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Risk factors for and impact of poststroke pneumonia in patients with acute ischemic stroke

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Abstract

Poststroke pneumonia (PSP) is a common complication of stroke and an important cause of death following stroke. However, the treatment of PSP remains inadequate due to severe impairment to the respiratory system by PSP. Thus, it is crucial to focus on preventing PSP to improve the prognosis of patients with stroke.

This prospective single-center Cohort study aimed to investigate the risk factors for pulmonary infection following an ischemic stroke and identify whether PSP significantly influences the prognosis of patients after stroke.

Altogether, 451 patients who were treated for acute ischemic stroke in the First Affiliated Hospital of Chongqing Medical University in China between April 2017 and April 2018 were enrolled. Clinical data from the patients from admission to 3 months after discharge were collected. PSP was the primary outcome and poor prognosis or death at 3 months following discharge was the secondary outcome observed in this study. We performed logistic regression analyses to identify the risk factors for PSP and test an association between pneumonia and poor prognosis or death after stroke.

Our findings revealed the following risk factors for PSP: atrial fibrillation odds ratio (OR) = 2.884, 95% confidence intervals (CI) = 1.316–6.322), being bedridden (OR = 2.797, 95%CI = 1.322–5.921), subject to an invasive procedure (OR = 12.838, 95%CI = 6.296–26.178), massive cerebral infarction (OR = 3.994, 95%CI = 1.496–10.666), and dysphagia (OR = 2.441, 95%CI = 1.114–5.351). Pneumonia was a risk factor for poor prognosis (OR = 2.967, 95%CI = 1.273–6.915) and death (OR = 5.493, 95%CI = 1.825–16.53) after stroke.

Hence, since pneumonia increases the risk of poor prognosis and death following acute ischemic stroke, preventing, and managing the risk factors for PSP may improve the prognosis and reduce the mortality after stroke.

Abbreviations: CI = confidence interval, COPD = chronic obstructive pulmonary disease, CT = computed tomography, IQR = inter-quartile ranges, MRI = magnetic resonance imaging, MRS = modified Rankin scale, NIHSS = National Institute of Health Stroke Scale, OR = odd's ratio, PSP = poststroke pneumonia.

Keywords: acute ischemic stroke, death, pneumonia, prognosis, risk factors

1. Introduction

Stroke is the third leading cause of death and disability worldwide; it is estimated that approximately 5 million people die of stroke and its related complications every year.[1] With an incidence of 10%, poststroke pneumonia (PSP) is the most common of all stroke-related complications.[2] PSP reportedly leads to poor clinical outcomes[1–8] such as disturbed neurological function recovery and reduced activities of daily living. Moreover, PSP has been reported to be independently associated with a 3.06-fold increase in mortality after stroke.[4] While the prevention of PSP could mitigate mortality following stroke, pharmacological or antimicrobial interventions have hitherto been ineffective in preventing PSP, and the risk factors for PSP remain obscure.[9–14] Furthermore, it also remains unclear whether PSP has an impact on the prognosis and mortality at 3 months following stroke since most of the related research does not consider outcomes following discharge. A previous study reported that pneumonia following stroke is an independent risk factor for adverse outcomes after 3 months.[15] However, in Vargas study,[16] poststroke infections including pneumonia were not found to be associated with poor functional outcome at discharge. Recent data from Teh study[17] revealed that PSP is

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associated with a poor functional outcome on discharge and increased mortality in 1 year.

To identify clearly the risk factors of PSP – a prerequisite for developing interventions to prevent PSP – we compared a series of characteristics between patients with stroke with and without PSP. The outcomes of the patients were also analyzed to detect the impact of PSP on outcomes and mortality at 3 months following stroke onset.

