (20.8%)	<0.001
Baseline SBP, mmHg, median (IQR)	150.0 (135.0–168.0)	152.5 (137.0–165.0)	148.0 (130.0–171.5)	0.684
Baseline DBP, mmHg, median (IQR)	83.0 (79.0–93.0)	85.0 (80.0–92.3)	82.0 (77.5–97.0)	0.971
Baseline grade of kobuta water swallow test ≥ 3, n (%)	129 (81.1%)	93 (87.7%)	36 (67.9%)	0.003
WBC count, 10 ⁹ /L, median (IQR) ^a	12.07 (10.25–14.88)	12.56 (10.64–15.83)	11.36 (9.69–13.58)	0.027
Lymphocyte count, 10 ⁹ /L, median (IQR) ^a	1.21 (0.81–1.82)	1.14 (0.78–2.0)	1.27 (0.90–1.72)	0.578
Neutrophil count, 10 ⁹ /L, median (IQR) ^a	6.91 (5.0–9.9)	6.91 (4.88–10.06)	6.98 (5.05–8.98)	0.698
Stroke etiology, n (%)				
Atherosclerotic	98 (61.6%)	67 (63.2%)	31 (58.5%)	0.564
Cardioembolic	54 (34.0%)	34 (32.1%)	20 (37.7%)	0.477
Undetermined or others	7 (4.4%)	5 (4.7%)	2 (3.8%)	1
Occlusion site, n (%)				
Anterior circulation	137 (86.2%)	91 (85.8%)	46 (86.8%)	0.871
Posterior circulation	22 (13.8%)	15 (14.2%)	7 (13.2%)	
Intravenous alteplase use, n (%)	48 (30.2%)	33 (31.1%)	15 (28.3%)	0.714
Endovascular treatment, n (%)				
Mechanical thrombectomy	82 (51.6%)	53 (50.0%)	29 (54.7%)	0.575
Thrombus aspiration	111 (69.8%)	75 (70.8%)	36 (67.9%)	0.714
Balloon expansion	80 (50.3%)	50 (47.2%)	30 (56.6%)	0.262
Stent implantation	57 (35.8%)	37 (34.9%)	20 (37.7%)	0.726
Time from last known well, min, median (IQR)				
To arterial puncture	300.0 (185.5–436.3)	300.0 (185.0–420.0)	339.0 (196.5–552.5)	0.234
To reperfusion or procedure completion	364.0 (269.0–531.0)	357.0 (258.0–520.0)	394.5 (272.5–610.5)	0.26
Medications in perioperative period, n (%)				
Antiplatelet drug	93 (58.5%)	62 (58.5%)	31 (58.5%)	1
Anticoagulant drug	65 (40.9%)	43 (40.6%)	22 (41.5%)	0.909

(Continued)

TABLE 1 (Continued)

Characteristics	Total	PaO ₂ /FiO ₂ ≤ 240	PaO ₂ /FiO ₂ > 240	<i>p</i> value
	(<i>N</i> = 159)	(<i>N</i> = 106)	(<i>N</i> = 53)	
Statin or other lipid-lowering drug	140 (88.1%)	92 (86.8%)	48 (90.6%)	0.489
Antihypertensive drug	115 (72.3%)	80 (75.5%)	35 (66.0%)	0.21
Antidiabetic drug	17 (10.7%)	12 (11.3%)	5 (9.4%)	0.717
Antibiotic drug	159 (100%)	106 (100%)	53 (100%)	1

DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; IQR, interquartile range; NHISS, National Institutes of Health Stroke Scales; NLR, neutrophil-lymphocyte ratio; SAP, stroke-associated pneumonia; SBP, systolic blood pressure; WBC, white blood cell. ^aWorst laboratory values after diagnosed as SAP.

