

# Analysis of risk factors and prognosis of post-stroke pulmonary infection in integrated ICU

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**Abstract.** – **OBJECTIVE:** The incidence of SAP (stroke-associated pneumonia) is high in integrated ICU (Intensive Care Unit), and it might result in sepsis, which exacerbates the clinical outcome and increases mortality. It is necessary to investigate the epidemiological features of post stroke infection and sepsis, identify the risk factors and analyze the prognosis.

**PATIENTS AND METHODS:** We retrospectively analyzed the data of 329 patients with cerebral infarction or cerebral hemorrhage, from seven tertiary university hospitals in Suzhou, Jiangsu Province, between January 1, 2016, and December 31, 2016. Basic demographic and clinical data including common health evaluation, stroke severity, microbiological parameters, surgical interventions and treatments were recorded for the analysis. SAP was diagnosed according to the criteria and recommendation from American Heart Association (AHA).

**RESULTS:** 188 (66.4%) patients suffered pneumonia, 124 patients were diagnosed as SAP. Compared with SAP, patients with non-SAP pulmonary infection had prolonged mechanical ventilation time, prolonged central venous catheter indwelling time, and higher incidence of sepsis (17.7% vs. 48.4%). 53 patients (18.7%) developed sepsis during hospitalization, whose mortality rate during hospitalization and the occurrence of neurologic dysfunction at 3 months were significantly increased ( $p < 0.05$ ). 130 positive results of

sputum cultures were found. The detected pathogens were mainly gram-negative bacteria. The pathogenic detection rate of non-SAP patients with pulmonary infection was higher (78.1%). The in-hospital mortality was 16.3% and the related risk factors were higher NIHSS score at admission, lower GCS score at admission, pulmonary infection (especially non-SAP pulmonary infection) and sepsis during hospitalization.

**CONCLUSIONS:** The incidence of pulmonary infection after stroke in the integrated ICU is high, and it is easy to be complicated with sepsis, prolonging the mechanical ventilation time, central venous catheter indwelling time and hospitalization time, and the prognosis of long-term neurological function is relatively poor. The definition of stroke-associated pneumonia has implications for the classification of clinical infections, the prediction of possible pathogenic pathogens, and the guidance of anti-infective treatment.

*Key Words:*

Stroke, Stroke-associated pneumonia (SAP), Sepsis, Integrated ICU, Prognosis.

## Introduction

Stroke leads to higher disability and mortality<sup>1,2</sup>. Pneumonia is considered to be one of the

major causes of death after stroke<sup>3</sup>. Poststroke pneumonia also increases the financial burden on the medical system. The annual cost of this complication approaches USD 459 million<sup>4</sup> and the average cost of hospitalization is USD 27,633<sup>5</sup>. These factors reflect the importance of preventing post-stroke pneumonia. Due to severe disturbance of consciousness and various complications, patients with severe stroke need to be admitted to the intensive care unit (ICU). Apart from prolonging in-hospital stay, post-stroke pneumonia is an important risk factor for adverse outcome<sup>5</sup>. In 2015, stroke associated pneumonia (SAP) was redefined according to recommendations of the Pneumonia in Stroke Consensus Group on diagnosis of stroke-associated pneumonia: nonventilated patients with pneumonia complicating in the first 7 days after stroke onset. Aspiration and stroke-induced immunodepression are the major pathogenesis<sup>6</sup>.

In the ICU, severe infections often lead to sepsis, a syndrome of organ dysfunction caused by dysregulated host response to infection. Stroke patients admitted to the ICU are at high risk for infections, such as disturbance of consciousness, aspiration, indwelling of various iatrogenic catheters, immunodepression, etc., and these might result in sepsis. Treatment options on sepsis are limited as stroke patients are prone to various complications and nerve function damage, which result in worse outcome. The mortality rate of stroke patients in the ICU is as high as 36-52.2%<sup>7-9</sup>.

To our knowledge, there were no data on epidemiology, risk factors, and outcome parameters of patients with SAP admitted to the integrated ICU in China. The aims of this study were (1) to investigate the epidemiologic features of SAP and sepsis in stroke patients in the ICU of Suzhou area, (2) to identify risk factors, and analyze outcome parameters. This would help in the prevention and treatment of these patients.

