

Risk Factors for Stroke-associated Pneumonia in a Chinese Population: a Prospective Cohort Study

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Abstract: Background-Pneumonia is a major cause of in-hospital morbidity and mortality in acute stroke population. We aimed to identify the risk factors related to stroke-associated pneumonia (SAP) in a Chinese stroke population. **Materials and Methods-**We prospectively investigated SAP for all the consecutive acute ischemic stroke patients admitted within 7 days from onset to hospital during Jan 2009 to Dec 2012. Data were from the database of the Henan Province Stroke Registry. Univariate and multivariable logistic regression analysis were used to assess the association of demographics, co-morbidities, and clinical characteristics with SAP. **Results-**Among 1142 eligible patients, the mean age was 60.3 ± 13.1 years, and 36.7% of the patients were female. The overall in-hospital SAP was 18.8%. Subjects who developed pneumonia were older (mean \pm SD age, 65.6 ± 11.9 vs. 59.1 ± 13.1 years), had higher modified National Institutes of Health Stroke Scale scores (Median, 9 vs. 3), and a longer length of stay (22.4 ± 12.3 vs. 14.0 ± 7.4 days). After adjusting for potential confounders, age (OR, 1.02; 95%CI, 1.00-1.04), dysphagia (OR, 11.76; 95%CI, 7.21-19.19), admission NIHSS score (OR, 1.11; 95%CI, 1.0-1.16) and length of stay (OR, 1.07; 95%CI, 1.05-1.10) were associated with a higher risk of SAP. **Discussions-**SAP is associated with older age, dysphagia, admission NIHSS score and length of stay. Simple assessment of these variables could be used to identify patients at high risk of developing pneumonia after stroke.

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Key words: risk factor; stroke-associated pneumonia; acute ischemic stroke

1. Introduction

Stroke is the second leading cause of death worldwide,¹ and is the first leading cause of death in China.² Pneumonia is a major cause of in-hospital morbidity and mortality in acute stroke population,³⁻¹² and attributes to increase the length of hospital stay and hospitalization cost.¹³⁻¹⁵

Some studies have identified several factors being independently associated with stroke-associated pneumonia (SAP) in acute stroke, such as older age, stroke severity, dysphagia, impaired level of consciousness, diabetes mellitus, stroke subtypes and so on.^{12, 15-19} However, these studies were limited to based on either retrospective data collection or small cohort. We aimed to prospectively identify the risk factors related to SAP in a Chinese stroke population, and moreover to explore its influence on the length of stay.

2. Materials and Methods:

2.1 Patients selection:

Patients included in this study were from the database of the Henan Province Stroke Registry (HNSR), which is a prospective single-center hospital-based cohort study of consecutive patients who had transient ischemic attack (TIA) and acute ischemic stroke (stroke onset to hospital ≤ 7 days).²⁰

Detailed baseline data were registryed prospectively using paper case report forms designed specifically for this study. Standardized case report forms were used for data collection in the HNSR cohort,

and were completed by neurologists with similar levels of training and experience. The including criteria were listed in the following: (1) age ≥ 18 years; (2) hospitalized with a primary diagnosis of acute ischemic stroke according to World Health Organization criteria²¹; (3) stroke confirmed by CT or MRI.

The study was approved by the central Institutional Review Board at the first affiliated hospital of Zhengzhou university. All patients or their designated relatives were informed about study participation, and informed written consent was obtained.

2.2 Data definitions:

The following variables were analyzed for the present study: (1)demographics (age and sex); (2)stroke risk factors: hypertension (history of hypertension or antihypertensive medication use), diabetes mellitus (history of diabetes mellitus or antidiabetic medication use), dyslipidemia (history of dyslipidemia or lipid-lowering medication use), atrial fibrillation (history of AF or documentation of AF at admission), coronary heart disease, history of stroke and TIA, current smoking, and excess alcohol consumption (≥ 2 standard alcohol beverages per day); (3)admission stroke severity based on National Institutes of Health Stroke Scale score (NIHSS); (4)symptom of dysphagia or abnormal of swallowing water test; (5)stroke subtype: according to the Oxfordshire Community Stroke Project criteria (OCSP);²² (6)complications: pneumonia; (7)length of hospital stay.