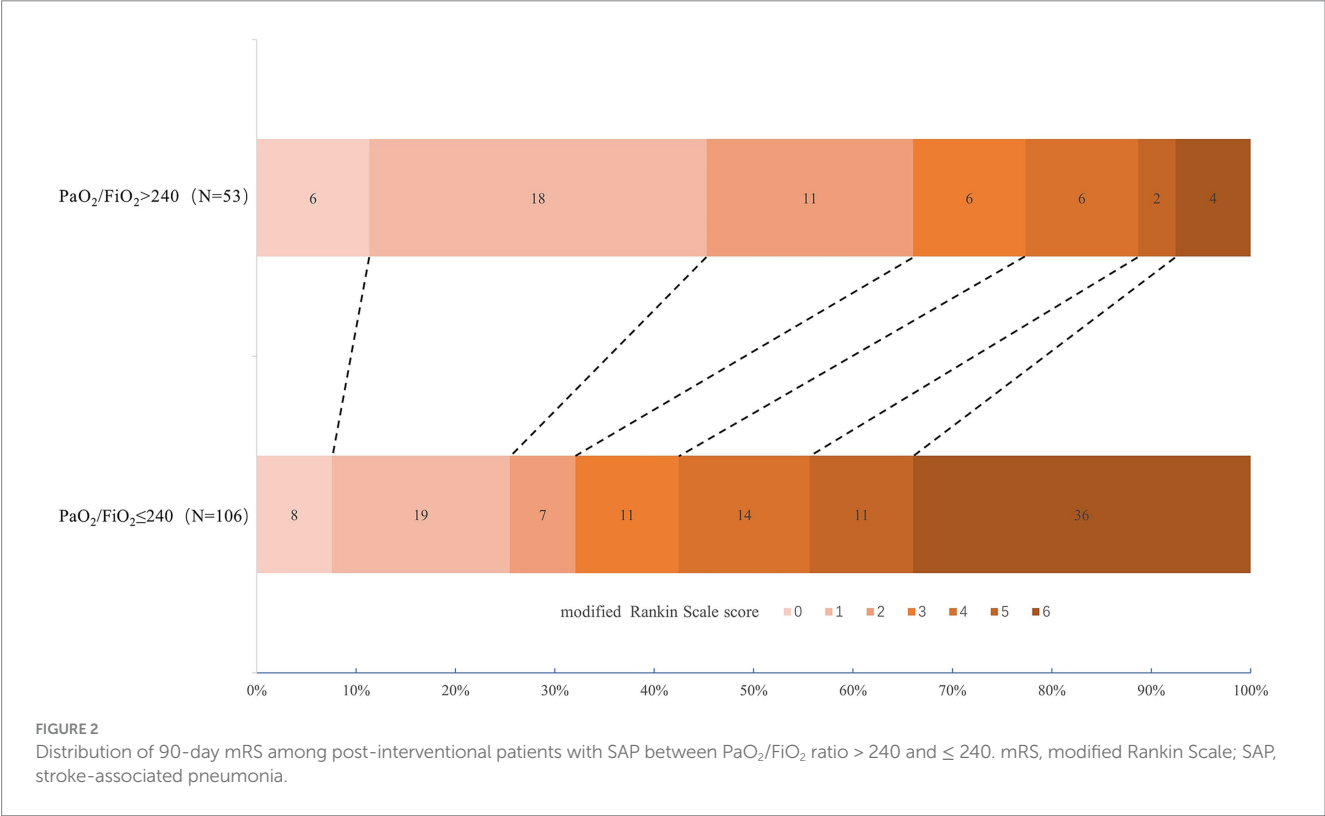


TABLE 2 Main clinical prognostic indicators according to PaO₂/FiO₂ ratio.

Parameters	PaO ₂ /FiO ₂ ≤ 240	PaO ₂ /FiO ₂ > 240	<i>p</i> value	OR (95%CI) ^a	<i>p</i> value ^a
	(<i>N</i> = 106)	(<i>N</i> = 53)			
mRS 0–2 at 90 days, <i>n</i> (%)	34 (32.1%)	35 (66.0%)	<0.001	0.5 (0.219–1.141)	0.1
sICH, <i>n</i> (%)	15 (14.2%)	3 (5.7%)	0.111	1.339 (0.319–5.612)	0.69
Length of stay, d, median (IQR)	13 (10–20)	10 (7–13)	<0.001	1.074 (1.01–1.143)	0.024
Mortality at 90 days, <i>n</i> (%)	36 (34.0%)	5 (9.4%)	0.001	1.702 (0.541–5.354)	0.363

CI, confidential interval; GCS, Glasgow Coma Scale; mRS, modified Rankin Scale; NHISS, National Institutes of Health Stroke Scales; OR, odds ratio; SAP, stroke-associated pneumonia; sICH, symptomatic intracerebral hemorrhage; WBC, white blood cell. ^aAdjusted for ages, baseline NHISS scores, baseline GCS scores of 3–8, baseline grade of kobuta water swallow test ≥ 3, and ln-transformed WBC counts after diagnosis of SAP.

