Original Article

Epidemiologic Features, Risk Factors, and Outcomes of Respiratory Infection in Patients with Acute Stroke

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Abstract

Objective: The objective of this study is to explore risk factors for stroke-associated pneumonia (SAP) and their impact on prognosis. **Materials and Methods:** The data collected from a retrospective review of 257 patients with acute cerebral infarction between January 2014 and December 2016 were included in this study. Data were collected for clinical, demographic, and coexisting parameters. Univariate and multivariate logistic regression analyses were performed. **Results:** Elderly age (odds ratio [OR]: 1.096, 95% confidence interval [CI]: 1.023–1.174), dysphagia (OR: 2.805, 95% CI: 1.614–4.875), and long-term bedridden status (OR: 120.425, 95% CI: 29.689–488.466) were significantly associated with SAP. Among these risk factors, long-term bedridden status had the highest prognostic value (area under the curve = 0.908) for developing SAP. Furthermore, pneumonia, in turn, strongly predicted poor prognosis at discharge and after 3 years. **Conclusions:** Pneumonia seems to be a major complication in stroke patients. A better understanding of its risk factors is important for prevention and early recognition. Further studies are needed to clarify the optimal preventive treatment for SAP patients.

Keywords: Dysphagia, pneumonia, stroke

Introduction

Poststroke infection is one of the most common complications, with 30%–65% of patients diagnosed in the postacute phase. Pneumonia and urinary tract infections are the most frequent sources.[1] Stroke-associated pneumonia (SAP) is the leading cause of death in the 1st month after stroke, accounting for approximately 30% of the 30-day mortality.[2] Furthermore, apart from increasing the length and cost of hospital stays, SAP is also established as an independent risk factor for adverse outcomes.[3-5] Therefore, the ability to identify the risk factors of SAP could aid in targeting preventive and therapeutic interventions to improve patient outcomes in daily clinical practice and stroke logistics and to facilitate more appropriate patient selection for clinical trials.

A diverse set of risk factors that may predispose an individual to early SAP was identified in recent studies, including older age, severity of neurologic impairment, dysphagia, and diabetes mellitus.[6-9] However, despite the high level of significance of SAP, risk factors for developing SAP have not been fully elucidated. In addition, the impact of SAP on long-term outcomes is still uncertain. Therefore, in this study, we focused on clinical data from 257 stroke patients in our Department of Neurology, assessing a sample with a comprehensive series of indicators, including sex, age, long-term bedridden status, invasive operation, lesion location, scores of consciousness, and neurological function and coexisting conditions. This study further explored the associations between these risk factors and patient outcomes, aiming to determine independent high-risk factors for SAP and to potentially lower the occurrence of nosocomial infection.

Materials and Methods

Subjects

Our study included 257 patients with acute cerebral infarction between January 2014 and December 2016. Patient ages ranged from 45 to 93 years (mean ± standard deviation [SD], 72 ± 10.8 years). There were 155 males and 102 females. Diagnosis based on clinical features supported by brain computed tomography (CT) or magnetic resonance imaging scanning had to be the vascular event and not secondary complications. Patients were excluded due to the following reasons: (1) patients had a diagnosis other than stroke, (2) patients were treated for > 24 h in a referring hospital after the onset of a qualifying vascular event, (3) patients with a stay shorter than 72 h, (4) patients regarded as having poor prognosis on admission and whose treatment was restricted to palliative care, (5) patients with pulmonary infections before the onset of stroke, and (6) patients preventively administered antibiotics before the onset of stroke.

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Bedside swallowing assessment

Bedside swallowing function was assessed by the modified water swallow test recommended by the medical examination guidelines issued by the Japan Stroke Society.[10] The modified water swallow test was performed by pouring 3 mL of chilled water into the oral vestibule of the patients and then instructing them to swallow, if possible; then, the patient was given more water and was asked to swallow again. The worst swallowing attempt was evaluated, and a score over 2 was considered abnormal.

Activity of daily living assessment

Activity of daily living (ADL) was scored according to the modified Barthel index, which included ten items and could be divided into four functional grades (0, 5, 10, and 15) according to whether the patients needed help or not.[11] The total score of ADL was 100; the higher the score was, the greater the independence of the patient.

