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Clinical Management and Pathophysiological Foundations of Stroke-Associated Pneumonia: A Comprehensive Review

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Abstract— *Stroke-associated pneumonia (SAP) is a critical complication occurring within the first seven days following an acute stroke, significantly influencing mortality, morbidity, and the economic burden on healthcare systems. This review aims to provide a comprehensive guide for clinicians and researchers on the etiology, diagnosis, and management of SAP. A systematic evaluation of existing literature indicates that SAP affects approximately 8.6% to 14.3% of stroke patients, with higher rates observed in those with severe neurological deficits and dysphagia. The pathophysiology of SAP consists of stroke-induced immunodepression syndrome (SIDS) and mechanical risk factors, such as oropharyngeal aspiration. Diagnostic progress has been marked by the implementation of the Pneumonia in Stroke Consensus (PISCES) criteria, which distinguish between probable and definite cases based on radiological evidence. Despite the efficacy of early dysphagia screening in reducing pneumonia incidence, large-scale randomized trials such as PASS and STROKE-INF have demonstrated that preventive antibiotic therapy does not improve functional outcomes. Management strategies must therefore prioritize multidisciplinary care bundles, including standardized oral hygiene, early mobilization, and tailored antibiotic therapy guided by clinical stability rather than universal prophylaxis.*

Keywords— *Stroke-associated Pneumonia (SAP); Stroke-induced immunodepression; Post-stroke complications.*

I. INTRODUCTION

The post-acute course of patients experiencing a cerebrovascular event is often complicated by secondary medical conditions that extend beyond the primary neurological injury [1]. Among these, stroke-associated pneumonia (SAP) represents one of the most critical complications, acting as a major determinant of adverse outcomes during both the acute and subacute recovery periods[2]. First described by Hilker et al. in 2003, SAP encompasses a range of lower respiratory tract infections (LRTIs) that develop within the initial seven days following stroke onset [1]. Whereas infections were historically attributed to immobility-related factors, accumulating evidence now highlights a sophisticated neuro–immune mechanism in which cerebral injury induces systemic immunosuppression to mitigate neuroinflammation, inadvertently increasing susceptibility of the lungs to pathogenic invasion[3].

The epidemiological burden of SAP is considerable. Worldwide incidence estimates range from 8.6% to 21.4% among unselected stroke populations, with rates approaching 50% in vulnerable subgroups such as elderly patients and those with extensive brainstem involvement [1]. The development of SAP is linked to a threefold rise in 30-day mortality and independently predicts long-term functional impairment, markedly diminishing the likelihood of favorable neurological recovery [4]. In addition to its clinical consequences, SAP exerts a substantial economic impact; in the United Kingdom, the average cost per episode has been estimated at £14,371, largely driven by prolonged hospitalization—approximately seven additional days—and the need for comprehensive multidisciplinary management [4].

Despite growing scientific attention, important challenges in diagnosis and treatment remain unresolved. Infectious manifestations in acute stroke patients are frequently subtle and non-specific, while conventional chest radiography—the longstanding diagnostic reference—often produces inconclusive findings in immobilized individuals [2]. Moreover, the inability of large randomized trials to demonstrate benefit from prophylactic antibiotic use has prompted a strategic shift toward non-pharmacological prevention strategies and the development of more precise risk stratification tools [5]. Accordingly, this review consolidates current evidence on the underlying mechanisms, risk assessment, evolving diagnostic approaches, and multidisciplinary management of SAP, with the goal of enhancing clinical decision-making and improving patient survival outcomes.

II. REVIEW CONTENT

A. Epidemiological Profile and Prognostic Consequences

The reported prevalence of stroke-associated pneumonia (SAP) varies considerably, largely influenced by differences in applied diagnostic definitions and the demographic composition of the studied populations [1]. Large-scale bibliometric reviews encompassing almost two decades of literature have documented incidence rates ranging from 8.6% to 14.3% [1]. In contrast, studies focusing on patients with acute ischemic stroke (AIS) accompanied by dysphagia consistently demonstrate substantially higher rates, underscoring the critical role of compromised airway protection in this subgroup [3].

The onset of SAP follows a distinct temporal pattern, with the highest risk concentrated in the early phase of hospitalization [6]. Analyses derived from the VISTA database

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reveal that approximately two-thirds of post-stroke pneumonia cases emerge within the first seven days, with a median time to diagnosis of four days [6]. This period coincides with maximal neurological deficits, peak stroke-induced immunosuppression, and increased exposure to invasive interventions, including nasogastric tube placement [1].