2. Material and methods

2.1. General data

The present single-center prospective cohort study enrolled a total of 451 patients (mean age, 67 ± 12.9 years; 294 men) who were diagnosed with acute ischemic stroke and admitted to our department in The First Affiliated Hospital of Chongqing Medical University between April 2017 and April 2018. Written informed consent was obtained from all participants, as well as approval from the ethics committee of The First Affiliated Hospital of Chongqing Medical University. Clinical data were collected from the enrolled patients with ischemic stroke from their admission to our hospital through the third month following their discharge. The patients discharged were followed up by telephone or home visit at the third month. Patients with miss data in the follow-up has been excluded. Ischemic stroke was diagnosed based on the diagnostic criteria specified by the guidelines for the diagnosis and treatment of ischemic stroke published by the Chinese Journal of Neurology.[18]

2.2. Methods

The clinical data collected from the patients included medical history, vital signs, routine blood test results, biochemistry panel findings, electrocardiogram or dynamic electrocardiogram, head computed tomography/ magnetic resonance imaging (CT/MRI), chest X-ray photographs, pulmonary CT, National Institute of Health Stroke Scale (NIHSS) scores at admission, modified Rankin scale (MRS) scores at admission and 3-month follow-up, A^2DS^2 scores, swallowing function assessment, and sputum culture results. Swallowing function was assessed using the water swallowing test,[19] wherein a grade ≥3 indicated swallowing dysfunction. Massive cerebral infarction was defined as an area of cerebral infarction >4 cm^2, an infarction surface that affected more than 2 lobes, or an affected area greater than one-half of the brain on the same side or two-thirds that of the brain on both sides. An invasive procedure was defined as actions that established a channel between the inside of the body and the outside, such as gastric tube feeding and mechanical ventilation. Confusion at admission was defined as unable to normally communicate with others. The following information of the patients including age, sex, length of stay, atrial fibrillation, dysarthria, history of chronic obstructive pulmonary disease (COPD), being bedridden, use of dehydrant, use of antacid, smoking, drinking, and coronary heart disease were sought from the medical record system.

2.3. Diagnostic criteria for PSP

Diagnoses of PSP were rendered according to the recommendations published by the Pneumonia in Stroke Consensus Group [20]. The patients had to present at least one of the following:

1. fever >38°C with no other recognizable underlying cause;
2. leukopenia (<4000 white blood cells [WBC]/mm^3) or leukocytosis (>12000 WBC/mm^3); and
3. for adults ≥70 years of age, altered mental status with no other recognizable underlying cause.

The patients had to present at least 2 of the following:

1. new-onset purulent sputum, change in the character of sputum over a 24-hour period, increased respiratory secretions, or increased suctioning requirements;
2. new onset or worsening of cough, dyspnea, or tachypnea (respiratory rate >25/minutes);
3. rales, crackles, or bronchial breath sounds; and
4. worsening gas exchange (e.g., O_2 desaturation [PaO_2/FiO_2 ≤240] or increased oxygen requirements).

Patients required at least 2 serial chest radiographs with at least one of the following: new or progressive and persistent infiltration, consolidation, or cavitation. For patients without an underlying pulmonary or cardiac disease, 1 definitive chest radiograph was acceptable. Moreover, patients with diseases that shared clinical manifestations with pneumonia, including tuberculosis, pulmonary tumor, non-infective interstitial lung disease, pulmonary edema, pulmonary embolism, and pulmonary atelectasis were excluded.

2.4. Patients were grouped according to A2DS2, NIHSS, and MRS scores

Patients' conditions at admission were routinely scored with the A2DS2 scoring tool: age ≥75 years = 1, atrial fibrillation = 1, dysphagia = 2, male sex = 1, NIHSS score of 0 to 4 = 0, NIHSS score of 5 to 15 = 3, and NIHSS score of > 15 = 5. The A2DS2 score was further dichotomized as low (0–4) and high (5–10) scores. Stroke severity was categorized according to NIHSS scores: mild or moderate (NIHSS score ≤ 15) and severe (NIHSS score > 15). The MRS scoring tool was used to assess the outcomes of the patients at three months; scores of 2 to 6 indicated a poor prognosis.