Collection of clinical data

In addition to the bedside swallow assessment and ADL assessment scores, the following clinical data were collected from medical records: (1) demographics: age and gender; (2) clinical characteristics: invasive operation and long-term bedridden status; (3) lesion location (supratentorial, infratentorial, and supra- and infratentorial); (4) scores reflecting consciousness and neurological function: the Glasgow Coma Scale (GCS) and the National Institute of Health Stroke Scale (NIHSS); and (5) coexisting conditions: heart failure, coronary artery disease, hypertension, diabetes mellitus, atrial fibrillation, renal dysfunction, hypokalemia, hypercholesteremia, hyperlipidemia, hypoproteinemia, and malnutrition. In addition, patients were followed up at 3 months after their stroke to determine survival and/or the development of pneumonia after discharge from the hospital.

Diagnosis of stroke-associated pneumonia

Pneumonia was diagnosed by the clinician team in close collaboration with the infection control practitioner based on the presence of respiratory tract infection symptoms or signs (cough, fever, crackles upon lung auscultation, and purulent tracheal secretion), laboratory test results (increased inflammatory markers and reduced oxygen saturation), microbiologic evidence (tracheal specimens and blood cultures), and typical radiological evidence (chest X-ray or CT). SAP was considered if it presented during the patients' hospitalization for their stroke.

Statistical analysis

The data were analyzed using the Statistical Product and Service Solutions software (SPSS, version 20.0, Chicago, IL, USA). The results are shown as the mean ± SD for the number of assays indicated and as the count (percentage) for categorical variables. *t*-tests or Mann–Whitney U-tests were used for univariate analysis of continuous variables, the Chi-square test was used for univariate analysis of categorical variables, and binary logistic regression analysis was used for multivariate analysis. Receiver operator characteristic (ROC) curves were used to assess the predictive accuracy of the parameters that were statistically significant in univariate and multivariate analysis [Figure 1]. Significance was set at a $P < 0.05$.

Results

Infection characteristics and patient clinical data

Of 257 patients included in the study, 107 (41.6%) acquired an infection, with the lungs being by far the most frequent site of infection (97, 90.7%), followed by the urinary tract (10, 9.3%) (3 patients had both respiratory and urinary tract infections). In 41.6% of the infections, a causative organism was identified, with Gram-negative (74.8%) *Klebsiella pneumoniae* being the most common, accounting for 31.8% of all microorganisms [Table 1].

The population used in the SAP study (median age ± SD: 72 ± 10.8 years) consisted of 148 (59.9%) males and 99 (40.1%) females, of which 97 patients were diagnosed with SAP (median age ± SD: 76 ± 9.5 years), consisting of 59 (60.8%) males and 38 (39.2) females. Of the 97 SAP patients, 51 (52.6%) acquired an infection within the first 7 days after stroke onset. All recorded patients fulfilled the inclusion criteria and thus were eligible for this analysis. The clinical characteristics of the patients are summarized in Table 2.

Risk factors for stroke-associated pneumonia

We further investigated which parameters were associated with an increased risk of acquiring SAP. In a univariate analysis, the demographic parameter (age), clinical parameters (invasive operation and long-term bedridden status), neurologic parameters (GCS, NIHSS, water swallow test score, and ADL score), and several comorbidities (heart failure, hypokalemia, and hypoproteinemia) were associated with the development of SAP ($P < 0.05$) [Table 3]. In multivariate analysis, age (odds ratio [OR]: 1.096, 95% confidence interval [CI]: 1.023–1.174), long-term bedridden status (OR: 120.425, 95% CI: 29 689–488.466), and water swallow test score (OR: 2.805, 95% CI: 1.614–4.875) were independent predictors of acquiring SAP [Table 4]. Surprisingly, the lesion location of the stroke was not significant in either the univariate or the multivariate analysis, and baseline neurological parameters (GCS, NIHSS, and ADL score) were not associated with increased risk of SAP in multivariate analysis [Tables 3 and 4].

The predictive power of age, long-term bedridden status, and water swallow test score was determined by ROC curve analysis. The results demonstrated that long-term bedridden status had the highest prognostic value (area under the curve [AUC] = 0.908), followed by the water swallow test score (AUC = 0.825) and age (AUC = 0.687), indicating that these three risk factors are good predictors for the development of pneumonia during hospitalization in patients with stroke.