In terms of prognosis, the development of SAP represents a severe adverse turning point in stroke recovery. Affected patients exhibit markedly higher in-hospital mortality, with rates approaching 45%, compared with approximately 12% among those without infectious complications [7]. Among survivors, SAP substantially impairs rehabilitation potential by promoting physical deconditioning, persistent fatigue, and a systemic inflammatory milieu that may amplify ongoing neuroinflammatory processes, ultimately limiting neuroplasticity and functional recovery [8].

B. Pathophysiological Basis: The Neuro–Immune Interface

The development of stroke-associated pneumonia (SAP) reflects a multifactorial process that extends beyond simple passive aspiration, arising from a coordinated breakdown of both local airway defences and systemic immune mechanisms [3]. This process is principally driven by two interrelated pathways: impairment of airway protection due to swallowing dysfunction and profound immune dysregulation known as stroke-induced immunodepression syndrome [3]. Following an acute cerebrovascular insult, the central nervous system initiates protective responses aimed at limiting neuroinflammation; however, these responses paradoxically suppress systemic immune function, rendering patients highly vulnerable to infection [3]. Communication between the injured brain and the immune system is mediated through activation of the sympathetic nervous system, parasympathetic pathways, and the hypothalamic–pituitary–adrenal axis. Sustained catecholamine release leads to a rapid decline in circulating lymphocytes, while vagally mediated cholinergic signaling suppresses pro-inflammatory cytokine production by pulmonary macrophages, weakening first-line antibacterial defenses [9]. Concurrently, stress-induced glucocorticoid secretion exacerbates lymphocytopenia and lowers the threshold for pulmonary infection, allowing even minimal bacterial exposure to precipitate severe pneumonia. In parallel, damage to cortical swallowing centers or the brainstem disrupts coordination of the oropharyngeal phase of deglutition, resulting in silent aspiration of colonized secretions [3]. Given that dysphagia affects approximately 50–65% of patients in the acute stroke phase and confers a 3- to 11-fold increased risk of pneumonia, the convergence of immune suppression and mechanical aspiration forms the central pathophysiological basis of SAP [10].

C. Diagnostic Standards and Terminology

One of the longstanding challenges in the clinical management of stroke-associated pneumonia (SAP) has been the absence of uniform terminology and diagnostic definitions. To address this issue, the Pneumonia in Stroke Consensus (PISCES) group introduced standardized diagnostic criteria adapted from the Centers for Disease Control and Prevention (CDC) framework [2]. These criteria clearly delineate SAP based on a defined temporal window, limiting the diagnosis to lower respiratory tract infections that develop within the first seven days following stroke onset [2].

The diagnostic framework incorporates both systemic and respiratory parameters. Systemic involvement is identified by the presence of at least one indicator such as fever, leukopenia, or leukocytosis [2]. Respiratory criteria require a minimum of two clinical features, including purulent sputum production, deterioration of cough, dyspnea, tachypnea, or evidence of worsening gas exchange [2]. While chest radiography remains the cornerstone imaging modality for SAP diagnosis, its sensitivity is often suboptimal during the early stages of infection [2]. Consequently, current recommendations advise repeat imaging after 48 hours when initial radiographic findings are inconclusive despite strong clinical suspicion [2]. In parallel, novel biomarkers such as the neutrophil-to-lymphocyte ratio (NLR) have gained attention for their potential to more accurately reflect the immunosuppressive milieu that characterizes SAP [11].

D. Risk Stratification and Predictive Models

Timely recognition of patients at elevated risk is a fundamental element in the prevention of stroke-associated pneumonia (SAP), prompting the development of several clinical scoring instruments to support risk assessment. Among these tools, the AIS-APS score is consistently regarded as one of the most robust predictors of SAP, particularly within ischemic stroke populations [12]. This model integrates variables such as age, National Institutes of Health Stroke Scale (NIHSS) score, Glasgow Coma Scale, sex, and the presence of dysphagia, yielding an area under the receiver operating characteristic curve (AUC) of approximately 0.79 [12].

The A2DS2 score is widely adopted because of its practicality and ease of use, incorporating age, atrial fibrillation, dysphagia, sex, and NIHSS score [12]. A threshold score of ≥ 5 is commonly used to identify high-risk patients and has been associated with a marked increase in in-hospital mortality [12]. In contrast, the ISAN score emphasizes pre-stroke functional independence alongside sex, age, and stroke severity as measured by NIHSS, demonstrating an exceptionally high negative predictive value approaching 100% [12].