2.5. Statistical analysis

The variables followed normal distribution as determined by the Kolmogorov-Smirnov test. The Chi-Squared test was used to test the differences in categorical variables between the groups. Categorical variables were reported as numbers(n) and percentages of the total (%). Continuous variables that did not follow a normal distribution were expressed as medians with inter-quartile ranges (IQR). The Mann–Whitney *U* test was used to compare continuous variables between groups. Multivariate logistic regression model was used to screen risk factors of pulmonary infection, poor prognosis (MRS scores of 2–6 at the 3-month follow up), and death at 3 months following discharge according to a stepwise method. Statistical analyses were performed using SAS 9.4 software (Copyright © 2016 SAS Institute Inc. Cary, NC). Significant differences were indicated by $\alpha \leq 0.05$.

3. Results

3.1. Risk factors for PSP

The data of 587 patients with the diagnosis of "ischemic stroke" were extracted from the computerized patient record system; 136

Table 1

Characteristics of the study population (n = 451).

Characteristics	PSP (n = 98)	Non-PSP (n = 353)	*P* value
Age (year)			
≤65	115 (48.32)	78 (36.62)	.012
>65	123 (51.68)	135 (63.38)	
Sex (Male) n%	245 (69.41)	49 (50.00)	<.001
Smoking, n (%)	187 (52.97)	35 (35.71)	.002
Drinking, n (%)	85 (24.08)	16 (16.33)	.103
Previous stroke, n (%)	85 (24.08)	28 (28.57)	.364
History of COPD, n (%)	24 (6.80)	13 (13.27)	.039
Diabetes mellitus, n (%)	119 (33.71)	25 (25.51)	.123
Hypertension, n (%)	210 (59.49)	57 (58.16)	.813
Coronary heart disease, n (%)	54 (15.30)	26 (26.53)	.01
Dyslipidemia, n (%)	117 (22.14)	23 (23.47)	.067
Atrial fibrillation, n (%)	40 (11.33)	45 (45.92)	<.001
Massive cerebral infarction, n (%)	12 (3.40)	49 (50.00)	<.001
Dysarthria, n (%)	186 (52.69)	76 (77.55)	<.001
Dysphagia, n (%)	33 (9.35)	48 (48.98)	<.001
Confusion at admission, n (%)	33 (9.35)	59 (60.20)	<.001
Bedridden, n (%)	56 (15.86)	73 (74.49)	<.001
Use of dehydrant, n (%)	46 (13.03)	62 (63.27)	<.001
Use of antacid, n (%)	113 (32.01)	71 (72.45)	<.001
Invasive operation, n (%)	38 (10.76)	81 (82.65)	<.001
Length of stay (day)			
≤14	247 (69.97)	48 (48.98)	<.001
>14	106 (30.03)	50 (51.02)	
Admission MRS score (IQR)	4 (2–6)	14 (7–20)	<.001
Admission NIHSS score, n (%)			
≤15	346 (98.02)	51 (52.04)	<.001
>15	7 (1.98)	47 (47.96)	
Admission A^2DS^2 score, n (%)			
0–4	293 (83.00)	29 (29.59)	<.001
5–10	60 (17.00)	69 (70.41)	

COPD = chronic obstructive pulmonary disease, IQR = interquartile range.

patients were excluded since the time from ischemic stroke onset was over 7 days. Of the 451 patients with acute ischemic stroke, 98 were diagnosed with PSP. All 451 patients completed follow-up at 3 month, and the data of the patients were analyzed. Table 1 shows the baseline characteristics according to the onset of PSP during the 3-month follow-up. The following characteristics significantly differed between the PSP and non-PSP groups: age, sex, length of stay, atrial fibrillation, dysarthria, history of COPD, being bedridden, use of dehydrant, use of antacid, subject to an invasive procedure, smoking, drinking, massive cerebral infarction, coronary heart disease, dysphagia, confusion at admission, MRS score (IQR) at admission, NIHSS score at admission, and A^2DS^2 score at admission.

