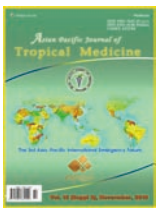

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An updated Chinese consensus statement on stroke−associated pneumonia 2019

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The concept of stroke-associated pneumonia (SAP) was first brought out by Hilker in 2003, which is the most important risk factor of mortality after stroke[1,2]. SAP causes prolonging hospitalization time and increasing medical expenses[3], which is a large burden for families and society. Due to the absence of an agreed concept for SAP in China and abroad previously, the variation in diagnostic criteria is considerable[4]. Therefore, in clinical practice, the prevention of SAP may be inadequate, and SAP patients may not be diagnosed timely or receive appropriate anti-infective treatment. The above situation may lead to a poor prognosis in patients. A multidisciplinary expert group composed of specialists in neurology, respiratory, infectious diseases, and intensive care was established in 2009 to discuss and formulate the Chinese consensus of SAP consensus 2010 edition[5] to improve the awareness and standardize the clinical diagnosis and treatment of SAP in China. In recent years, increasing researches on SAP provide more clinical evidence, and the accumulated evidence in the Chinese population is also increasing. Therefore, the specialists in neurology, emergency, respiratory, infectious diseases, intensive care, updated and revised the original consensus together to meet the needs of SAP clinical and prevention work. This version of the consensus is based on the 2010 version; the overall framework and major updates of SAP are determined after several working sessions. This version of the consensus combines the latest research progress and relevant guidelines at home and abroad, and the practical experience and research data on SAP prevention and treatment in China are used as much as possible; it is also revised by extensive solicitation of opinions and repeated discussions. We hope this consensus can provide a reference for the clinical treatment and prevention of SAP (Figure 1).

1. Definition and epidemiology

The consensus published by the Pneumonia in Stroke Consensus Group in 2015 suggests defined SAP as pneumonia occurring within the first seven days after stroke onset in non-ventilated patients without previous pulmonary infection. Pneumonia onset in stroke patients is highly associated with post-stroke body dysfunctions, and inflammation caused by infection is an important factor in exacerbating brain injury after stroke[6]. SAP can also cause other serious complications such as sepsis and gastrointestinal bleeding[7].

Foreign epidemiological data[7-10] show that the incidence of SAP is 7% to 38%. Ji *et al*[6,11] found that the incidence of SAP was 11.4% in ischemic stroke patients and 16.9% in hemorrhagic stroke patients, according to the China National Stroke Registry. The research of Xu *et al*[12] showed that the incidence of SAP was 35.97%, and it is much higher than the incidence of hospital-acquired lower respiratory tract infection (1.76%-1.94%). SAP

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increases 3-fold in the 30-day mortality in stroke patients, while 1-year and 3-year risk of mortality also increase[10,13].

Recommendation: Stroke-associated pneumonia is defined as pneumonia, which occurs within the first seven days after stroke onset in non-ventilated patients without previous pulmonary infection.

2. Risk factors and prediction model

SAP risk prediction can help choose interventions to reduce the incidence of high-risk patients[14]. Stroke-induced immunosuppression and dysphagia are major independent risk factors for SAP[15]; other risk factors include but are not limited to age, gender, smoking history, the severity, type and location of stroke, level of consciousness, dysphagia, feeding method, antacid application, admission to intensive care unit (ICU), hypertension, diabetes, history of chronic respiratory disease, history of atrial fibrillation[9,16,17]. A number of studies have applied multivariate regression models to design various scoring methods to predict SAP risk since 2012[6,8,18-20]. This Consensus recommends the scoring method based on Chinese population data by Ji *et al*. to assess the risk of Chinese patients (Table 1)[6,11]. This prediction model has been validated by related researches[14,20].

Recommendation: It is recommended to apply an AIS-APS, ICH-APS scoring method to assess SAP risk in Chinese stroke patients.

3. Pathogenesis

The pathogenesis of SAP is highly related to the body dysfunction caused by stroke, and it is specific comparing with community-acquired pneumonia and hospital-acquired pneumonia. Aspiration caused by the disturbance of consciousness and dysphagia after stroke, as well as stroke-induced immunosuppression, are considered as the most important pathogenesis of SAP[21]. A total of 40%-70% patients will show symptoms such as consciousness decrease, dysphagia, protective reflex decline, lower esophageal sphincter dysfunction, swallow-breathing coordination decline, cough reflex decline; therefore, it is easy to aspirate nasopharynx and oropharynx secretions, and stomach contents into the lungs and cause SAP[22,23]. Early identification of dysphagia can provide evidence for decision-making in nutrition management; early swallowing rehabilitation can reduce pulmonary complications[24].