E. Prevention of Stroke-Associated Pneumonia

Prevention represents the most effective approach to reducing the burden of stroke-associated pneumonia (SAP), and current evidence supports a comprehensive, multidisciplinary preventive framework rather than reliance on pharmacological prophylaxis [1]. Central to this strategy is the early identification and management of dysphagia, which constitutes the most impactful non-pharmacological intervention. Clinical guidelines recommend that all acute stroke patients be maintained on nil per os (NPO) status until a formal swallowing assessment is completed, preferably within the first 24 hours of hospital admission [10]. The use of standardized dysphagia screening tools has demonstrated high sensitivity in identifying aspiration risk, and the implementation of structured swallowing protocols has been associated with a reduction in

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pneumonia incidence of up to 40% [10]. In contrast, large randomized controlled trials have consistently shown that routine antibiotic prophylaxis does not confer meaningful clinical benefit. The PASS trial, which enrolled 2,550 patients randomized to receive ceftriaxone or standard care, failed to demonstrate improvement in three-month functional outcomes despite lowering overall infection rates [5]. Likewise, the STROKE-INF trial did not show significant reductions in pneumonia incidence or functional recovery [13]. Collectively, these findings underscore a paradigm shift away from indiscriminate antibiotic prevention toward targeted, non-pharmacological measures as the cornerstone of SAP prevention.

F. Treatment and Management of Stroke-Associated Pneumonia

Once stroke-associated pneumonia (SAP) is confirmed, prompt initiation of therapy is essential, with management strategies individualized according to the suspected causative pathogens and the patient's overall clinical condition [14]. Empirical antimicrobial selection should be informed by the timing of pneumonia onset. Early-onset SAP, occurring within the first 72 hours after stroke, typically necessitates coverage for community-acquired organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae* [2]. In contrast, late-onset SAP, developing between days four and seven, requires broader antimicrobial coverage targeting hospital-acquired pathogens, including *Pseudomonas aeruginosa* and members of the *Enterobacterales* group [14]. In this context, amoxicillin/clavulanic acid is commonly utilized as an empirical option due to its broad-spectrum activity [7]. Regarding treatment duration, accumulating evidence supports shorter antibiotic courses of five to seven days, as these have been shown to be non-inferior to prolonged therapy in patients who achieve clinical stability, while also offering advantages such as increased antibiotic-free days and a reduced risk of secondary antimicrobial resistance [15].

III. CONCLUSION

Stroke-associated pneumonia continues to represent a major challenge in the care and recovery of patients with acute stroke. This review highlights that although prophylactic antibiotic strategies have not shown meaningful improvements in functional outcomes, a carefully coordinated multidisciplinary approach can substantially reduce the risk of this complication. Optimal management relies on the early implementation of structured dysphagia assessments, strict mechanical oral care measures, and the use of validated risk prediction tools to enhance clinical surveillance. By moving away from indiscriminate preventive therapies toward targeted risk stratification and integrated rehabilitative strategies, clinicians can meaningfully enhance both survival rates and long-term functional autonomy among stroke survivors.

APPENDIX

TABLE I. Summary of Major SAP Clinical Trials

Trial Name	Primary Intervention	Population	Major Finding
PASS (2015)	Ceftriaxone (2g, 4 days)	General stroke	No functional benefit [5].
STROKE-INF (2015)	Various antibiotics	Dysphagic stroke	No reduction in pneumonia [13].
PRECIOUS [2024]	Metoclopramide	Elderly (NGT)	No reduction in pneumonia [6]

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REFERENCES

[1] R. Hilker, C. Poetter, N. Findeisen, J. Sobesky, A. Jacobs, M. Neveling, W. D. Heiss, "Nosocomial pneumonia after acute stroke: implications for neurological intensive care medicine," Stroke, vol. 34, no. 4, pp. 975-981, 2003.

[2] C. J. Smith, A. K. Kishore, A. Vail, A. Chamorro, J. Garau, S. J. Hopkins, M. Di Napoli, Lalit Kalra, Peter Langhorne, Joan Montaner, Christine Roffe, Anthony G. Rudd, Pippa J. Tyrrell, Diederik van de Beek, Mark Woodhead, Andreas Meisel, "Diagnosis of stroke-associated pneumonia: recommendations from the pneumonia in stroke consensus group," Stroke, vol. 46, no. 8, pp. 2335-2340, 2015.