240. ROC curve analysis suggested that the AUC, sensitivity, and specificity of combined indicators in predicting SAP with PaO₂/FiO₂ ratio ≤ 240 was 0.753 (95% CI, 0.676–0.83; *p* < 0.001), 0.613, and 0.811, respectively. The Hosmer-Lemeshow goodness-of-fit test indicated that the combined model showed a satisfactory level of goodness of fit (*p* = 0.892, χ^2 = 3.593).

TABLE 3 Logistic regression analyses of potential risk factors for SAP with PaO₂/FiO₂ ratio ≤ 240.

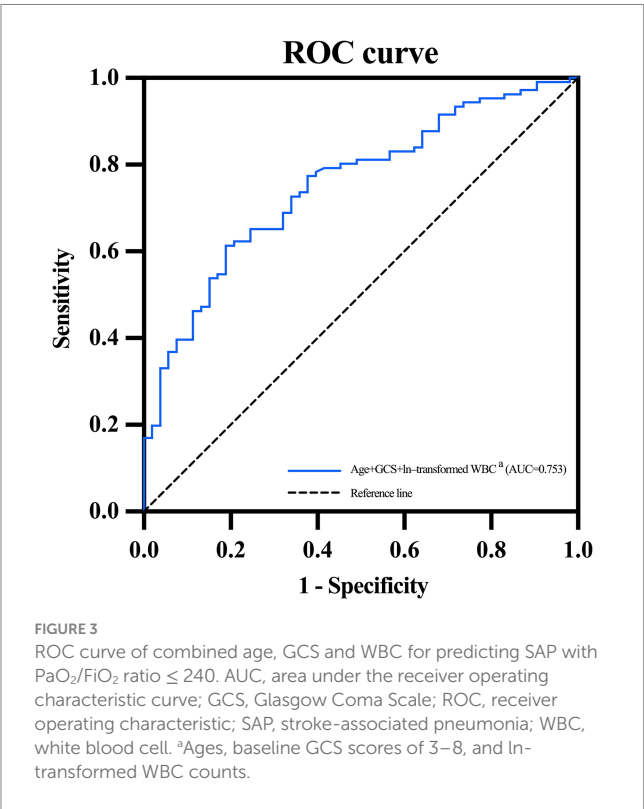
Parameters	Univariate regression		Multivariate regression ^a	
	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Age	1.046 (1.018–1.076)	0.001	1.043 (1.011–1.077)	0.009
NHIS score	1.076 (1.023–1.133)	0.005	1.039 (0.98–1.102)	0.198
GCS scores of 3–8	3.965 (1.844–8.523)	<0.001	2.802 (1.214–6.465)	0.016
Grade of kobuta water swallow test ≥ 3	3.378 (1.491–7.657)	0.004	1.173 (0.448–3.072)	0.746
ln-transformed WBC counts	3.787 (1.354–10.587)	0.011	3.977 (1.226–12.896)	0.021

CI, confidential interval; GCS, Glasgow Coma Scale; NHIS, National Institutes of Health Stroke Scales; OR, odds ratio; SAP, stroke-associated pneumonia; WBC, white blood cell. ^aAdjusted for ages, baseline NHIS scores, baseline GCS scores of 3–8, baseline grade of kobuta water swallow test ≥ 3, and ln-transformed WBC counts after diagnosis of SAP.

TABLE 4 AUC and diagnostic accuracy of combined age, GCS, and WBC for SAP with PaO₂/FiO₂ ratio ≤ 240.