Impaired cellular immunity function induced by stroke is an important internal mechanism of SAP. Systemic immune responses after acute stroke can prevent further inflammatory stimuli and protect brain tissue, but it also causes immunosuppression and therefore leads to stroke-induced immunosuppression syndrome and infection. Immunoregulatory mediators are released after stroke-induced brain injury, including IL-lβ, TNF-α, IL-6, as well as calcitonin gene-related peptide, neuropeptide, vasoactive intestinal peptide, and others. These immunoregulatory mediators act on blood vessels, adrenal glands, and nerve endings and cause the release of norepinephrine, glucocorticoids, acetylcholine from these areas. The above three substances act on receptors on immune cells such as NK cells, Th1, Th2, and macrophages, and down-regulate the immune function of these cells. Therefore, these cells weaken immune function, resulting in systemic immunosuppression and making people prone to infection. In addition, the right cerebral hemisphere is also associated with the activation of T lymphocytes, and the decrease in the number and activation of T lymphocytes increases the probability of infection in patients[25].

Systemic immune responses after acute stroke can prevent further inflammatory stimuli and protect brain tissue, but cause immunosuppression and cause stroke-induced immunosuppression syndrome and infection.

Bedridden may also lead to SAP. Stroke patients are often bedridden for limb paralysis, and endotracheal secretion is stagnated and accumulated at basis pulmonis, so the bacteria are easy to reproduce, causing SAP.

4. Pathogen

Stroke patients may have persistent aspiration due to disturbance of consciousness and abnormal swallowing function; aspirated material includes not only secretions from the oropharynx, but also nasal secretions, food left in the mouth, contents of the gastrointestinal tract, and refluxed digestive fluid. El-Solh *et al*[26] applied the method of protective bronchoalveolar lavage to study the etiology of aspiration pneumonia. They found the most common pathogens were G-bacilli (49%), anaerobes (16%) and *Staphylococcus aureus* (12%); the most common anaerobes were *Prevotella* and *Clostridium*; 22% were mixed infection, of which 20% were mixed infection of two pathogens, and 2% were mixed infection of three pathogens. Thus, analyzed from this evidence, SAP pathogens are mainly G-bacteria, such as *Klebsiella pneumonia*, *Escherichia coli*; mixed infection of various bacteria and anaerobes is common. Besides, pathogens are often changeable during the disease process, and it is difficult to detect pathogens; multi-drug resistant bacteria are prone to occur. There is no large-scale multicenter epidemiological data worldwide currently.

Recommendation: The pathogen SAP is mainly G-bacteria, and mixed infections of various bacteria and anaerobic bacteria are common. Besides, the pathogens during the disease process are often changeable.

Table 1. Risk prediction model for stroke-associated pneumonia.

Scoring method	Risk factors and corresponding scores		Prediction of stroke-associated pneumonia
Acute ischemic stroke-associated pneumonia score (AIS-APS)	Age≤59 years old: 0 points; 60–69: 2 points; 70–79: 5 points; ≥80: 7 points. History of atrial fibrillation: 1 point; history of congestive heart failure: 3 points; history of chronic obstructive pulmonary disease (COPD): 3 points; Smoke history: 1 point. Modified Rankin Scale score≥3 before this stroke: 2 points. Glasgow Coma Score 9–15: 0 points; 3–8: 3 points. Swallowing dysfunction: 3 points. Stroke subtype is lacunar infarct: 0 points; anterior circulation infarct: 0 points; Total anterior circulation infarct: 2 points; posterior circulation infarct: 2 points. Blood glucose at admission≥11.1 mmol/L: 2 points.		Score 0–6: extremely low risk Score 7–13: low risk Score 14–20: moderate risk Score 21–27: high risk Score 28–35: extremely high risk (the total score ranges from 0–35)
Intracerebral hemorrhage-associated pneumonia score (ICH-APS)	A	Age≤59 years old: 0 points; 60–69: 2 points; 70–79: 3 points; ≥80: 5 points. Smoking: 1 point; Excessive drinker: 1 point; COPD: 5 points. Incapable of looking after oneself before stroke (mRS ≥3 points): 2 points. Glasgow coma scale at admission is 3–8: 2 points; 9–12: 2 points; 13–14: 2 point; 15: 0 points. National Institute Health stroke scale score at admission is 0–5: 0 points; 6–10: 1 point; 11–15: 2 point; ≥16: 3 points. Dysphagia: 2 points. Sublingual cerebral hemorrhage: 1 point; hemorrhage breaking into the ventricle: 1 point; hematoma volume (mL): sublingual cerebral hemorrhage<10 or supratentorial cerebral hemorrhage<40-point; sublingual cerebral hemorrhage 10–20 or supratentorial cerebral hemorrhage 40–70-point; sublingual cerebral hemorrhage>20 or supratentorial cerebral hemorrhage>70-point.	Score 0–3: extremely low risk Score 4–7: low risk Score 8–11: moderate risk Score 12–15: high risk Score≥16: extremely high risk
	B	Age≤59 years old: 0 points; 60–69: 2 points; 70–79: 3 points; ≥80: 5 points. Smoking: 1 point; Excessive drinker: 1 point; COPD: 6 points. Incapable of looking after oneself before stroke (mRS ≥3 points): 2 points. Glasgow coma scale at admission is 3–8: -point; 9–12: -point; 13–14: - point; 15: - point. National Institute Health stroke scale score at admission is 0–5: 0 points; 6–10: 1 point; 11–15: 3 point; ≥16: 5 points. Dysphagia: 3 points. Sublingual cerebral hemorrhage: 1 point; hemorrhage breaking into the ventricle: - point; hematoma volume (mL): sublingual cerebral hemorrhage<10 or supratentorial cerebral hemorrhage<40 is 0 points; sublingual cerebral hemorrhage 10–20 or supratentorial cerebral hemorrhage 40–70 is 1 point; sublingual cerebral hemorrhage>20 or supratentorial cerebral hemorrhage>70 is 2 points.	Score 0–3: extremely low risk Score 4–7: low risk Score 8–11: moderate risk Score 12–15: high risk Score≥16: extremely high risk