The factors related to PSP were further analyzed with multivariable logistic regression. We observed the following possible risk factors for PSP (Table 2): atrial fibrillation (odds ratio [OR] = 2.884, 95% confidence interval [CI] = 1.316–6.322), being bedridden (OR = 2.797, 95% CI = 1.322–5.921), subject to an invasive procedure (OR = 12.838, 95%CI = 6.296–26.178), massive cerebral infarction (OR = 3.994, 95%CI = 1.496–10.666), and dysphagia (OR = 2.441, 95% CI = 1.114–5.351). On the other hand, age, sex, length of stay, dysarthria, history of COPD, use of dehydrant, use of antacid, smoking, drinking, coronary heart disease, confusion at admission, MRS score (IQR) at admission, NIHSS score at admission, and A^2DS^2 score at admission were ruled out as risk factors for PSP.

Table 2

Multivariable logistic regression of factors related to PSP.

Characteristics	OR (95%CI)	*P* value
Intercept		<.001
Atrial fibrillation	2.884 (1.316–6.322)	.008
Bedridden	2.797 (1.322–5.921)	.007
Invasive operation	12.838 (6.296–26.178)	<.001
Massive cerebral infarction	3.994 (1.496–10.666)	.006
Dysphagia	2.441 (1.114–5.351)	.026

3.2. Risk factors of poor prognosis and death at 3 months

We further aimed to elucidate the risk factors of poor prognosis or death to understand better the effect of PSP on the prognosis of stroke. In our study, the univariate analysis of death and poor prognosis of the patients was conducted first (Tables 3 and 4). Following this, the variables with $P < .05$ were included in the multivariate logistic regression model, and the variables were screened by stepwise method. Multivariable logistic regression showed that pneumonia (OR = 2.967, 95%CI = 1.273–6.915), previous stroke (OR = 2.113, 95%CI = 1.199–3.722), being bedridden (OR = 6.091, 95%CI = 2.792–13.288), MRS score at admission (OR = 2.196, 95%CI = 1.721–2.802), and massive

Table 3

Prognosis of patients with stroke at 3 months.

Characteristics	MRS at 3 months 0–1	MRS at 3 months 2–6	*P* value
Age (y)			
≤65	115 (48.32)	78 (36.62)	.012
>65	123 (51.68)	135 (63.38)	
Sex (male) n%	171 (71.85)	123 (57.75)	.002
Smoking, n (%)	171 (71.85)	123 (57.75)	.063
Drinking, n (%)	62 (26.05)	39 (18.31)	.049
Previous stroke, n (%)	62 (26.05)	39 (18.31)	.003
History of COPD, n (%)	17 (7.14)	20 (9.39)	.385
Diabetes mellitus, n (%)	71 (29.83)	73 (34.27)	.313
Hypertension, n (%)	139 (58.40)	128 (60.09)	.715
Coronary heart disease, n (%)	54 (15.30)	26 (26.53)	.042
Dyslipidemia, n (%)	78 (32.77)	62 (29.11)	.401
Atrial fibrillation, n (%)	25 (10.50)	60 (28.17)	<.001
Massive cerebral infarction, n (%)	2 (0.84)	59 (27.70)	<.001
Dysarthria, n (%)	115 (48.32)	147 (69.01)	<.001
Dysphagia, n (%)	16 (6.72)	65 (30.52)	<.001
Confusion at admission, n (%)	14 (5.88)	78 (36.62)	<.001
Bedridden, n (%)	10 (4.20)	119 (55.87)	<.001
Use of dehydrant, n (%)	27 (11.34)	81 (38.03)	<.001
Use of antacid, n (%)	64 (26.89)	120 (56.34)	<.001
Invasive operation, n (%)	21 (8.82)	98 (46.01)	<.001
Length of stay (day)			
≤14	187 (78.57)	108 (50.70)	<.001
>14	51 (21.43)	105 (49.30)	
Admission MRS score (IQR)	3 (2–3)	5 (4–5)	<.001
Admission NIHSS score, n (%)			
≤15	237 (99.58)	160 (75.12)	<.001
>15	1 (0.42)	53 (24.88)	
Admission A^2DS^2 score, n (%)			
0–4	212 (89.08)	110 (51.64)	<.001
5–10	26 (10.92)	103 (48.36)	
PSP	11 (4.62)	87 (40.85)	<.001

COPD = chronic obstructive pulmonary disease, IQR = interquartile range, PSP = poststroke pneumonia.