## Patients and Methods

### *Data Source and Study Population*

The data of this study were from integrated ICU of seven General Hospitals in Suzhou City, Jiangsu Province (The Second Affiliated Hospital of Soochow University, Suzhou Municipal Hospital, The First People's Hospital of Taicang, Zhangjiagang First People's Hospital, First People's Hospital of Wujiang, The First People's Hospital of Kunshan, the First People's Hospital of Changshu). We analyzed the discharge records

for patients with ischemic stroke or cerebral hemorrhage admitted between January 1, 2016, and December 31, 2016. Neurologists and integrated ICU physicians were involved in the diagnosis and treatment of these patients. A cerebral computed tomography (CT) scan or magnetic resonance imaging (MRI) was required to confirm patients meet diagnostic criteria for ischemic stroke or cerebral hemorrhage. Patients with ischemic stroke or cerebral hemorrhage admitted to the ICU within 72 hours from onset and hospitalized for more than 48 hours were included in the study. Patients with traumatic brain injury (TBI), transient ischemic attacks (TIA), subarachnoid hemorrhage (SAH) and other diseases were excluded. By this approach, we identified 329 patients. Of these, we excluded 46 patients due to the following reasons: patients admitted ICU from onset to treatment for more than 72 hours (10 cases), and patients' total hospital stay was less than 48 hours (36 cases). Finally, 283 patients entered the study.

### *Clinical Characteristics and Study Process*

#### *Data collection*

According to standardized data collection process, all relevant clinical scores, diagnosis, treatment and follow-up results were recorded for patients included in the study. The medical history of each patient was collected through consultation. For patients who cannot be communicated due to aphasia, coma or other reasons, medical history data obtained through their family members. Patients completed cerebral CT scan or MRI in outpatient or emergency department. Clinical scores were completed to assess the severity of disease, including Glasgow Coma Scale (GCS) score, National Institute of Health stroke scale (NIHSS) score, Acute Physiology and Chronic Health Evaluation (APACHEII) score and Sequential Organ Failure Assessment (SOFA) score.

#### *Nerve Function Parameters*

Get the scores of the Glasgow Coma Scale (GCS) and National Institute of Health Stroke Scale (NIHSS). By the TOAST standard<sup>10</sup>, types of ischemic stroke were divided into five subtypes, including cardiogenic cerebral embolism, formatting large artery atherosclerosis, small artery occlusion (lacunar infarcts), ischemic stroke caused by other reasons and unexplained ischemic stroke. By the etiology, the subtypes of cerebral hemorrhage included hypertension, arterial amyloidosis,

intracranial arteriovenous malformation, coagulation disorders (including caused by oral anticoagulant), formatting cerebral sinus thrombosis complicated with cerebral hemorrhage, other reasons and some unknown reasons. Bleeding amount of hemorrhage brain stroke patients was calculated by the related parameter of the area of lesion by the first CT check<sup>11</sup>. According to the different lesion locations, the lesions were divided into supratentorial lesions and infratentorial lesions.

#### *SAP Diagnoses*

SAP diagnoses were based on the diagnostic advice of AHA stroke-associated pneumonia in 2015 and the improved advice of CDC standard are recommended for SAP diagnoses. (1) Suspected SAP: meet the CDC diagnoses standard without the typical features in chest X-ray film for first check and review (maybe without review), ruling out of other diagnosis. (2) Confirmed SAP: meet the CDC diagnoses standard and show the typical features in chest X-ray film at least once. Besides SAP, the diagnoses of mechanical ventilation patients should obey the existing standard of ventilator-associated pneumonia (VAP)<sup>12</sup>. The pulmonary infection caused by invasion mechanical ventilation for 48 h was diagnosed with VAP. After 7 days of stroke, patients should be diagnosed with hospital-acquired pneumonia (HAP) with the existing standard of hospital acquired pneumonia<sup>12</sup>. In our study, VAP and HAP were collectively called non-SAP pulmonary infection.

#### *Sepsis Diagnoses*

The sepsis diagnoses were based on the guidelines of sepsis-3.0 standard<sup>13</sup> by Society of Critical Care Medicine (SCCM) in 2016, and at the same time consulting the Surviving Sepsis Campaign in 2012<sup>14</sup>.

#### *Collection of Pathogenic Specimens*

For all diagnosed pulmonary infection patients (including suspected SAP patients), we cultured and examined the sputum specimens and fiberoptic airway secretion, also the positive results of the first cultured were recorded.