5. Diagnosis

5.1. Clinical manifestation

Newly emerged pulmonary infection symptoms within the first seven days after stroke onset inpatients without mechanical ventilation: (1) fever, temperature 38 ℃; (2) newly emerged or aggravated cough, dyspnea, or shortness of breath; (3) newly emerged purulent sputum, sputum properties changes, or respiratory secretion increases or needs for sputum suction increases within 24 hours; (4) rales or crackles or bronchorespiratory sounds are found during lung auscultation; (5) age≥70 years old, change in consciousness state without other definite causes.

5.2. Laboratory and imaging inspection

Peripheral blood leukocytes≥10 000×10^9/L or≤4 000×10^9/L, with or without left shift; imaging result shows newly emerged or progressing infiltrating shadow, and chest CT can be performed if necessary. Zhang *et al*[27] found leukocyte count and C-reactive protein (CRP) of SAP patients are significantly higher than patients without SAP, and the rising of CRP independently is associated with poor outcomes, as well as the increased mortality and infection risk. Procalcitonin is a better predictor for infection compared with CRP. A higher procalcitonin level indicates a more serious bacterial infection and a higher possibility of bacterial infection and sepsis[28].

5.3. Pathogen examinations

Collect qualified lower respiratory secretions (neutrophils count >25/low-power field, epithelial cell count <10/low-power field, or ratio of the above two >2.5:1), protected specimen brush, bronchoalveolar lavage fluid, or aseptic body fluid (blood or pleural effusion) before applying anti-infective drugs, and send for pathogenic microorganism examination. Among the above sampling method, sputum expectoration is more acceptable for patients and their families, as this sampling method is noninvasive; therefore, it is more common in clinical application. Before sputum samples collection, patients need to remove dentures, dental trays, *etc*., and clean oral cavity; patients need to cough deeply and expectorate, and it is better to have medical staff guidance during this sample collecting process. Patients who cannot expectorate spontaneous need claps on their backs to expel sputum. Sputum samples were sent for examination once a day, and sputum smear and culture were conducted for 2-3 consecutive days; laboratory treatment needs to be done within 1-2 hours after sample collection. Blood culture is an essential method for diagnosing bloodstream infections. Blood samples should be collected 2-3 sets each time for adult patients, and each set should be collected from different puncture sites. Blood samples collected from the same puncture site are usually injected into aerobic and anaerobic culture flasks, respectively, and the blood volume per bottle is 8-10 mL to increase the positive rate. For complication with pleural effusion, it is feasible to send pleural cavity puncture to routine and biochemical examinations, smear (such as Gram staining, acid-fast staining), culture, and other tests.

If necessary, blood samples should be sent to detect antibodies or nucleic acid of atypical pathogens (mycoplasma, chlamydia, and legionella); the definite diagnosis can be made if the serum IgM antibody is positive or the titer of serum specific IgG antibody in acute and recovery period rises four-fold or higher. Respiratory secretions (nose/throat swabs) should be sent for corresponding viral antigens or nucleic acid detection or virus culture, when during the epidemic of respiratory viruses and with epidemiological exposure history[29].

Recommendation: It is recommended to conduct pathogen examinations proactively to optimize SAP anti-infective treatment strategies.

5.4. Diagnostic criteria

The SAP diagnostic criteria referred to the improved criteria by the Centers for Disease Control and Prevention[30] are as follows:

At least meet one of the following criteria: (1) Fever without other clear cause (body temperature≥38 ℃); (2) Leukopenia (≤4 000×10^9/L) or leukocytosis (≥10 000×10^9/L); (3) Age≥70 years old, change in consciousness state without other clear cause;

And at least meet two of the following criteria: (1) Newly emerged purulent sputum properties changes or respiratory secretion increases or needs for sputum suction increases within 24 hours; (2) Newly emerged or aggravated cough, dyspnea, or shortness of breath (respiratory rate > 25 times/minute); (3) Find rales or crackles or bronchorespiratory sounds during lung auscultation; (4) Impaired gas exchange (such as hypoxemia (PaO_2/FiO_2≤300), increase in oxygen demand;

Chest imaging meet one of the following criteria: Newly emerged or progressing infiltrating shadow, solid shadow or ground glass shadow (For patients without underlying cardiopulmonary disease), a chest imaging test with any of the above imaging features is acceptable.