Table 4

Comparison between death and non-death groups.

Characteristics	Death (44)	Non-death (n = 407)	*P* value
Age (y)			
≤65	185 (45.45)	8 (18.18)	.001
>65	222 (54.55)	36 (81.82)	
Sex (male) n%	275 (67.57)	19 (43.18)	<.001
Smoking, n (%)	206 (50.61)	16 (36.36)	.072
Drinking, n (%)	95 (23.34)	6 (13.64)	.142
Previous stroke, n (%)	102 (25.06)	11 (25.00)	.993
History of COPD, n (%)	30 (7.37)	7 (15.91)	.075
Diabetes mellitus, n (%)	135 (33.17)	9 (20.45)	.086
Hypertension, n (%)	243 (59.71)	24 (54.55)	.508
Coronary heart disease, n (%)	67 (16.46)	13 (29.55)	.031
Dyslipidemia, n (%)	132 (32.43)	8 (18.18)	.052
Atrial fibrillation, n (%)	60 (14.74)	25 (56.82)	<.001
Massive cerebral infarction, n (%)	34 (8.35)	27 (61.36)	<.001
Dysarthria, n (%)	228 (56.02)	34 (77.27)	.007
Dysphagia, n (%)	56 (13.76)	25 (56.82)	<.001
Confusion at admission, n (%)	58 (14.25)	34 (77.27)	<.001
Bedridden, n (%)	90 (22.11)	39 (88.64)	<.001
Use of dehydrant, n (%)	78 (19.16)	30 (68.18)	<.001
Use of antacid, n (%)	151 (37.10)	33 (75.00)	<.001
Invasive operation, n (%)	81 (19.90)	38 (86.36)	<.001
Length of stay (day)			
≤14	260 (63.88)	35 (79.55)	.038
>14	147 (36.12)	9 (20.45)	
Admission MRS score (IQR)	3 (2–4)	5 (5–5)	0
Admission NIHSS score, n (%)			
≤15	378 (92.87)	19 (43.18)	<.001
>15	29 (7.13)	25 (56.82)	
Admission A^2DS^2 score, n (%)			
0–4	313 (76.90)	9 (20.45)	<.001
5–10	94 (23.10)	35 (79.55)	
PSP	62 (15.23)	36 (81.82)	<.001

COPD = chronic obstructive pulmonary disease, IQR = interquartile range, PSP = poststroke pneumonia.

cerebral infarction (OR = 5.673, 95% CI = 1.179–27.291) were risk factors for poor prognosis following acute ischemic stroke (Table 5). Multivariable logistic regression further revealed a strong association between PSP and death at 3 months (OR = 4.305, 95% CI = 1.825–16.53). Hospital stays of ≤14 days (OR = 13.544, 95%CI = 4.626–39.658), atrial fibrillation (OR = 3.496, 95%CI = 1.332–9.18), being bedridden (OR = 8.6, 95% CI = 2.302–32.122), and confusion at admission (OR = 4.305, 95%CI = 1.376–13.472) were also identified as high risk factors for death after stroke (Table 5).

4. Discussion

PSP is a strong predictor for poor prognosis and mortality after acute ischemic stroke, and elucidating the risk factors for PSP is a prerequisite for developing interventions to prevent PSP. This study identified atrial fibrillation, bedridden status, subject to an invasive procedure, massive cerebral infarction, and dysphagia as risk factors for PSP. Furthermore, while the long-term impact of PSP on the outcome of stroke patients remains unclear, an association between PSP and poor prognosis or death at 3 months after discharge from the hospital following treatment of stroke was observed.