#### *Calling Back Interview*

After being discharged, patients were followed-up by the phone call and assessed the neurological function outcomes adopting the modified Rankin Scale (mRS)<sup>15</sup>. If the score of mRS  $\geq 5$ , the outcomes of neurological function were poor.

#### *Ethics*

All patients and their entrusted agent informed consent entered the study voluntarily. The study was approved by Suzhou Medical Association and funded by Changshu, Jiangsu Province-Health Bureau. Also get the strong support from Critical Care Medicine and the Young Commission of Suzhou.

#### *Statistical Analysis*

Evaluate the dichotomy through the same grades or percentage and check by chi-square test. The measurement of abnormal distributions was described by interquartile range (IQR). If the results of single-variable test were significant, the multivariate analysis and the stepwise logistic regression analysis were evaluated. Through the logistic regression, get the results of parametric estimation, Wald chi-square test and odds ratio in the related variables through logistic regression model. The findings were analyzed using the statistical software SPSS. Statistical significance was defined at  $p < 0.05$ .

## **Results**

#### *Patient Baseline*

283 patients stroke patients were enrolled in our study with male sex ( $n=191$ ) included median age 65.6 years. And 124 (58.7%) patients were  $\geq 65$ . Among all patients, 136 (48.1%) patients were ischemic stroke and 147 (51.9%) were hemorrhagic stroke. The intracranial lesions location of 242 (85.5%) patients were in supratentorial area and 89 (28.2%) patients underwent neurosurgery interventions. 11 (8.8% of ischemic stroke) patients were taken intravenous thrombolysis therapy. The main reasons of ischemic stroke included the large pathology (38.2%) and small artery (34.6%). And the main reason of hemorrhagic stroke was hypertension. The main complication was hypertension (73.5%) of hemorrhagic stroke patients. The epidemiologic characteristics of patients were shown in Table I.

#### *Treatment and Pulmonary Infection*

188 patients (66.4%) developed pulmonary infection during hospitalization. 124 patients were diagnosed as SAP (accounting for 66.0% of the patients of pulmonary infection), with 100 patients confirmed SAP by clear imaging findings, and 24 patients were probably SAP. 165 patients (58.3%) underwent endotracheal intubation due to critical illness, with the mechanical ventilation

**Table I.** Basic data of patients.

		%	Range	IQR
Total	283			
Male	191	67.5		
Age (range, IQR)	65.6		34-94	56-76
Age $\geq$ 65 years	166	58.7		
NIHSS at admission (range, IQR)	18.7		0-41	8-28
GCS at admission (range, IQR)	8.6		3-15	5-12
APACHEII at admission (range, IQR)	17.4		2-46	10-23
SOFA at admission (range, IQR)	3.1		0-14	2-7
Ischemic stroke	136	48.1		
Supratentorial lesions	124	91.2		
thrombolysis	11	8.1		
decompressive craniectomy	3	2.2		
Pathogeny				
1 Cardiac cerebral embolism	47	34.6		
2 Macroarteriopathy	52	38.2		
3 Arteriolar lesions (including lacunar infarction)	28	20.6		
4 Other reasons	1	0.7		
5 Unknown reasons	8	5.9		
Hemorrhagic stroke	147	51.9		
Supratentorial lesions	118	80.3		
Blood loss (mL) (range, IQR)	35.3		2-120	13-50
Hematoma evacuation	86	58.5		
Decompressive craniectomy	84	57.1		
External ventricular drainage	68	46.3		
Pathogeny				
1 Hypertension	108	73.5		
2 Arterial amyloidosis	7	4.8		
3 Intracranial arteriovenous malformation	4	2.7		
4 Coagulation disorders (including caused by oral anticoagulants)	1	0.7		
5 Cerebral hemorrhage complicated by venous sinus thrombosis	1	0.7		
6 Other reasons	4	2.7		
7 Unknown reasons	22	15		
Combined disease				
Cardiac insufficiency	14	4.9		
Chronic obstructive pulmonary disease	4	1.4		
Renal insufficiency	9	3.2		
Hepatic insufficiency	3	1.1		
Hypertension	207	73.1		
Diabetes mellitus	58	20.5		
Atrial fibrillation	60	21.2		
Malignant tumor	16	5.7		

IQR: interquartile range.

support for an average of 9 days. Among the mechanically ventilated patients, 60 patients (31.9%) developed pulmonary infection 48 hours after mechanical ventilation and were diagnosed as VAP. 4 patients were diagnosed as HAP and 53 patients (18.7%) developed sepsis during hospitalization. The relevant treatment measures and pulmonary infection were shown in Table II.