Parameters	AUC	95% CI	<i>p</i> -value	Sensitivity	Specificity
Age + GCS + WBC ^a	0.753	0.676–0.83	<0.001	0.613	0.811

AUC, area under the receiver operating characteristic curve; CI, confidence interval; GCS, Glasgow Coma Scale; ROC, receiver operating characteristic; SAP, stroke-associated pneumonia; WBC, white blood cell. ^aAges, baseline GCS scores of 3–8, and ln-transformed WBC counts after diagnosis of SAP.



Discussion

In the current study, firstly, we found that SAP with PaO₂/FiO₂ ratio ≤ 240 was robustly correlated with the prolonged hospitalization among acute stroke patients after EVT. Then, the occurrence of SAP with PaO₂/FiO₂ ratio ≤ 240 was revealed in independent relevance to advanced age, low GCS scores, and high WBC count after diagnosis of SAP.

Growing evidence stressed the pivotal role of SAP on the high risk of poor clinical outcomes among stroke patients (14, 15), with a large-scale study of SAP showing a 4.72-fold increase in in-hospital death

related to severe stroke (16). The possible explanations could be given: First, after stroke onset, patients are predisposed to SAP due to immune dysregulation (17). SAP can also induce systemic inflammation, and thus enhance autoreactive immune responses against central nervous system antigens (18, 19). Second, SAP may have a direct and negative impact on perfusion and metabolism in the ischemic brain, especially when occurring hypotension and hypoxia (20, 21). The interaction between AIS and SAP is assumed to largely deteriorate patient conditions, thereby leading to poorer prognosis (6, 22).

Our investigation into the clinical outcomes of post-interventional patients with SAP depending on PaO₂/FiO₂ ratio were shown in accordance with previous observations on SAP (6, 22, 23). Notably, the PaO₂/FiO₂ ratio serves as a typical indicator to evaluate the severity of gas exchange in lung diseases, such as acute respiratory distress syndrome and pneumonia (24, 25). At such circumstances of lung diseases, diffuse alveolar damage may develop in lungs, then decreasing lung compliance and impairing gas-exchange function (26). We speculate that the above pathophysiological process of lung injury may also get involved in the progression of SAP among post-interventional patients, which was indicated by the decreased PaO₂/FiO₂ ratio.

Prior studies identified several independent predictors for occurring SAP among patients with stroke, such as existence of dysphagia, increased values of inflammatory mediators, and concurrent comorbidities (27–29). Our study further revealed that advanced age, low GCS scores, and high WBC count after diagnosis of SAP could significantly elevate the risk of developing SAP with lower PaO₂/FiO₂ ratio after EVT.

The underlying plausibility could be lent to our findings. Firstly, aging weakens the control of immunometabolic responses to severe infection and persistent inflammation, while stroke-induced immunodepression can be exacerbated by inflammation-related immunosenescence during aging as well (30). Aging may thus increase the possibility of worsening post-stroke infections (30), which could be supported by our observation that older ages might increase the occurrence of SAP with lower PaO₂/FiO₂ ratio. Secondly, post-stroke infection and inflammation may persistently and directly damage major organ functions, including acute lung injury (31). As lung injury advances in SAP, inflammatory response escalates in lung tissue, leading

to further impairment of alveolar gas-exchange function (31). Of note, high peripheral WBC count often serves as a routine and reliable indicator for systemic inflammatory status of SAP (32). Accordingly, the strong relevance of higher WBC counts to SAP with decreased $\text{PaO}_2/\text{FiO}_2$ ratio in our study may largely support the above pathophysiological process. Besides, elevated peripheral WBC counts can also independently predict extubation failure for acute stroke patients (33), which is in accordance with our finding. Thirdly, impaired consciousness attributed to stroke decreases the capacity to drive central respiratory function and airway self-clearance (34, 35). Central respiratory depression may directly result in the occurrence of hypoxemia via hypoventilation, while loss of airway self-protection may increase the risk of silent aspiration of secretions or gastric contents (34, 35). In such circumstances, gas-exchange function may easily deteriorate among patients with SAP, which can be corroborated by our result that SAP patients with low GCS were more likely to develop reduced $\text{PaO}_2/\text{FiO}_2$ ratio.