Table 1: Infection characteristics

Infection	*n* (%)
Focus (total)	107
Pneumonia	97 (90.7)
Urinary tract infection	10 (9.3)
Infectious diarrhea	1 (0.9)
Bacteremia	2 (1.9)
Defined microorganism	
Gram positive	26 (24.3)
Streptococcus viridans	5 (4.7)
Staphylococcus aureus	16 (15.0)
Staphylococcus saprophyticus	2 (1.9)
Staphylococcus hominis	2 (1.9)
Staphylococcus epidermidis	1 (0.9)
Gram negative	80 (74.8)
Klebsiella pneumoniae	34 (31.8)
Pseudomonas aeruginosa	12 (11.2)
Acinetobacter baumannii	18 (16.8)
Lofel acinetobacter	4 (3.7)
Haemophilus parainfluenzae	2 (1.9)
Escherichia coli	2 (1.9)
Others	8 (7.4)
Fungus	10 (9.3)
Candida albicans	10 (9.3)

Table 2: Baseline characteristics of respiratory infection

Clinical data	Value (*n* or mean±SD)
Demographics	
Gender (*n*)	
Male	144
Female	103
Age (year)	72±10.8
Clinical characteristics (*n*)	
Invasive operation	60
Long-term bedridden	86
Score of consciousness and neurological function	
GCS score at admission	13.3±2.3
NIHSS score at admission	5.6±6.5
Water swallow test score at admission	2.0±1.7
ADL score at admission	72.9±23.7
Coexisting conditions (*n*)	
Heart failure	17
Coronary heart disease	9
Hypertension	206
Diabetes mellitus	99
Atrial fibrillation	39
Renal dysfunction	25
COPD	3
Hypokalemia	23
Hypercholesteremia	19
Hyperlipidemia	63
Hypoproteinemia	28
Malnutrition	16

GCS=Glasgow Coma Scale, NIHSS=National Institute of Health Stroke Scale, ADL=Activity of daily living, COPD=Chronic obstructive pulmonary disease, SD=Standard deviation

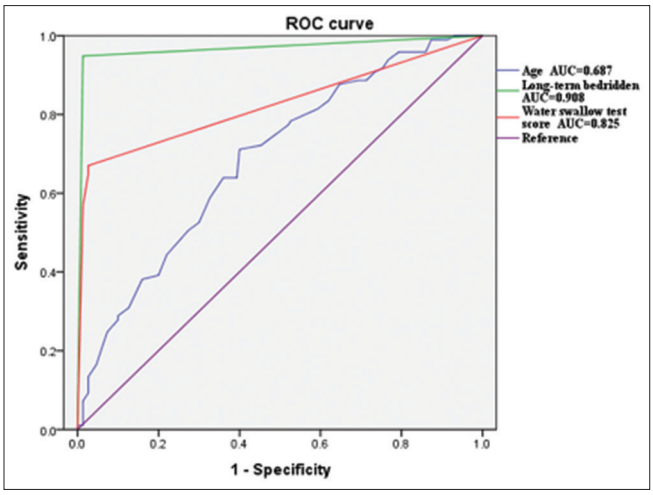

Figure 1: Receiver operating characteristic curves of age, long-term bedridden status and water swallow test score for the prediction of stroke-associated pneumonia

Association of pneumonia with outcome at discharge and after 3 years

As pneumonia can be regarded as a major complication in stroke patients, we correlated its occurrence with outcome at discharge and after 3 years. Unfavorable outcomes were defined as re-hospitalization or death. In this study, SAP patients had significantly worse outcomes at discharge ($P = 0.0033$) and after 3 years ($P < 0.0001$). Furthermore, we analyzed the association between pneumonia and mortality after 3 years, and the results showed that patients with pneumonia had an increased mortality rate after 3 years ($P < 0.0001$) [Table 5].

As demonstrated in Table 5, pneumonia was closely related to poor prognosis. To further explore risk factors of unfavorable outcomes, all demographics, coexisting conditions and clinical characteristics listed in Table 2 for stroke patients with pneumonia, were analyzed for their association with inhospital mortality and unfavorable outcomes. Invasive operation, heart failure, and atrial fibrillation were significantly correlated with inhospital mortality in univariate analyses, while only heart failure was significant in the multivariate analysis [Table 6]. Similarly, age, heart failure, and atrial fibrillation were significantly associated with unfavorable outcomes after 3 years, and atrial fibrillation was an independent predictor according to multivariate analysis [Table 7].