In this study, SAP was diagnosed by treating physician according to the Centers for Disease Control and Prevention criteria for hospital-acquired pneumonia.²³ Only hospital-acquired pneumonia was documented and pneumonia before stroke was not considered. Data on in-hospital SAP was prospectively recorded.

2.3 Outcomes:

The main outcome of interest was in-hospital SAP.

2.4 Statistical analysis:

The Shapiro-Wilk test was used to check the normality of continuous variables. Student *t* test was used in the case of normality, and Mann-whitney test was used in the case of abnormality. The differences between categorical variables were analyzed by χ^2 test. Univariate and multivariable logistic regression was performed to determine the independent predictors of SAP after acute ischemic stroke. Variables associated with SAP at a significance level of 0.1 in univariate analysis were included in a multivariable logistic regression model using a stepwise backward elimination procedure.

All tests were 2-tailed and statistical significance was determined at an α level of 0.05. Statistical analyses were performed with the SPSS 16.0.

3. Results:

From Jan 2009 to Dec 2012, a total of 1142 eligible patients were included in our analysis. The mean age of the patients was 60.3 ± 13.1 years, of whom 419 patients (36.7%) were female. The overall in-hospital SAP was 18.8%, and the incidence of dysphagia was 19.0%. SAP patients had larger mean age (65.6 ± 11.9 vs. 59.1 ± 13.1 years; $p < 0.001$), larger NIHSS score (Median, 9 vs. 3; $p < 0.001$) and longer length of stay (22.4 ± 12.3 vs. 14.0 ± 7.4 days; $p < 0.001$) compared to non-SAP patients. The detailed baseline characteristics of the HNSR were summarized in the Table 1.

The univariate logistic regression analysis showed that age, AF, dysphagia, admission NIHSS score, history of stroke or TIA, diabetes mellitus, OCSP subtype and length of stay were associated with SAP (shown in the Table 2). Variables associated with SAP at a significance level of 0.1 in univariate analysis were included in a multivariable logistic regression model using a stepwise backward elimination procedure. The multivariate logistic regression analysis demonstrated age (OR, 1.02; 95%CI, 1.00-1.04, $p < 0.022$), dysphagia (OR, 11.76; 95%CI, 7.21-19.19, $p < 0.001$), admission NIHSS score (OR, 1.11; 95%CI, 1.0-1.16, $p < 0.001$) and length of stay (OR, 1.07; 95%CI, 1.05-1.10, $p < 0.001$) that were associated with a higher risk of SAP (Shown in the Table 3).

4. Discussions:

SAP is a common medical complication after acute ischemic stroke. In the present study, we prospectively identified the risk factors of SAP. The incidence of SAP in the present study was 18.8%, which is consistent with previous reports.^{12, 19, 24, 25}

Several risk factors for SAP have been identified. Consistent with these studies, we confirmed that in-hospital SAP was significantly associated with older age, dysphagia, history of stroke, NIHSS score and length of stay. As shown in previous studies, older age was independently associated with poststroke pneumonia. This might be due to the fact that advanced age is associated with more severe neural symptoms, impaired swallowing functions and the cough reflex.²⁶ Stroke severity as measured by the NIHSS is a well-known factor influencing probability of poststroke pneumonia.²⁷ A higher NIHSS score is associated with a deteriorated level of consciousness and decreased bulbar reflexes making aspiration more likely.²⁸ Correspondingly, dysphagia was verified as a predictor of poststroke pneumonia in previous studies.²⁹ Patients with dysphagia are prone for aspiration, which, in turn, is a strong risk factor for pneumonia. Several studies reported that length of stay was highly associated with SAP, and our study also confirmed it. The result showed that SAP was not associated with AF. However, the association of AF with SAP has been shown in only one study.³⁰ AF is a proxy for cardioembolic stroke, which is associated with cortical infarctions and higher stroke severity.³¹

There were also some limitations in this study. Firstly, this is a single center study that could have selected bias. Secondly, the exact date of new-onset SAP during hospitalization wasn't documented, the present study just showed that the length of stay was highly associated with SAP, but could not come to a conclusion as to whether patients with a longer length of stay was more likely to develop pneumonia or whether diagnosis of pneumonia led to a longer hospitalization.