5.5. SAP severity assessment

The assessment on the severity of SAP is important for choosing antibiotic sempirically and treatment sites, as well as determining prognosis. CURB-65 (C: confusion, U: uremia, R: respiratory rate, B: blood pressure) and pneumonia severity index (PSI) can be applied to assessment (Table 2).

Recommendation: The combined application of CURB-65 and

Table 2. Scoring systems of stroke-associated pneumonia severity assessment.

Scoring system	Prediction index	Risk assessment	Characteristics
CURB-65	Five items in total, 1 item for 1 point 1. Disturbance of consciousness 2. Blood urea nitrogen>7 mmol/L 3. Respiratory rate >30 times/min 4. Systolic blood pressure <90 mmHg or diastolic blood pressure≤60 mmHg 5. Age ≥65 years old	Low risk: score 0–1; treated in the outpatient clinic or general ward Moderate risk: score 2; treated in the general ward High risk: score 3–5; treated in ICU	The scoring system is simple, sensitive and, easy to operate
Pneumonia severity index	Age plus the sum of all risk factors (minus 10 points for female): 1. Living in nursing home: 10 points 2. Underlying diseases: tumor: 30 points; liver disease: 20 points; congestive heart failure: 10 points; cerebrovascular disease: 10 points; kidney disease: 10 points 3. Signs: change of consciousness: 10 points; respiratory rate >30 times/min; systolic blood pressure <90 mmHg; Temperature <35 ℃ or ≥40 ℃: 15 points; pulse ≥125 times/min: 10 points 4. Laboratory inspection: pH of arterial blood< 7.35: 30 points; Blood urea nitrogen ≥11 mmol/L: 20 points; blood sodium <130 mmol/L: 20 points; blood glucose ≥14 mmol/L: 10 points; hematocrit <30%: 10 points; PO_2<60 mmHg: 10 points 5. Chest imaging: hydrothorax: 10 points	Low risk: level Ⅰ (≤50), level Ⅱ (51–70), level Ⅲ (71–90); treated in general ward Moderate risk: level Ⅳ (91–130); treated in ICU High risk: level Ⅴ (>130); treated in ICU	The scoring system is complex, with high sensitivity and specificity

CURB-65: C, confusion; U, uremia; R, respiratory rate; B, blood pressure.

PSI is recommended to assess disease severity to guide further treatment of the patient.

5.6. Differential diagnosis

Hospital-acquired pneumonia (HAP): The patient does not have pre-existing infection nor in the incubation period of infection at the admission, but the parenchymal inflammation in pulmonary initiated by bacteria, fungi, mycoplasma, viruses, protozoa, or other pathogens occurs after 48 hours since admission. There are some overlap or intersection between HAP and SAP to some extent, but the patient group of HAP is more extensive than SAP, and SAP refers to pneumonia in patients after stroke, regardless of whether they are admitted to the hospital or not. For hospitalized SAP patients, their disease onset time is earlier (can be within 48 hours after admission), and their time window for disease onset is shorter (only within 7 days after stroke onset).

Community-acquired pneumonia: Inflammation of infectious pulmonary parenchyma (including the alveolar wall, *i.e.*, pulmonary interstitium in a broad sense) occurs outside the hospital, including pneumonia which is caused by pathogens with a definite incubation period and onset within the average incubation period (within 48 hours) after admission. SAP refers to pneumonia in patients after stroke, but it is not associated with whether these patients are hospitalized. Some community-acquired pneumonia patients combined with acute stroke should be differentiated with SAP; their pathogenic characteristics may be quite different.

Ventilator-associated pneumonia: Pneumonia occurred after 48 hours of mechanical ventilation with endotracheal intubation or tracheotomy or within 48 hours of artificial airway removal. In cases of pulmonary infection after mechanical ventilated stroke patients, diagnosis and treatment should be carried out according to ventilator-associated pneumonia-related principles.

Chemical pneumonitis: Chemically toxic pneumonitis caused by inhalation of chemical irritant gases, liquids, or organic dust. Inhalation of large amounts of gastric contents can lead to chemical pneumonitis, but only when inhaling large quantities of substances with low pH value (pH< 2.5). The disease is characterized by sudden onset of dyspnea, hypoxemia, tachycardia, auscultation of extensive wheezing, and popping sounds in both lungs. Airway secretions

ofchemical pneumonitis patients are often thin, and infection-related laboratory tests and pathogen tests are negative.

6. Treatment and management

6.1. General treatment

1) Treatment of primary disease: Corresponding treatment for stroke, including treatment such as thrombolysis for ischemic stroke, hematoma clearance and intracranial pressure reduction for hemorrhagic stroke.

2) Diluting sputum and sputum drainage: Apply expectorants such as ambroxol hydrochloride, acetylcysteine, and carbocisteine, to dilute sputum.