Atrial fibrillation has previously been identified as an independent risk factor for in-hospital acquired pneumonia and stroke.[21,22] During atrial fibrillation, irregular atrial activities can decrease cardiac output and cause pulmonary congestion, which can further promote pulmonary infection.[22] A previous study reported that 83% of all patients with stroke exhibit hemiplegia.[23] Severe hemiplegia can cause a patient to become bedridden, and this can diminish drainage of sputum and thus significantly increase the risk of hypostasis pneumonia. Patients with a large cerebral infarction on head CT/MRI are likely to become bedridden and manifest dysphasia and disturbance of consciousness: all 3 are associated with a higher risk of developing pneumonia.[3,24] Stroke-induced dysphagia could lead to aspiration, which also contributes to the onset of pneumonia: 40% to 70% of patients with stroke develop dysphagia within 3 days of the stroke episode, aspiration is manifested in 40% of those who aspirate, and approximately one-third of those who aspirate develop pneumonia.[19] Invasive procedures are administered to protect patients with various complications such as eating disorders, dyspnea, and dysuresia. Invasive procedures administered to protect patients increase the risk of PSP; this association may be partly attributable to forming a direct channel between the body and the outside world, thereby, increasing the risk of infection.[19,25,26] Consistent with our findings, Harms et al[19] and Matz et al[21] demonstrated that invasive procedures, being bedridden, and dysphagia are risk factors for PSP. However, in contrast with our findings, several previous studies did not identify atrial fibrillation and massive cerebral infarction as risk factors for PSP.[22,27] This could be due to regional differences.

Age, sex, length of stay, dysarthria, history of COPD, use of dehydrant, use of antacid, smoking, coronary heart disease, confusion at admission, MRS score at admission, NIHSS score at admission, and A^2DS^2 score at admission were not risk factors for PSP. Among these, sex, length of stay, and smoking have not

Table 5

Multivariable logistic regression of factors related to outcome.

	Variable	OR (95%CI)	*P* value
Poor prognosis at 3 months (MRS score 2–6)	Previous stroke	2.113 (1.199–3.722)	.01
	Bedridden	6.091 (2.792–13.288)	<.001
	Massive cerebral infarction	5.673 (1.179–27.291)	.03
	Admission MRS score	2.196 (1.721–2.802)	<.001
	PSP	2.967 (1.273–6.915)	.012
Death in 3 months	Hospital stay≤14 days	13.544 (4.626–39.658)	<.001
	Atrial fibrillation	3.496 (1.332–9.18)	.011
	Bedridden	8.6 (2.302–32.122)	.001
	Confusion at admission	4.305 (1.376–13.472)	.012
	PSP	5.493 (1.825–16.53)	.002

been confirmed as risk factors for PSP by several studies,[21,22,24] while whether the use of antacid, confusion at admission, NIHSS score at admission, and A^2DS^2 score at admission are risk factors for PSP remains controversial.[21,24,25] We suspect that the variance in findings is due to difference in distributions of race and clinical conditions within the study populations.

While several studies have confirmed that pneumonia seriously affects a patient's prognosis and increases the risk of death during hospitalization.[4,15,18,28] it was unclear whether PSP influences outcomes and mortality at 3 months after discharge from the hospital. Consistent with a prior study,[28] our findings showed that pneumonia remained a risk factor for poor prognosis and mortality at 3 months following the stroke episode.

Thus, the prevention for onset of PSP seems to be vital for the prognosis of patients with stroke. In Vermeij JD and Schwarz S studies, preventive antibiotics did not lower the incidence of pneumonia and had no significant effect on the prognosis.[9,29] Considering the high incidence of dysphagia following stroke, a recent study suggested that metoclopramide might reduce the rate of pneumonia and partly improve clinical outcomes in patients with subacute stroke fed via nasogastric tube.[30] Besides, Angiotensin-Converting Enzyme Inhibitors may be effective in reducing the risk of pneumonia following stroke, especially in Asian populations.[31] In addition to pharmacological interventions, prolonged precautionary measures such as increasing substance *P* levels, oral care, and swallowing rehabilitation, are considered to be significant for preventing PSP.[32] Nevertheless, there is no consensus on the use of drugs following stroke to prevent PSP onset.