Discussion

Stroke is a global health problem and is a major cause of death and disability in the adult population. One of the most common complications of stroke is respiratory infection, which can lead to considerably higher health-care costs and adverse outcomes. In this study, we explored a comprehensive range of risk factors implicated in the development of SAP. We included demographic, clinical, and neurologic factors and coexisting conditions. Of the ten factors (age, invasive

Table 3: Univariate analysis of variables associated with respiratory infection after stroke

Variables	No infection (%)	Infection (%)	*P*
Demographics			
Gender (male)	91 (61.7)	53 (54.6)	0.8533
Age (year ≥72)	60 (40.0)	68 (70.1)	<0.0001
Clinical characteristics			
Invasive operation	11 (7.3)	49 (50.5)	<0.0001
Long-term bedridden	6 (4.0)	80 (82.5)	<0.0001
Score of consciousness and neurological function at admission			
GCS score (<13)	7 (4.7)	45 (46.4)	<0.0001
NIHSS score (≥5)	24 (16.0)	60 (28.6)	<0.0001
Water swallow test score (>2)	4 (2.7)	65 (67.0)	<0.0001
ADL score (<73)	125 (83.3)	62 (63.9)	0.0005
Lesions			
Supratentorial lesion	115 (76.7)	78 (80.4)	0.5310
Infratentorial lesion	18 (12)	9 (9.3)	0.5394
Supra- and infratentorial lesion	17 (11.3)	20 (20.6)	0.0667
Coexisting conditions			
Heart failure	5 (3.3)	12 (12.3)	0.0061
Coronary heart disease	5 (3.3)	4 (4.1)	0.7461
Hypertension	127 (84.7)	79 (81.4)	0.5061
Diabetes mellitus	69 (46.0)	30 (30.9)	0.3993
Atrial fibrillation	22 (14.7)	17 (17.5)	0.5473
Renal dysfunction	12 (8.0)	13 (13.4)	0.1692
COPD	1 (0.6)	2 (2.1)	0.3283
Hypokalemia	9 (6)	14 (14.4)	0.0259
Hypercholesteremia	10 (6.7)	9 (9.3)	0.4519
Hyperlipidemia	41 (27.3)	22 (22.7)	0.4126
Hypoproteinemia	4 (2.7)	24 (24.7)	<0.0001
Malnutrition	11 (7.3)	5 (5.2)	0.4969

GCS=Glasgow Coma Scale, NIHSS=National Institute of Health Stroke Scale, ADL=Activity of daily living, COPD=Chronic obstructive pulmonary disease

Table 4: Logistic regression modeling of risk factors for respiratory infection after stroke

Variables	OR	95% CI	*P*
Age	1.096	1.023–1.174	0.009
Invasive operation	4.225	0.775–23.020	0.096
Long-term bedridden	120.425	29.689–488.466	<0.001
GCS score	0.719	0.344–1.503	0.380
NIHSS score	0.815	0.599–1.111	0.815
Water swallow test score	2.805	1.614–4.875	<0.001
ADL score	0.997	0.926–1.073	0.929
Heart failure	1.659	0.230–11.960	0.616
Hypokalemia	1.640	0.222–12.101	0.627
Hypoproteinemia	0.945	0.811–1.100	0.463

GCS=Glasgow Coma Scale, NIHSS=National Institute of Health Stroke Scale, ADL=Activity of daily living. OR=Odds ratio, CI=Confidence interval

Table 5: Univariate analysis between respiratory infection and outcome at discharge and after 3 years

Variables	No infection (%)	Infection (%)	*P*
Inhospital mortality	0	6 (6.2)	0.0033
Unfavorable outcome after 3 years	45 (30.0)	56 (57.7)	<0.0001
Mortality after 3 years	14 (9.3)	32 (33.0)	<0.0001

operation, long-term bedridden status, GCS, NIHSS, water swallow test score, ADL score, heart failure, hypokalemia, and hypoproteinemia) that were identified as being associated with an increased risk of developing SAP, three (age, long-term bedridden status, and water swallow test score) were confirmed as independent predictors by multivariate analysis. Then, ROC curve analysis further proved that the three indicators are good prognostic predictors for SAP.