### ***Analysis of Risk Factors for Pulmonary Infection and Sepsis***

Elderly patients (> 65 years) and patients with deep disturbances of consciousness (low GCS score) were more likely to have pulmonary infection ( $p < 0.05$ ). Compared with non-infected patients, patients with pulmonary infection had prolonged central venous catheter indwelling time,

ICU stay time and total hospitalization time. However, pulmonary infection did not significantly increase the fatality rate during hospitalization and the incidence of adverse neurological outcomes at 3 months ( $p \geq 0.05$ ). Once combined with sep-

sis, the neurological disability outcome increased significantly at 3 months (50.9% vs. 33.9%). The comparison of statistically significant risk factors for pulmonary infection and sepsis was shown in Table III.

**Table II.** Treatment measures and infections.

		%	Range	IQR
ICU length of stay (Day) (Range, IQR)	11.9		1-69	4-16
Total hospital stay (Day) (Range, IQR)	20.3		2-159	7-23
Urinary catheter (Percentage)	259	91.5		
Urinary catheter indwelling time (Day) (Range, IQR)	11.7		1-60	4-17
Central venous catheter (Percentage)	171	60.4		
Central venous catheter indwelling time (Day) (Range, IQR)	6.2		1-48	4-8
Number of mechanical ventilation patients (Percentage)	165	58.3		
Mechanical ventilation time (Day) (Range, IQR)	9.1		1-55	3-12
Enteral nutrition support time (Day) (Range, IQR)	14.3		1-73	6-19
Gastric tube retention time (Day) (Range, IQR)	5.8		1-25	4-7
Naso intestinal tube retention time (Day) (Range, IQR)	8.5		1-65	5-14
Service time of antacids (Day) (Range, IQR)	9.9		1-35	4-14
Pulmonary infection (percentage of patients)	188	66.4		
SAP (percentage of patients with pulmonary infection)	124	66		
Diagnosis as SAP	100			
Probably SAP	24			
VAP (percentage of patients with pulmonary infection)	60	31.9		
HAP (percentage of patients with pulmonary infection)	4	2.1		
Number of sepsis cases (percentage of patients)	53	18.7		

IQR: interquartile range

**Table III.** Analysis of pulmonary infection and sepsis factors.

	Pulmonary infection	%	Non-pulmonary infection	%	<i>p</i>	sepsis	%	Non-sepsis	%	<i>p</i>
Total	188		95			53		230		
age > 65 years	122	65	44	46.3	<b>0.003</b>	33	62.2	130	57.8	NS
ICU length of stay (Day)	13.8		8.3		<b>&lt;0.001</b>	13.9		11.5		NS
Total hospital stay (Day)	23.2		14.7		<b>0.001</b>	27.8		18.6		<b>0.005</b>
GCS at admission	8.1		9.6		<b>0.002</b>	8.4		8.6		NS
Urinary catheter indwelling time (Day)	14.2		6.8		<b>&lt;0.001</b>	15.6		10.8		<b>0.003</b>
Central venous catheter indwelling time (Day)	7.5		3.5		<b>&lt;0.001</b>	10.6		5.1		<b>&lt;0.001</b>
Mechanical ventilation time (Day)	6.7		3.6		<b>&lt;0.001</b>	8.5		4.6		<b>0.002</b>
Enteral nutrition support time (Day)	17.1		7.3		<b>&lt;0.001</b>	17.7		13.3		<b>&lt;0.001</b>
Service time of antacids (Day)	8.1		7.4		NS	7.7		7.1		NS
Death during hospitalization	37	20	9	9.5	<b>0.028</b>	17	32.1	30	13	<b>&lt;0.001</b>
Poor prognosis at 3 months	75	40	29	30.5	NS	27	50.9	78	33.9	<b>0.021</b>