3) Oral management: Strengthening oral care and comprehensive management (using normal saline, chlorhexidine or povidone-iodine mouthwash to wash or/and brush teeth, tongue surface, and other parts in oral cavity) can reduce the conditionally pathogenic bacteria in the oropharynx, avoid their displacement and translocation, and reduce or prevent the risk of lung infection.

4) Oxygen therapy and respiratory support: Monitoring the patients' blood oxygen saturation or blood gas analysis dynamically; blood oxygen saturation should be maintained at 94%, and the oxygen partial pressure should be maintained above 70 mmHg. Continues nasal catheter oxygen or high-flow nasal cannula oxygen therapy can be given when hypoxemia occurs. If conventional oxygen therapy is ineffective, give mechanical ventilation in case of severe hypoxemia or respiratory failure (partial oxygen pressure 60 mmHg). Note: stroke with consciousness disturbance is a contraindication of noninvasive mechanical ventilation.

5) Symptomatic treatment: When body temperature is above 38.5℃, give antipyretic or physical cooling and liquid supplement, relieve cough and asthma, as well as other symptomatic treatments.

Recommendation: Treat primary disease actively; strengthen oral care and comprehensive management in order to reduce or prevent the risk of lung infection.

6.2. Early nutrition support therapy

Give digestible and nutritious food or nutrient solution within 24 to 48 hours after disease onset to maintain water-electrolyte balance. Try to take food orally. If the patient is unable to take food by mouth, it is recommended to use continuous enteral nutrition, and it is more beneficial for patients in severe status to use this sequential treatment from initial enteral administration of short peptide preparation to whole protein preparation. If there is any contraindication of oral feeding or enteral nutrition, it is necessary to start parenteral nutrition within 3–7 days; If the patient can tolerate enteral nutrition, intravenous nutrition will not be applied. The energy supply for non-bedridden patients with mild symptoms is 25–35 kcal/kg/d, and that of patients with severe symptoms in the acute stress periodis 20-25 kcal/kg/d. For the patients without complications, the protein intake should be at least 1 g/kg/d; the fat intake should not exceed 35% of the total energy intake, and preparation rich in polyun saturated fatty acids should be applied. Dietary fiber intake should be as close as possible to 25–30 g/d. In order to avoid overfeeding, it is not recommended to give the total nutrition goal too early; the nutrition standard can reach total nutrition goal within 3-7 days[31].

Recommendation: Try to give food orally within 24–48 hours after stroke onset; If the patient is unable to take food by mouth, continuous enteral nutrition is recommended; If the patient can tolerate enteral nutrition, intravenous nutrition will not be applied.

Recommendation: If there is any contraindication of oral feeding or enteral nutrition, it is necessary to start parenteral nutrition within 3–7 days.

6.3. Anti-infective treatment

The principle of anti-infective treatment in SAP is the combination of empirical treatment and targeted anti-infective treatment. The initial empirical treatment should be timely and sufficient. At the same time, the pathogen examination should be highly valued, to obtain early and accurate evidence for targeted anti-infective treatment and optimizing the anti-infective treatment plan.

Empirical anti-infective treatment should be initiated within 6 hours of the pneumonia occurrence, or as soon as possible; otherwise, it will increase the mortality and prolong the hospitalization time of patients[32]. Intravenous preparation is recommended for the initial empirical anti-infective treatment. During this period, the medication should be adjusted in time on the basis of therapeutic response and etiology information. According to the CURB-65 or PSI scale, a combination of β-lactamswith β-lactamase inhibitor (for instance, amoxicillin/clavulanate, piperacillin/tazobactam, cefoperazone/sulbactam), cephamycins (for instance, cefoxitin, cefmetazole) and oxacephems (latamoxef or flomoxef) are preferred for patients with mild to moderate SAP. The course of treatment is 5–7 days generally. For patients who are assessed as severe SAP by CURB-65 or PSI scale, medications such as ertapenem, meropenem, imipenem, and biapenem are preferred; the avenge course of treatment is 7–10 days.

According to the risk factors assessment of drug-resistant bacteria or microbial culture, if the pathogen was assessed or confirmed to be methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Acinetobacter*, or carbapenem-resistant *Enterobacter* (CRE), the course of treatment should be prolonged to 10 to 21 days[5]. Vancomycin, norvancomycin, linezolid, orteicoplanin can be used in MRSA infection. Anti-*Pseudomonas carbapenems* (such as piperacillin/tazobactam, cefoperazone/sulbactam, ceftazidime,

cefepime, imipenem, meropenem) are recommended for the treatment of *Pseudomonas aeruginosa* infection, and combination of quinolones (ciprofloxacin, levofloxacin, for instance) or aminoglycosides are recommended if necessary. The drug resistance rate of *Acinetobacter* is generally high, so sulbactam preparations (such as cefoperazone/sulbactam, ampicillin/sulbactam), carbapenems, tigecycline, or polymyxins can be applied for treatment or even the combination treatment with the medications mentioned above. Ceftazidime/avibactam, polymyxin, or tigecycline can beapplied in CRE infected patients. Combination therapy can be considered when mixed anaerobic infections; and nitroimidazoles (such as levornidazole, metronidazole, tinidazole) are preferred for the treatment of anaerobic bacteria.