In conclusion, our study prospectively identified the risk factors related to SAP in a Chinese stroke population. Simple assessment of these variables could be used to identify patients at high risk of developing pneumonia after stroke.

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Tables

Table 1. Baseline Characteristics of the HNSR Cohort.

Characteristic	HNSR Cohort (n=1142)	SAP Patients (n=215)	Non-SAP Patients (n=927)
Age, mean(SD), y	60.3 ± 13.1	65.6 ± 11.9	59.1 ± 13.1
Sex, no.(%), y			
Male	723(63.3)	135(62.8)	588(63.4)
Female	419(36.7)	80(37.2)	339(36.6)
NIHSS, median(IQR)	4(1-7)	9(5-15)	3(1-6)
Dysphagia, no.(%)	217(19.0)	146(67.9)	71(7.7)
Comorbidities, no.(%)			
Hypertension	673(58.9)	127(59.1)	546(58.9)
Diabetes mellitus	343(30.0)	82(38.1)	261(28.2)
Atrial fibrillation	51(4.5)	25(11.6)	26(2.8)
Previous stroke	299(26.2)	74(34.4)	225(24.3)
Previous TIA	53(4.6)	15(7.0)	38(4.1)
Dyslipidemia	94(8.2)	14(6.5)	80(8.6)
Coronary heart disease	115(10.1)	22(10.2)	93(10.0)
Excess alcohol consumption	270(23.6)	45(20.9)	225(24.3)
Current smoking	336(29.4)	58(27.0)	278(30.0)
Length of stay, mean(SD), d	15.7(9.3)	22.4 ± 12.3	14.0 ± 7.4
Pneumonia, no.(%)	215(18.8%)		

HNSR, Henan Province Stroke Registry; SD, standard deviation; NIHSS, National Institutes of Health Stroke Scale; IQR, interquartile range.

Table 2. Risk Factors for SAP by Univariate Logistic Regression.

Characteristics	N	Pneumonia	OR (95%CI)	P Value
Age, y	1142	100%	1.04(1.03-1.06)	<0.001*
Male sex	723	18.7%	0.97(0.72-1.32)	0.861
Dysphagia	217	67.3%	25.51(17.53-37.12)	<0.001*
Comorbidities				
Atrial fibrillation	51	49.0%	4.56(2.58-8.07)	<0.001*
Hypertension	673	18.9%	1.01(0.75-1.36)	0.964
Diabetes mellitus	343	23.9%	1.57(1.15-2.15)	0.004*
Previous stroke	299	24.7%	1.64(1.19-2.25)	0.002*
Previous TIA	53	28.3%	1.76(0.95-3.25)	0.071*
Dyslipidemia	94	14.9%	0.74(0.41-1.33)	0.309
Coronary heart disease	115	19.1%	1.02(0.63-1.67)	0.930
Excess alcohol consumption	270	16.7%	0.83(0.58-1.19)	0.299
Current smoking	336	17.3%	0.86(0.62-1.20)	0.382
NIHSS on admission	1142	100%	1.20(1.17-1.24)	<0.001*
OCSP subtype				
LACI	222	12.2%	1.0(reference)	
PACI	403	19.4%	1.73(1.08-2.78)	0.021*
TACI	40	37.5%	4.33(2.03-9.23)	<0.001*
POCI	256	23.0%	2.16(1.32-3.55)	0.002*
Length of stay	921	20.4%	1.10(1.08-1.12)	<0.001*

OR, Odds Ratio; CI, Confidence Interval; TIA, Transient Ischemic Attack; NIHSS, National Institutes of Health Stroke Scale score; OCSP, Oxfordshire Community Stroke Project; LACI, Lacunar infarction; PACI, Partial anterior circulation infarct; TACI, Total anterior circulation infarct; POCI, Posterior circulation infarct.

Table 3. Risk Factors for SAP by Multivariate Logistic Regression.

Risk factor	OR	OR (95%CI)	P Value
Age(1 year increase)	1.02	1.00-1.04	0.022
Dysphagia	11.76	7.21-19.19	<0.001
Admission NIHSS score(1 increase)	1.11	1.06-1.16	<0.001
Length of stay	1.07	1.05-1.10	<0.001

OR, Odds Ratio; NIHSS, National Institutes of Health Stroke Scale score.

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