NS: no significance

**Table IV.** Risk factors analysis of SAP group and non-SAP group.

	SAP group	%	Non-SAP group	%	p
Total	124		64		
Sex (male)	83	66.9	47	73.4	NS
age > 65 years	84	67.7	42	65.6	NS
ICU length of stay (Day)	12.8		15.7		NS
Total hospital stay (Day)	20.9		27.8		NS (0.054)
APACHE II at admission	16.8		20		0.005
SOFA at admission	17.3		22.4		0.002
NIHSS at admission	8.4		7.6		NS
Urinary catheter indwelling time (Day)	13.4		15.8		NS
Central venous catheter indwelling time (Day)	5.7		10.9		<0.001
Mechanical ventilation time (Day)	5.3		9.4		0.003
Enteral nutrition support time (Day)	14.2		18.3		NS
Gastric tube retention time (Day)	5.7		6.4		0.08
Service time of antacids (Day)	7.5		7.3		NS
Sepsis	22	17.7	31	48.4	<0.001
Death during hospitalization	20	16.1	17	26.6	NS
Poor prognosis at 3 months	43	34.7	32	50.0	NS (0.055)

NS: no significance

### **Analysis of Risk Factors for SAP and non-SAP Pulmonary Infection**

Among the 124 SAP patients, 64 patients underwent invasive mechanical ventilation and pulmonary infection occurred before 48 hours after mechanical ventilation and were still diagnosed as SAP. 60 patients had invasive mechanical ventilation due to severe disturbance of consciousness and high risk of asphyxia. They developed pulmonary infection 48 hours after mechanical ventilation and were diagnosed as VAP. Moreover, 4 patients with non-mechanical ventilation developed pulmonary infection after 7 days of onset and were diagnosed with HAP. In this study, VAP and HAP were unified as non-SAP pulmonary infection. In comparison with SAP group, non-SAP pulmonary infection group patients had prolonged mechanical ventilation time, deep vein catheter indwelling time, and higher incidence of sepsis (17.7% vs. 48.4%) ( $p < 0.05$ ), relatively poor neurological disability outcome at 3 months (69.2% vs. 55.1%), but the difference was not statistically significant ( $p = 0.071$ ) (as shown in Table IV).

### **Pathogen Distribution of Respiratory Secretions**

Of all 188 patients with pulmonary infections, 130 patients were found positive results in the

pathogen distribution of respiratory secretions. The pathogens detected were mainly Gram-negative bacteria, accounting for 86.2% of all microorganisms. The first three bacteria were *Klebsiella pneumoniae* (20.7%), *Acinetobacter baumannii* (11.2%) and *Pseudomonas aeruginosa* (5.9%). Compared with SAP patients, non-SAP pulmonary infection patients had higher pathogenic detection rate (63.7% vs 78.1%), with the positive rates of *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and fungi in pathogenic composition increased. The characteristics of the pathogen spectrum were shown in Table V and Figure 1.

### **Analysis of Prognostic Risk Factors**

Stroke patients admitted to ICU are critically ill and usually had poor prognosis. In this study, the mortality rate of patients during hospitalization was 16.3%. Of the 237 patients who were discharged alive, 41 patients (17.3%) had severe disability (mRS score of 5), accompanied by severe disturbance of consciousness and incontinence, prolonged bedridden, and requiring continuous health care. Risk factors associated with mortality during hospitalization were higher NIHSS score at admission, lower GCS score at admission, pulmonary infection (especially non-SAP pulmonary infection) and sepsis during hospitalization (Ta-

**Table V.** Distribution of pathogens.

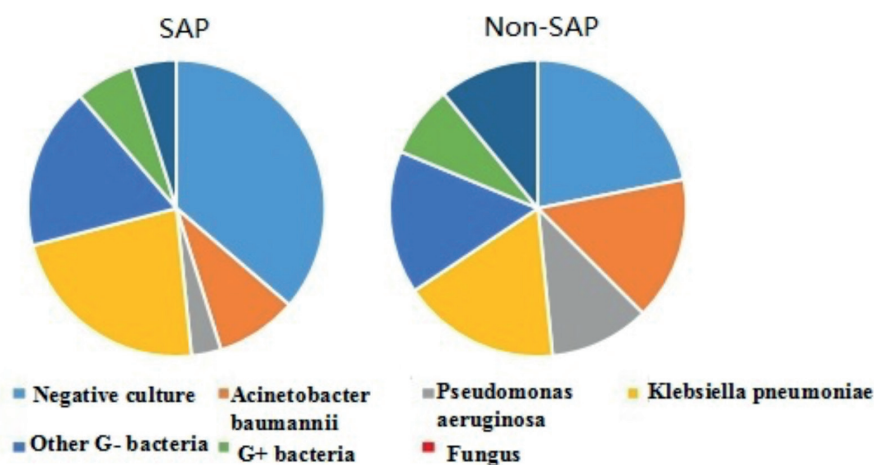
	SAP group	%	Non-SAP group	Total	%	(Total)
Negative culture	45	36.3	14	21.9	59	31.4
Acinetobacter baumannii	11	8.9	10	15.6	21	11.2
Pseudomonas aeruginosa	4	3.2	7	10.9	11	5.9
Klebsiella pneumoniae	28	22.6	11	17.2	39	20.7
Other G- bacteria	22	17.7	10	15.6	32	17.0
G+ bacteria	8	6.5	5	7.8	13	6.9
Fungus	6	4.8	7	10.9	13	6.9
Total	124		64		188	