If the pathogen examinations confirm atypical pathogens (*Mycoplasma*, *Chlamydia*, or *Legionella*) infections in SAP patients, they can be treated with quinolones (such as levofloxacin and moxifloxacin), macrolides (such as azithromycin) or tetracycline antibiotics (such as doxycycline and minocycline). It should be noted that quinolones have central nervous system side effects, especially in patients with severe strokes, lesions adjacent to the cortex, or previous epilepsy history. More detail of the above content is shown in Table 3&4.

Efficacy evaluation and adjustment of the empirical anti-infective treatment plan: the therapeutic effect of the anti-infective treatment can be evaluated by leukocyte count, body temperature, blood oxygen saturation, and other indicators, and comprehensive analysis of above indicators can be used to guide clinical medication. Chest imaging often lags behind the improvement of clinical indicators. With effective treatment, SAP patients usually have significant clinical improvement within 48–72 hours, and the anti-infective treatment plan can be adjusted at this time. If the etiological examinations have been carried out, narrow-spectrum anti-infective drugs should be applied according to the etiological examination results, especially for the patients who initially used carbapenem broad-spectrum antibiotics. If the pathogen has been examined, a narrow-spectrum anti-infective treatment should be used after 72 hours according to the results of the pathogen examination, especially for patients who initially used broad-spectrum carbapenem antibiotics.

Recommendation: Initialize anti-infection therapy as soon as possible once the SAP diagnosis is established.

7. Prevention

For stroke patients who are estimated as high-risk and extremely high-risk by AIS-APS and ICH-APS predictive model, to strengthen SAP prevention is essential. Preventive measures include but are not limited to: In order to prevent cross-infection, medical staff should preform standardize hand washing before and after contact with patients, wear gloves and masks, wear isolation gowns if necessary, place patients with special infections in isolation rooms. This consensus emphasizes the following aspects considering the specific characteristics of SAP:

7.1. Semi–recumbent position

Research focusing on ICU patients with mechanical ventilation found that to elevate head-of-bed for 30º to 45º reduces the incidence of aspiration comparing with patients in the prone position[33]. Therefore, the semi-recumbent position (elevating head-of-bed for 30º to 45º) is preferred in stroke patients when without contraindications, such as pelvic and spinal diseases.

7.2. Swallowing function assessment and training

Hinchey *et al*[34] conducted a study on 2 532 patients with acute ischemic stroke, and they found that screening and training swallowing function reduced the incidence of pneumonia significantly ($P<0.01$). Early assessment, screening, and rehabilitation of swallowing function after acute stroke can help reduce pneumonia[24].

7.3. Airway management

In terms of nursing, it is necessary to turn over, clap back, change position (postural drainage of sputum), and perform suctioning regularly. Mechanical and physical methods such as the simulated cough machine can be selected to promote the discharge of respiratory tract secretions. In patients with severe hypoxemia (partial pressure of oxygen$\leqslant$60 mmHg) caused by sputum deposition, and can't be improved by oxygen inhalation through nasal catheter or mask, artificial airways can be placed in patients who need sputum drainage. Patients who are assessed as able to improve within 1–2 weeks can receive oral or nasal intubation; otherwise, they are given a tracheotomy (a sputum suction tube can be applied to suction the distal airway secretion, which is more conducive to sputum removal). Patients with sputum deposition or aspiration can be conducted suction by bronchoscope; the frequency of operation is adjusted according to the individual sputum volume of each patient, from once a day initially to once every other day or once a week as the sputum decreases. Argyle nasopharyngeal airway should be applied to keep the airway unobstructed in patients with upper airway obstruction caused by tongue falling backward and short neck with obesity. High-flow nasal cannula oxygen therapy has gradually become an important means of oxygen therapy and airway management because of its high flow of inhaled gas, good humidification, and a certain level of positive end-expiratory pressure[35]. It can be applied actively.

Table 3. Recommended empirical anti-infective treatment for stroke-associated pneumonia.