Apart from PSP, previous stroke, being bedridden, MRS score at admission, and massive cerebral infarction were risk factors for poor prognosis at 3 months following stroke. Hospital stays of $\leq$14 days, atrial fibrillation, being bedridden, and confusion at admission were associated with death at 3 months following the stroke episode. The risk factor of a short hospital stay could be ascribed to the death of patients during hospitalization or poor financial situations; patients who could not afford treatment would have had to leave the hospital before completion of their treatment. In addition to these results in our study, Wen-Jun study showed that serum 25-hydroxyvitamin D is an independent prognostic predictor for outcome and death at 3 month in Chinese patients with acute ischemic stroke.[33] Haris study suggested that the recovery time from stroke symptoms to neurological integrity in ICU patients with stroke was significantly shorter than in the regular floor patients.[34] Thus, more comprehensive data should be included to identify the prognostic predictors of outcome after stroke in the future.

A limitation of our study is that the location of the patients' infarctions was not considered. Furthermore, postcyclic infarction could induce consciousness disorders and dysphagia, which could increase the risk of pneumonia, poor prognosis, and death following stroke. There was a lack of imaging data for some patients; however, this factor was not considered in our analysis. Finally, our nonrandomized single-center study duty features the inherent limitation of a potential selection bias.

5. Conclusion

Atrial fibrillation, invasive operation, cerebral infarction involving a large area, and dysphagia are risk factors for PSP, which is a strong predictor for poor prognosis and mortality following acute ischemic stroke. Patients with a high risk of developing PSP may warrant closer monitoring and intervention.

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References

[1] Armstrong JR, Mosher BD. Aspiration pneumonia after stroke: intervention and prevention. Neurohospitalist 2011;1:85–93.
[2] Westendorp WF, Nederkoorn PJ, Vermeij JD, et al. Post-stroke infection: a systematic review and meta-analysis. BMC Neurol 2011;11:110.
[3] Hug A, Dalpke A, Wieczorek N, et al. Infarct volume is a major determiner of post-stroke immune cell function and susceptibility to infection. Stroke 2009;40:3226–32.
[4] Ingeman A, Andersen G, Hundborg HH, et al. In-hospital medical complications, length of stay, and mortality among stroke unit patients. Stroke 2011;42:3214–8.
[5] Katzan IL, Cebul RD, Husak SH, et al. The effect of pneumonia on mortality among patients hospitalized for acute stroke. Neurology 2003;60:620–5.
[6] Koennecke HC, Belz W, Berfelde D, et al. Factors influencing in-hospital mortality and morbidity in patients treated on a stroke unit. Neurology 2011;77:965–72.
[7] Wilson RD. Mortality and cost of pneumonia after stroke for different risk groups. J Stroke Cerebrovasc Dis 2012;21:61–7.
[8] Azurmendi L, Lapierre-Fetaud V, Schneider J, et al. Proteomic discovery and verification of serum amyloid A as a predictor marker of patients at risk of post-stroke infection: a pilot study. Clin Proteomics 2017;14:27.
[9] Schwarz S. Prophylactic antibiotic therapy for preventing poststroke infection. Neurotherapeutics 2016;13:783–90.
[10] Shi K, Wood K, Shi FD, et al. Stroke-induced immunosuppression and poststroke infection. Stroke Vasc Neurol 2018;3:34–41.
[11] Liu L, Xiong XY, Zhang Q, et al. The efficacy of prophylactic antibiotics on post-stroke infections: an updated systematic review and meta-analysis. Sci Rep 2016;6:36656.
[12] Westendorp WF, Vermeij JD, Vermeij F, et al. Antibiotic therapy for preventing infections in patients with acute stroke. Cochrane Database Syst Rev 2012;1:CD008530.
[13] Westendorp WF, Vermeij J-D, Zock E, et al. The preventive antibiotics in stroke study (PASS): a pragmatic randomised open-label masked endpoint clinical trial. Lancet 2015;385:1519–26.
[14] Zheng F, Spreckelsen NV, Zhang X, et al. Should preventive antibiotics be used in patients with acute stroke? A systematic review and meta-analysis of randomized controlled trials. PLoS One 2017;12:e0186607.
[15] Aslanyan S, Weir CJ, Diener HC, et al. Pneumonia and urinary tract infection after acute ischaemic stroke: a tertiary analysis of the GAIN International trial. Eur J Neurol 2004;11:49–53.