ble VI). Logistic regression analysis (Table VII) showed that lower GCS scores were independent predictors of death during hospitalization. Risk factors for poor neurological prognosis at 3 months were higher APACHE II, NIHSS score, lower GCS score at admission, and sepsis during hospitalization (Table VI). Logistic regression analysis (Table VII) showed that higher APACHE II score, lower GCS score at admission were independent predictors of poor neurological outcomes at 3 months.

## Discussion

The annual stroke mortality was as high as 1.5 million in China. About 75% of the surviving patients had varying degrees of disability, of which 50% were moderately or severely disabled<sup>16</sup>. Suzhou was a developed city in eastern China with the high level of medical conditions, and the incidence of stroke was relatively high. The pur-

pose of this study was to describe the epidemiological characteristics, risk factors and prognosis of stroke patients admitted to ICU in regional general hospitals. Although there were many epidemiological studies on sepsis in the integrated ICU, as far as we know, there was no multi-center study on pulmonary infection in a specific population of stroke treated in the integrated ICU. There were some differences between integrated ICU and neurological ICU (neurologic intensive care unit, NICU), such as the type of disease, the occurrence of infection, and the pathogen spectrum of infection. The epidemiological data on post-stroke infection in neurology or NICU might not be suitable for stroke patients in the integrated ICU. This was also the reason of selecting the stroke patients in the integrated ICU as the objects in this study. In most foreign NICU studies, the prevalence of pulmonary infection after stroke was between 9.5 and 56.6%<sup>17-22</sup>. In the integrated ICU study, the prevalence of pulmonary infection after stroke was 17%-50%<sup>23-27</sup>. The prevalence

**Figure 1.** Pathogen spectrum.

of pulmonary infection in this study was 66.4%, higher than those studies, which might be related to the local stroke epidemiology, the severity of stroke included in this study, and the research in integrated ICUs.

In this study, a total of 36 patients were excluded who were hospitalized for less than 48 hours. Some of these patients died within 48 hours after onset, and the others had extremely poor neurological function (GCS score 3-5). They could not benefit from surgical intervention and were expected to die in the short term. Their family members chose to give up treatment after informing the severity of the disease. Such choices might weaken the effect of stroke lesions, while enhanced the effect of pulmonary infection and sepsis on prognosis. The influence of age on prognosis was weakened (because the patient's family members considered the cost, prognosis and ethical issues, the elderly patients might be selected for palliative treatment instead, this study failed to indicate age as a strong predictor of prognosis). Moreover, it also explained why some neurological parameters (such as NIHSS score at admission to predict neurological prognosis at 3 months) in logistic regression analysis (Table 7) could not show the independent prediction of patient outcomes.

The term of "stroke-associated pneumonia" was first proposed by Hilker et al<sup>17</sup> to describe the pulmonary infection occurring within 72 hours of admission. Teramoto<sup>28</sup> classified SAP as acute SAP (within one month after stroke) and chronic SAP (one month after stroke). There were also other definitions<sup>18</sup>, which confused and could not conducive to systematic evaluation and comparison of pulmonary infection after stroke in different studies. The stroke-associated pneumonia was re-defined by AHA "Diagnosis of Stroke-Associated Pneumonia"<sup>6</sup>. This study used this definition to diagnose SAP and compared it with non-SAP pulmonary infection such as VAP and HAP. In terms of pathogenesis, SAP was related to aspiration<sup>28</sup> and the stroke-induced immune function inhibition<sup>29</sup>. The defined time was within one week after stroke onset or within 48 hours after mechanical ventilation, which was closer to the defined time of community acquired infection (CAP). Non-SAP pulmonary infection (including VAP and HAP) were essentially in-hospital acquired infections<sup>6</sup> and were closely related to invasive interventions such as mechanical ventilation. In this study, patients with non-SAP pulmonary infection were more likely to develop sepsis than those with SAP, leading to poor outcomes (especially mortality during