Pathogens	Recommend antibiotics		Antibiotic dosages
	Monotherapy	Combination therapy	
Methicillin sensitive pathogens *Staphylococcus aureus* *Streptococcus pneumoniae* *Haemophilus influenzae* Antibiotic sensitive *Enterobacter* *Escherichia coli* *Klebsiella pneumoniae*	β-lactams/β-lactamase inhibitor or cephamycins and oxacephems or moxifloxacin		Piperacillin/tazobactam 4.5 g/6–8 h Ampicillin/sulbactam 1.5 g/6–8 h Piperacillin/sulbactam 2.5 g/6 h Amoxicillin/clavulanate 1.2 g/6–8 h Cefoxitin 1–2 g/6–8 h Cefmetazole 1–2 g/6–8 h Cefatriaxone 2–4 g/d
Multidrug-resistant pathogens *Pseudomonas aeruginosa* Enterobacteriaceae producing ESBLs	β-lactams/β-lactamase inhibitor or anti-*Pseudomonas* cephalosporins or anti-*Pseudomonas* carbapenems		Cefoperazone/sulbactam 2–3 g/8–12 h Ceftazidime/avibactam 2.5 g/8 h Cefepime 2 g/8–1 h Ceftazidime 2 g/8 h Latamoxef 1–2 g/8 h Flomoxef 0.5–1 g/12 h Ertapenem 1 g/d Imipenem 0.5 g/6 h or 1 g/8 h Meropenem 1 g/8 h Biapenem 0.3–0.6 g/8–12 h Netilmicin 100–200 mg/8–12 h Etimicin 100 mg/8–12 h
Acinetobacter	Sulbactam preparation or carbapenem or tigecycline or polymyxin		
MRSA	Vancomycin or norvancomycin or linezolid		
CRE	Polymyxin or tigecycline or ceftazidine/avibactam		
Anaerobic bacteria Prevotella, clostridium	Levornidazole or metronidazole, tinidazole	Ceftriaxone+nitroimidazoles or Levofloxacin+nitroimidazoles or Levofloxacin+clindamycin or Anti-*Pseudomonas* cephalosporins+aminoglycosides	
Atypical pathogens	Levofloxacin or moxifloxacin or azithromycin		
Patient with severe conditions or sepsis	Non-anti-*Pseudomonas* carbapenem or anti-*Pseudomonas* carbapenem is preferred		
			Levofloxacin 500 mg/d Moxifloxacin 400 mg/d Azithromycin 250 mg/d, double the first dose Vancomycin 15 mg/kg/12 h Norvancomycin 400 mg/6 h or 800 mg/12 h Linezolid 600 mg/12 h Levornidazole 0.5 g/8–12 h Metronidazole 0.5 g/6–8 h Tinidazole 0. 8g/d Tigecycline 50 mg/12 h, double dose on the first day Polymyxin 2.5 mg/kg for first dose, after that 1.5 mg/kg/12 h

Note: In the initial empirical treatment, the medication should be adjusted correspondingly based on the etiological data and response to treatment. MRSA: methicillin-resistant *Staphylococcus aureus*; CRE: carbapenem-resistant *Enterobacter*. ESBLs: extended-spectrum β-lactamases; β-lactams/β-lactamase inhibitor: piperacillin/tazobactam, ampicillin/sulbactam, piperacillin/sulbactam, amoxicillin/clavulanate, cefoperazone/sulbactam, ceftazidime/avibactam; Anti-pseudomonas cephalosporins: such as cefoperazone/sulbactam, cefepime, ceftazidime; non-anti-pseudomonas carbapenem: ertapenem; anti-pseudomonas carbapenem: such as imipenem, meropenem, biapenem, panipenem; The above dosages are for patients with normal renal function; the dosages of netilmicin, etimicin, and vancomycin should be adjusted when renal function is abnormal.

Table 4. Risk factors for common drug-resistant bacterial infections.

Drug-resistant bacteria	Risk factors for drug-resistant bacterial infections
MRSA	MRSA colonization exists in the respiratory tract; therefore, the separation rate of MRSA in the medical unit is high
Pseudomonas aeruginosa	Impaired skin and/or mucosal barrier; receiving treatment with glucocorticoids or immunosuppressive agents, and with low immune function; chronic structural lung disease (bronchiectasis, COPD); severe pulmonary dysfunction; *etc.*
Acinetobacter baumannii	Severe underlying disease; *Acinetobacter baumannii* colonization
CRE	CRE colonization; used broad-spectrum antibiotics (such as carbapenem, fluoroquinolone, the third or fourth generation of cephalosporins, β-lactamase mixtures) in the past 90 d

MRSA: Methicillin-resistant *Staphylococcus aureus*; CRE: Carbapenem-resistant Enterobacter.

7.4. Feeding management

1) It is recommended to provide soft and thick food (such as rice paste, yogurt) for patients who take food orally, instead of viscous or thin liquid. Try to keep the chin down and the head to one side when eating; patients are encouraged swallowing a small amount of food each time, swallowing multiple times and coughing after each swallowing[36].

2) Confirming the position of feeding tube before feeding: Misplacement of the feeding tube, such as placement in the esophagus or misplacement into the bronchus, is one of the serious complications of feeding and can lead to pneumonia. X-ray examination is the gold standard to confirm the position of the feeding tube. In patients with coma, sedation, or weakness or disappeared cough reflexes, to conduct an X-ray examination before the first time of feeding is important. In the case of aspiration or suspected feeding tube displacement during feeding, the position of the feeding tube should be verified by X-ray examination again.