Our findings are important because we were able to confirm two predictive factors (age and water swallow test score) reported in previous studies.[12] It is important to note that some of the variation in findings among different studies (such as the lesion location of stroke and diabetes mellitus) can be attributed to differences in study design. In our study, we observed that SAP occurred in 65 (94.2%) of the 69 patients with abnormal initial water swallow test scores (>2). In contrast to this, SAP occurred in 32 (18.0%) of the 178 patients with normal initial water swallow test scores (≤2). Previous studies suggested that about 37%–74% patients with acute stroke had different degrees of dysphagia, and the incidence rate of aspiration could increase by 11.5 times. Aspiration pneumonia from dysphagia following stroke presents significant mortality and morbidity in that population. In addition, patients with dysphagia often need invasive

Table 6: Univariate and multivariate analysis of variables significantly associated with mortality at discharge

Variable	Univariate			Multivariate		
	Survivors (%)	Nonsurvivors (%)	*P*	OR	95% CI	*P*
Heart failure	6 (6.6)	6 (100)	<0.0001	32.360	2.414–433.820	0.009
Atrial fibrillation	12 (13.2)	5 (83.3)	0.0005	NS		
Invasive operation	43 (47.3)	6 (100)	0.0267	NS		

OR=Odds ratio, CI=Confidence interval, NS=Not significant

Table 7: Univariate and multivariate analysis of variables significantly associated with unfavorable outcome after 3 years

Variable	Univariate			Multivariate		
	Accept outcome (%)	Unfavorable outcome (%)	*P*	OR	95% CI	*P*
Age (>72)	23 (56.1)	45 (80.4)	0.0135	NS		
Heart failure	1 (2.4)	11 (19.6)	0.012	NS		
Atrial fibrillation	2 (4.9)	15 (26.8)	0.006	4.028	1.491–10.884	0.006

OR=Odds ratio, CI=Confidence interval, NS=Not significant

procedures, which also increase the risk of SAP.[2,12] Therefore, it is important to stress the necessary of swallow evaluation in acute stroke and the need to take precautions to reduce the rate of respiratory infection after stroke, such as reducing the number of invasive operations, strictly complying with aseptic requirements during operation, and providing enteral nutrition early for patients with dysphagia or aspiration.[13]

Stroke patients with severe leg paralysis are often bedridden in the acute and subacute phase, which increases the risk of hypostatic pneumonia and even multiple organ dysfunction, especially in elderly patients. Our results showed that 80 (82.5%) SAP patients had long-term bedridden status, which had the highest prognostic value (AUC = 0.908) for developing SAP. Thus, it is necessary to reduce the bedridden time as much as possible, to ensure appropriate positioning, to turn the body, and to improve the patients' daily living activities.

In addition to exploring risk factors for developing SAP, we also identify associations with pneumonia and outcomes at discharge and after 3 years. Our results showed that pneumonia is closely related to poor prognosis, and thus, we further explored risk factors for unfavorable outcomes in patients with SAP: heart failure and atrial fibrillation were independent predictors for mortality at discharge and unfavorable outcomes after 3 years, respectively. Therefore, regarding the impact of pneumonia on outcomes, the hypothesis was that pneumonia was a major complication and cause of stroke mortality, and this hypothesis was impressively underlined by a nearly quadruple mortality rate after 3 years (33% and 9.3%) in stroke patients with and without pneumonia, respectively.

The current study has several strengths. We believed it to be a comprehensive cohort study with the specific aim of identifying risk factors for SAP and providing ongoing data by means of follow-up for 3 months. The assessments of respiratory infection status were blinded to other clinical characteristics. However, the study had several limitations. First, our sample size was limited to 257 patients (150 stroke patients without infection, 97 stroke patients with respiratory infection, and 10 stroke patients with other organ infection) in one institution, and our findings will need to be validated in a larger population and multiple institutions. Second, as our data for identifying respiratory infection in patients after discharge from hospital were based on telephone inquiries and questionnaires, they were not as robust as those included in the hospital that were based on well-recognized criteria. Finally, we were also unable to perform critical assessments of swallowing impairments during the follow-up period.

Conclusions

In our study, we found that elderly age, dysphagia, and long-term bedridden status were significantly associated with pneumonia after stroke. Pneumonia, in turn, strongly predicted poor prognosis at discharge and after 3 years. These findings open new avenues in the management of patients with stroke who are at risk of developing pneumonia.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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