hospitalization). However, the prognosis of neurological function at 3 months evaluated by the modified Rankin score<sup>15</sup> were more dependent on the severity of neurological loss of patients. Therefore, infection and sepsis during hospitalization could not show their predictive value, as shown in table 7. ICU patients usually needed to keep one or more invasive catheter indwelling, which increased the risk of infection. In our study, the factors related to the occurrence and adverse outcome of pulmonary infection were prolonged mechanical ventilation time, central venous catheter indwelling time, but the prolonged urinary catheter and the use of antacids were not significantly related. Enteral nutrition support pipeline should be divided into two parts: gastric tube and naso-intestinal tube. Compared with patients without indwelling enteral nutrition support pipeline and those changed with naso-intestinal tube in the short term, the incidence of pulmonary infection and poor outcomes increased in patients with long-term gastric tube indwelling, which might be related to the swallowing dysfunction and digestive tract reflux. Some studies had similar conclusions<sup>23,24</sup>.

In our study, the positive detection rate of respiratory secretion culture pathogens in SAP group was lower than non-SAP pulmonary infection group, however, the proportion of *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and fungi in non-SAP pulmonary infection group was higher than SAP group. This was consistent with the clinical situation of hospital acquired infection. Therefore, the new definition of stroke-associated pneumonia<sup>6</sup> might be meaningful for classifying clinical infections, predicting possible pathogens and guiding anti-infective treatment, although it required further large-scale studies.

Most of the patients in our study completed the chest CT examination at the time of the first head CT examination in the Emergency Department. For patients unable to complete the synchronous chest CT examination at the first head CT examination, we conducted the chest CT examination at the time of the re-examination of the head CT according to the patient's specific conditions (such as vital signs, whether to receive surgical intervention). For patients unable to go out for a second imaging examination, a bedside chest X-ray was performed within 48 hours of admission, for that radiologists' reports on chest X-ray lung changes were reliable<sup>6</sup>. When the patient has new clinical symptoms of pulmonary infection (fever, change of sputum, chest physical signs, et al), chest CT examination or bedside chest X-ray were performed.

In our study, 53 patients (18.7%) developed sepsis during hospitalization. The results were similar to those of other studies. A large prospective study by Engel et al<sup>7</sup> showed that the incidence of sepsis in different professions was 23.4%. The diagnosis of sepsis in this study was based on the guidelines of sepsis-3.0 standard<sup>13</sup>, meanwhile we also consulted Sepsis-2.0 standard<sup>14</sup>. The main reason was that SOFA score in the sepsis-3.0 standard included the Glasgow Coma Scale (GCS) score, and the SOFA score was influenced by the GCS score. For patients with a decreased level of consciousness (GCS $\leq$ 14), the baseline SOFA score was at least 1 at admission. As the disease progresses, changes in the level of consciousness caused by stroke lesions might significantly affect the accuracy of SOFA score, and it was impossible to distinguish whether the degree of consciousness disorder caused by the stroke or the infection. Recently, Kantanen et al<sup>30</sup> used SOFA without GCS scores to exclude disturbance of consciousness and evaluate the correlation between non-central nervous system factors and prognosis. We attempted such data transformation, but it failed to show any independent predictive values for prognosis in the statistical analysis. How to eliminate disturbance of consciousness for diagnosing sepsis after stroke required more further studies.

### Research Limitations

Due to the limitations of clinical practice, the patient selection in this study could affect the extension of conclusions. It might be only suitable for patients with severe stroke in integrated ICU in some areas of China.

### Conclusions

The occurrence of pulmonary infection after stroke in the integrated ICU is high, and it is easy to be complicated with sepsis, prolonging the mechanical ventilation time, central venous catheter indwelling time and hospitalization time, and the prognosis of long-term neurological function is relatively poor. The definition of stroke-associated pneumonia<sup>6</sup> has implications for the classification of clinical infections, the prediction of possible pathogenic pathogens, and the guidance of anti-infective treatment.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

### Acknowledgements

This work was supported by the youth Program of Changshu Health Bureau: cswsq201401.

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