3) Post-pyloric feeding: In patients with pyloric obstruction, gastroparesis, esophageal reflux, or aspiration, using post-pyloric feeding may reduce the incidence of pneumonia[37].

4) It is recommended to provide nutritional support through percutaneous endoscopic gastrostomy or duodenostomy for those whose swallowing function isn't expected to recover within a long time (> 2–3 weeks)[38].

7.5. Application of medications

1) Reduce the use of glucocorticoids, proton pump inhibitors, H_2-receptor blockers, sedatives, and muscle relaxants[39].

2) Avoid prophylactic use of anti-infective medications: It is not recommended to apply anti-infective medications to prevent stroke-associated pneumonia in every country currently.

3) In Asian stroke patients, the use of an angiotensin-converting enzyme inhibitor (captopril) to control blood pressure can reduce the risk of aspiration pneumonia. It may work by increasing the substance Plevel, promoting cough, and improving swallowing reflex[40].

Recommendation: Elevating head-of-bed for 30º to 45º is an effective measure to prevent SAP.

Recommendation: Early assessment and training of swallowing function in stroke patients can reduce the incidence of SAP.

Recommendation: In patients with pyloric obstruction, gastroparesis, esophageal reflux or aspiration, the use of post-pyloric feeding can reduce the incidence of pneumonia.

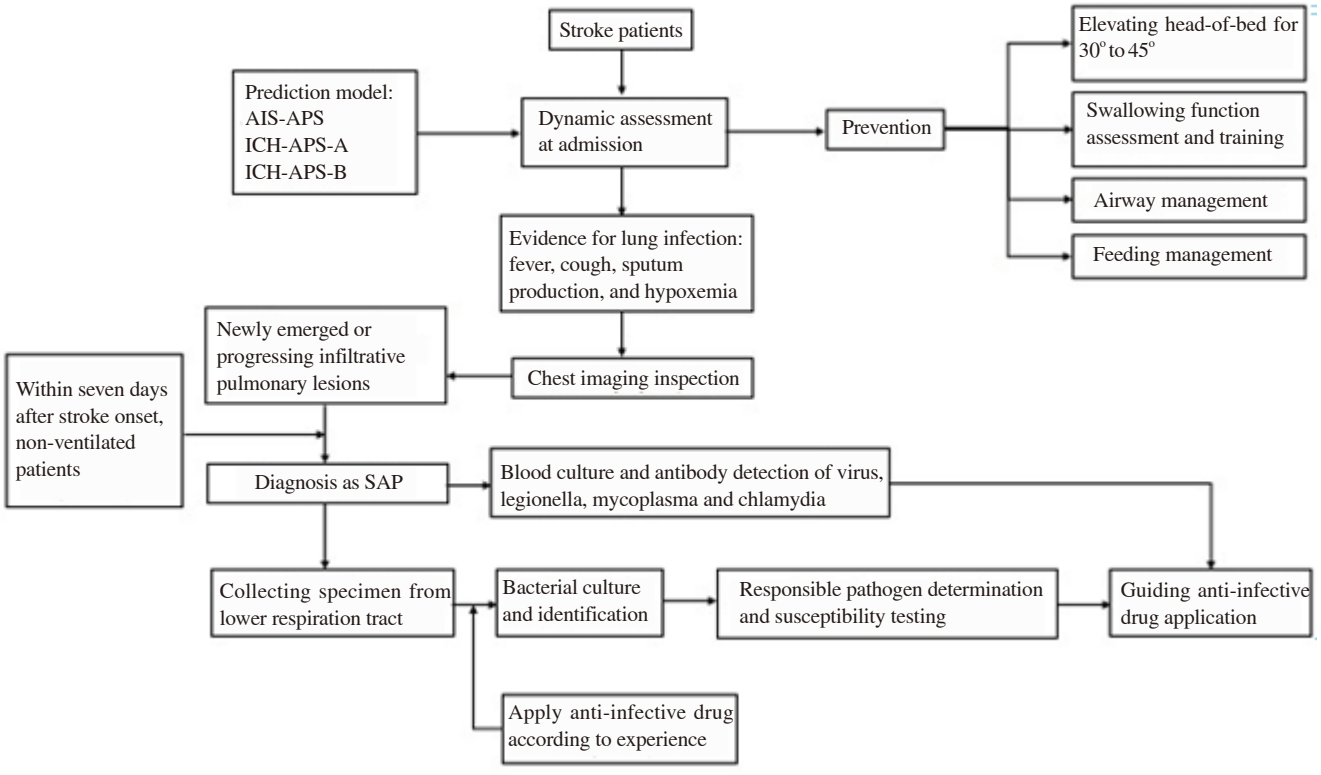

Figure 1. Flow chart for prevention, diagnosis, and treatment of stroke-associated pneumonia. SAP: stroke-associated pneumonia; AIS-APS: acute ischemic stroke-associated pneumonia score; ICH-APS: intracerebral hemorrhage-associated pneumonia score.

Appendix

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Conflicts of interest statement

The authors declare that there are no conflicts of interest.

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