[3] S. Hoffmann, H. Harms, L. Ulm, Darius G. Nabavi, Bruno-Marcel Mackert, Ingo Schmehl, Gerhard J. Jungehulsing, Joan Montaner, Alejandro Bustamante, Marcella Hermans, Frank Hamilton, Jos Göhler, Uwe Malzahn, Carolin Malsch, Peter U. Heuschmann, Christian Meisel, Andreas Meisel, "Stroke-induced immunodepression and dysphagia independently predict stroke-associated pneumonia – The PREDICT study," J. Cereb. Blood Flow Metab., vol. 37, no. 12, pp. 3671-3682, 2017.

[4] I. L. Katzan, N. V. Dawson, C. L. Thomas, M. E. Votruba, R. D. Cebul, "The cost of pneumonia after acute stroke," Neurology, vol. 68, no. 22, pp. 1938-1943, 2007.

[5] W. F. Westendorp, J. D. Vermeij, E. Zock, A. J. Quiroz, P. J. Nederkoorn, D. J. Dippel, H. B. van der Worp, D. van de Beek, "The Preventive Antibiotics in Stroke Study (PASS): a pragmatic randomised open-label masked endpoint clinical trial," Lancet, vol. 385, no. 9977, pp. 1519-1526, 2015.

[6] W. M. Sluis, J. C. de Jonge, Hendrik Reinink, Lisa J. Woodhouse, Willeke F. Westendorp, Philip M. Bath, Diederik van de Beek, H. Bart van der Worp, "Metoclopramide to Prevent Pneumonia in Patients With Stroke and a Nasogastric Tube: Data From the PRECIOUS Trial," Stroke, vol. 55, no. 10, pp. 2515-2522, 2024.

[7] J. Faura, Alejandro Bustamante, Francesc Miro, Joan Montaner, "Stroke-associated pneumonia according to mCDC criteria: impact on prognosis and antibiotic therapy," Front. Neurol., vol. 15, p. 1358628, 2024.

[8] R. J. Tinker, Craig J. Smith, C. Heal, Lalit Kalra, "Predictors of mortality and disability in stroke-associated pneumonia," Acta Neurol. Belg., vol. 121, no. 2, pp. 379-385, 2021.

[9] Jing Bai, Yusheng Zhao, Zihe Wang, Peng Qin, Jingjie Huang, Yupei Cheng, Chaoran Wang, Yuyan Chen, Longxiao Liu, Yuxing Zhang, Bangqi Wu, "Gut microbiota dysbiosis drives stroke-associated pneumonia: mechanisms and targeted therapeutic strategies," The Neurologist, vol. 30, no. 4, pp. 237-250, 2025.

[10] S. A. Eltringham, K. Kilner, M. Gee, K. Sage, B. D. Bray, Craig J. Smith, S. Pownall, "Impact of dysphagia assessment and management on risk of stroke-associated pneumonia: a systematic review," Cerebrovasc. Dis., vol. 46, no. 3-4, pp. 99-107, 2018.

[11] K. Nam, T. J. Kim, J. S. Lee, S. K. Kwon, H. J. Han, Y. S. Park, S. B. Ko, B. W. Yoon, "High neutrophil-to-lymphocyte ratio predicts stroke-associated pneumonia," Stroke, vol. 49, no. 8, pp. 1886-1892, 2018.

[12] Benjamin Hotter, Sarah Hoffmann, Lena Ulm, Christian Meisel, Alejandro Bustamante, Joan Montaner, Mira Katan, Craig J. Smith, Andreas Meisel, "Predictive value of scoring systems for stroke-associated pneumonia," Stroke, vol. 52, no. 1, pp. 120-129, 2021.

[13] Lalit Kalra, S. Irshad, J. Hodsoll, D. Smithard, D. Manawadu, "Prophylactic antibiotics after acute stroke for reducing pneumonia in patients with dysphagia (STROKE-INF): a prospective, cluster-

randomised, open-label, masked endpoint, controlled clinical trial," Lancet, vol. 386, no. 10006, pp. 1835-1844, 2015.

[14] A. K. Kishore, A. Vail, A. R. Jeans, Angel Chamorro, Mario Di Napoli, Lalit Kalra, Peter Langhorne, Christine Roffe, Willeke Westendorp, Paul J. Nederkoorn, Craig J. Smith, "Antibiotic treatment for pneumonia complicating stroke: Recommendations from the pneumonia in stroke consensus (PISCES) group," Eur. Stroke J., vol. 4, no. 4, pp. 318-328, 2019.

[15] T. S. Kadyrov, E. M. Mamytova, A. D. Mamytova, A. U. Toktomametova, M. A. Batyrov, N. T. Dzhaparalieva, "Etiopathogenesis, diagnosis and treatment strategies for stroke-associated pneumonia," Heart Vessels Transplant., vol. 8, no. 2, pp. 293-301, 2024.

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