Although the combined risk factors proposed in our study showed medium diagnostic power for SAP with $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 240 , our findings facilitate the early identification of high-risk patients with severe SAP. Currently, no efficient therapy (neither prophylactic antibiotics nor β -blockers) can be approached to prevent SAP onset (36, 37). It is notable that the early prediction of SAP may largely improve overall outcomes among patients with stroke (3). Consequently, the consideration of age, baseline GCS score and WBC level after diagnosis of SAP may account for the vital impact on stroke prognosis, which still requires further validation.

Our study had limitations. Firstly, a relatively small sample size from a monocentric EVT cohort. Other unnoticed confounding factors might not be included in the models. Or combination of another relevant parameters might increase diagnostic power for severe SAP. Secondly, this study excluded patients with a confirmed diagnosis of COVID-19, which could lead to a possible selection bias, because of the fact that all patients with COVID-19 were admitted or transferred to designated hospitals during the pandemic.

Conclusion

In this study, SAP with decreased $\text{PaO}_2/\text{FiO}_2$ ratio was revealed in significant association with the prolonged in-hospital stays among post-interventional patients with LVO. Advanced age, low GCS scores, and high WBC count after diagnosis of SAP could serve as independent risk factors for SAP with lower $\text{PaO}_2/\text{FiO}_2$ ratio after EVT. Future research is warranted to confirm our results.

Data availability statement

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

Ethics statement

The studies involving humans were approved by the Ethics Committees of Wuhan No. 1 Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the

requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because this was a retrospective study.

Author contributions

KT: Methodology, Data curation, Investigation, Formal analysis, Writing – original draft, Project administration. JL: Data curation, Conceptualization, Project administration, Writing – original draft, Investigation, Formal analysis, Methodology. YW: Formal analysis, Data curation, Writing – original draft, Methodology, Project administration, Investigation. ZG: Methodology, Project administration, Investigation, Writing – review & editing. YY: Project administration, Methodology, Writing – review & editing, Investigation. FG: Project administration, Writing – review & editing, Investigation, Methodology. YC: Writing – review & editing, Investigation, Project administration, Methodology. WL: Validation, Conceptualization, Writing – review & editing, Supervision, Investigation, Methodology, Resources, Funding acquisition, Project administration.

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Conflict of interest

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Supplementary material

The Supplementary material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fneur.2025.1598156/full#supplementary-material>