[16] Vargas M, Horcajada J, Obach V, et al. Clinical consequences of infection in patients with acute stroke: is it prime time for further antibiotic trials? Stroke 2006;37:461–5.
[17] Teh W, Smith C, Barlas R, et al. Impact of stroke-associated pneumonia on mortality, length of hospitalization, and functional outcome. Acta Neurologica Scandinavica 2018;138:293–300.
[18] Finlayson O, Kapral M, Hall R, et al. Risk factors, inpatient care, and outcomes of pneumonia after ischemic stroke. Neurology 2011;77:1338–45.
[19] Harms H, Prass K, Meisel C, et al. Preventive antibacterial therapy in acute ischemic stroke: a randomized controlled trial. PLoS One 2008;3: e2158.
[20] Smith CJ, Kishore AK, Vail A, et al. Diagnosis of stroke-associated pneumonia: recommendations from the pneumonia in stroke consensus group. Stroke 2015;46:2335–40.
[21] Matz K, Seyfang L, Dachenhausen A, et al. Poststroke pneumonia at the stroke unit - a registry based analysis of contributing and protective factors. BMC Neurol 2016;16:107.
[22] Zhu J, Zhang X, Shi G, et al. Atrial fibrillation is an independent risk factor for hospital-acquired pneumonia. PLoS One 2015;10:e0131782.
[23] Sui R, Zhang L. Risk factors of stroke-associated pneumonia in Chinese patients. Neurol Res 2011;33:508–13.
[24] Ashour W, Al-Anwar AD, Kamel AE, et al. Predictors of early infection in cerebral ischemic stroke. J Med Life 2016;9:163–9.
[25] Ho SW, Hsieh MJ, Yang SF, et al. Risk of stroke-associated pneumonia with acid-suppressive drugs: a population-based Cohort study. Medicine (Baltimore) 2015;94:e1227.
[26] Yuan MZ, Li F, Tian X, et al. Risk factors for lung infection in stroke patients: a meta-analysis of observational studies. Expert Rev Anti Infect Ther 2015;13:1289–98.
[27] Westendorp WF, Vermeij JD, Hilkens NA, et al. Development and internal validation of a prediction rule for post-stroke infection and poststroke pneumonia in acute stroke patients. Eur Stroke J 2018;3: 136–44.
[28] Wang PL, Zhao XQ, Yang ZH, et al. Effect of in-hospital medical complications on case fatality post-acute ischemic stroke: data from the China National Stroke Registry. Chin Med J Engl 2012;125:2449–54.
[29] Vermeij JD, Westendorp WF, Dippel DW, et al. Antibiotic therapy for preventing infections in people with acute stroke. Cochrane Database Syst Rev 2018;1:CD008530.
[30] Warusevitane A, Karunatilake D, Sim J, et al. Safety and effect of metoclopramide to prevent pneumonia in patients with stroke fed via nasogastric tubes trial. Stroke 2015;46:454–60.
[31] Shinohara Y, Origasa H. Poststroke pneumonia prevention by angiotensin-converting enzyme inhibitors: results of a meta-analysis of five studies in Asians. Adv Ther 2012;29:900–12.
[32] Teramoto S. Novel preventive and therapuetic strategy for poststroke pneumonia. Expert Rev Neurother 2009;9:1187–200.
[33] Tu WJ, Zhao SJ, Xu DJ, et al. Serum 25-hydroxyvitamin D predicts the short-term outcomes of Chinese patients with acute ischaemic stroke. Clin Sci (Lond) 2014;126:339–46.
[34] Kamal H, Ahmed MK, Zha A, et al. Strokes occurring in the hospital: symptom recognition and eligibility for treatment in the intensive care units versus hospital wards. Brain Circ 2020;6:196–9.