References

- Fan J, Li X, Yu X, Liu Z, Jiang Y, Fang Y, et al. Global burden, risk factor analysis, and prediction study of ischemic stroke, 1990–2030. *Neurology*. (2023) 101:e137–50. doi: 10.1212/WNL.0000000000207387
- Jovin TG, Li C, Wu L, Wu C, Chen J, Jiang C, et al. Trial of Thrombectomy 6 to 24 hours after stroke due to basilar-artery occlusion. *N Engl J Med*. (2022) 387:1373–84. doi: 10.1056/NEJMoa2207576
- Bouddhara T, Persondek L, Ablah E, Okut H, Lu L, Walker J. Post-stroke pneumonia: factors associated with readmission within 90 days of stroke discharge. *J Stroke Cerebrovasc Dis*. (2023) 32:107276. doi: 10.1016/j.jstrokecerebrovasdis.2023.107276
- Xu CY, Ye HW, Chen B, Wu YF, Cao Z, Ding Z, et al. Analysis of risk factors and prognosis of post-stroke pulmonary infection in integrated ICU. *Eur Rev Med Pharmacol Sci*. (2021) 25:856–65. doi: 10.26355/eurrev_202101_24654
- Suda S, Aoki J, Shimoyama T, Suzuki K, Sakamoto Y, Katano T, et al. Stroke-associated infection independently predicts 3-month poor functional outcome and mortality. *J Neurol*. (2018) 265:370–5. doi: 10.1007/s00415-017-8714-6
- Westendorp WF, Dames C, Nederkoorn PJ, Meisel A. Immunodepression, infections, and functional outcome in ischemic stroke. *Stroke*. (2022) 53:1438–48. doi: 10.1161/STROKEAHA.122.038867
- Westendorp WF, Nederkoorn PJ, Vermeij JD, Dijkgraaf MG, van de Beek D. Post-stroke infection: a systematic review and meta-analysis. *BMC Neurol*. (2011) 11:110. doi: 10.1186/1471-2377-11-110
- Tortum F, Tekin E, Gur A, Kerget B, Kasali K. Use of the PaO₂(2)/FiO₂(2) ratio in pulmonary embolism: evaluation of its correlation with pulmonary arterial computed tomography obstruction index. *Acad Radiol*. (2023) 30:893–9. doi: 10.1016/j.acra.2022.06.004
- Villar J, Fernandez C, Gonzalez-Martin JM, Ferrando C, Anon JM, Del Saz-Ortiz AM, et al. Respiratory subsets in patients with moderate to severe acute respiratory distress syndrome for early prediction of death. *J Clin Med*. (2022) 11:724. doi: 10.3390/jcm11195724
- Zinellu A, De Vito A, Scano V, Paliogiannis P, Fiore V, Madeddu G, et al. The PaO₂/FiO₂ ratio on admission is independently associated with prolonged hospitalization in COVID-19 patients. *J Infect Dev Ctries*. (2021) 15:353–9. doi: 10.3855/jidc.13288
- Whiting J, Edriss H, Yang S, Nugent K. Peak pressures and PaO₂/FiO₂ ratios are associated with adverse outcomes in patients on mechanical ventilators. *Am J Med Sci*. (2016) 351:638–41. doi: 10.1016/j.amjms.2016.01.028
- Smith CJ, Kishore AK, Vail A, Chamorro A, Garau J, Hopkins SJ, et al. Diagnosis of stroke-associated pneumonia: recommendations from the pneumonia in stroke consensus group. *Stroke*. (2015) 46:2335–40. doi: 10.1161/STROKEAHA.115.009617
- Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II) Second European-Australasian Acute Stroke Study Investigators. *Lancet*. (1998) 352:1245–51. doi: 10.1016/S0140-6736(98)08020-9
- Lobo Chaves MA, Gittins M, Bray B, Vail A, Smith CJ. Do stroke care processes modify clinical outcomes in patients with stroke-associated pneumonia? A registry cohort study in England and Wales. *Cerebrovasc Dis*. (2023) 52:21–7. doi: 10.1159/000524917
- Tinker RJ, Smith CJ, Heal C, Bettencourt-Silva JH, Metcalf AK, Potter JF, et al. Predictors of mortality and disability in stroke-associated pneumonia. *Acta Neurol Belg*. (2021) 121:379–85. doi: 10.1007/s13760-019-01148-w
- Gittins M, Lobo Chaves MA, Vail A, Smith CJ. Does stroke-associated pneumonia play an important role on risk of in-hospital mortality associated with severe stroke? A four-way decomposition analysis of a national cohort of stroke patients. *Int J Stroke*. (2023) 18:1092–101. doi: 10.1177/17474930231177881
- Iadecola C, Buckwalter MS, Anrather J. Immune responses to stroke: mechanisms, modulation, and therapeutic potential. *J Clin Invest*. (2020) 130:2777–88. doi: 10.1172/JCI135530
- Javidi E, Magnus T. Autoimmunity after ischemic stroke and brain injury. *Front Immunol*. (2019) 10:686. doi: 10.3389/fimmu.2019.00686
- DeLong JH, Ohashi SN, O'Connor KC, Sansing LH. Inflammatory responses after ischemic stroke. *Semin Immunopathol*. (2022) 44:625–48. doi: 10.1007/s00281-022-00943-7
- Verschoof MA, Groot AE, Vermeij JD, Westendorp WF, van den Berg SA, Nederkoorn PJ, et al. Association between low blood pressure and clinical outcomes in patients with acute ischemic stroke. *Stroke*. (2020) 51:338–41. doi: 10.1161/STROKEAHA.119.027336
- Bernhardt J, Godecke E, Johnson L, Langhorne P. Early rehabilitation after stroke. *Curr Opin Neurol*. (2017) 30:48–54. doi: 10.1097/WCO.0000000000000404
- Oh SE, Parikh NS. Recent advances in the impact of infection and inflammation on stroke risk and outcomes. *Curr Neurol Neurosci Rep*. (2022) 22:161–70. doi: 10.1007/s11910-022-01179-6
- Teh WH, Smith CJ, Barlas RS, Wood AD, Bettencourt-Silva JH, Clark AB, et al. Impact of stroke-associated pneumonia on mortality, length of hospitalization, and functional outcome. *Acta Neurol Scand*. (2018) 138:293–300. doi: 10.1111/ane.12956
- Zaccagnini G, Berni A, Pieralli F. Correlation of non-invasive oxygenation parameters with paO₂/FiO₂ ratio in patients with COVID-19 associated ARDS. *Eur J Intern Med*. (2022) 96:117–9. doi: 10.1016/j.ejim.2021.12.015
- Toffaletti JG, Rackley CR. Monitoring oxygen status. *Adv Clin Chem*. (2016) 77:103–24. doi: 10.1016/bs.acc.2016.06.003
- Bos LDJ, Ware LB. Acute respiratory distress syndrome: causes, pathophysiology, and phenotypes. *Lancet*. (2022) 400:1145–56. doi: 10.1016/S0140-6736(22)01485-4
- Patel UK, Kodumuri N, Dave M, Lekshminarayanan A, Khan N, Kavi T, et al. Stroke-associated pneumonia: a retrospective study of risk factors and outcomes. *Neurologist*. (2020) 25:39–48. doi: 10.1097/NRL.0000000000000269
- Banda KJ, Chu H, Kang XL, Liu D, Pien LC, Jen HJ, et al. Prevalence of dysphagia and risk of pneumonia and mortality in acute stroke patients: a meta-analysis. *BMC Geriatr*. (2022) 22:420. doi: 10.1186/s12877-022-02960-5
- Lv XN, Shen YQ, Li ZQ, Deng L, Wang ZJ, Cheng J, et al. Neutrophil percentage to albumin ratio is associated with stroke-associated pneumonia and poor outcome in patients with spontaneous intracerebral hemorrhage. *Front Immunol*. (2023) 14:1173718. doi: 10.3389/fimmu.2023.1173718
- Gallizioli M, Arbaizar-Roviro M, Brea D, Planas AM. Differences in the post-stroke innate immune response between young and old. *Semin Immunopathol*. (2023) 45:367–76. doi: 10.1007/s00281-023-00990-8
- Wang H, Zhang S, Xie L, Zhong Z, Yan F. Neuroinflammation and peripheral immunity: focus on ischemic stroke. *Int Immunopharmacol*. (2023) 120:110332. doi: 10.1016/j.intimp.2023.110332
- Wu B, Luo H, Li J, Chen Y, Liu J, Yu P, et al. The relationship between the Barthel index and stroke-associated pneumonia in elderly patients and factors of SAP. *BMC Geriatr*. (2024) 24:829. doi: 10.1186/s12877-024-05400-8
- Ho UC, Hsieh CJ, Lu HY, Huang AP, Kuo LT. Predictors of extubation failure and prolonged mechanical ventilation among patients with intracerebral hemorrhage after surgery. *Respir Res*. (2024) 25:19. doi: 10.1186/s12931-023-02638-5
- Patrizz A, El Hamamy A, Maniskas M, Munshi Y, Atadja L, Ahnstedt H, et al. Stroke-induced respiratory dysfunction is associated with cognitive decline. *Stroke*. (2023) 54:1863–74. doi: 10.1161/STROKEAHA.122.041239
- Robateau Z, Lin V, Wahlster S. Acute respiratory failure in severe acute brain injury. *Crit Care Clin*. (2024) 40:367–90. doi: 10.1016/j.ccc.2024.01.006
- Faura J, Bustamante A, Miro-Mur F, Montaner J. Stroke-induced immunosuppression: implications for the prevention and prediction of post-stroke infections. *J Neuroinflammation*. (2021) 18:127. doi: 10.1186/s12974-021-02177-0
- Vermeij JD, Westendorp WF, van de Beek D, Nederkoorn PJ. Post-stroke infections and preventive antibiotics in stroke: update of clinical evidence. *Int J Stroke*. (2018) 13:913–20. doi: 10.1177/1747493018798557