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ARTICLE

Predictors of pneumonia in acute stroke in patients in an emergency unit

Preditores de pneumonia em pacientes com AVC isquêmico numa unidade de emergência

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ABSTRACT

Objective: To evaluate the risk factors and comorbid conditions associated with the development of pneumonia in patients with acute stroke. To determine the independent predictors of pneumonia. **Method:** Retrospective study from July to December 2011. We reviewed all medical charts with diagnosis of stroke. **Results:** 159 patients (18-90 years) were admitted. Prevalence of pneumonia was 32%. Pneumonia was more frequent in patients with hemorrhagic stroke (OR: 4.36; 95%CI: 1.9-10.01, $p < 0.001$), higher National Institute of Health Stroke Scale (NIHSS) ($p = 0.047$) and, lower Glasgow Coma Score (GCS) ($p < 0.0001$). Patients with pneumonia had longer hospitalization ($p < 0.0001$). Multivariable logistic regression analysis identified NIHSS as an independent predictor of pneumonia (95%CI: 1.049-1.246, $p = 0.002$). **Conclusion:** Pneumonia was associated with severity and type of stroke and length of hospital stay. The severity of the deficit as evaluated by the NIHSS was shown to be the only independent risk factor for pneumonia in acute stroke patients.

Keywords: stroke, pneumonia, predictors, length of stay.

RESUMO

Objetivo: Avaliar os fatores de risco e as comorbidades associadas ao desenvolvimento de pneumonia em pacientes com acidente vascular cerebral (AVC) agudo. Determinar os preditores independentes de pneumonia. **Método:** Estudo retrospectivo, realizado entre julho e dezembro de 2011. Foi revisado todos os prontuários dos pacientes com diagnóstico de AVC. **Resultados:** 159 pacientes (18-90 anos) foram admitidos. A incidência de pneumonia foi de 32%. A incidência de pneumonia foi maior em pacientes com AVC hemorrágico (OR: 4,36; IC95%: 1,9-10,01, $p < 0,001$) e em pessoas com escore alto National Institute of Health Stroke Scale (NIHSS) ($p = 0,047$) e escores mais baixos da Escala de Coma de Glasgow (ECG) ($p < 0,0001$). Os pacientes com pneumonia tiveram maior tempo de internação ($p < 0,0001$). A análise de regressão logística identificou apenas o NIHSS como um preditor independente de pneumonia (IC95%: 1,049-1,246, $p = 0,002$). **Conclusão:** O diagnóstico de pneumonia foi associado a tipo e gravidade do AVC e com tempo de hospitalização. A gravidade do déficit, avaliada pela escala NIHSS mostrou ser o único fator de risco independente para pneumonia em pacientes com AVC agudo.

Palavras-chave: acidente vascular cerebral, pneumonia, preditores, tempo de internação.

Despite significant achievements in the acute management and treatment of stroke, it remains the third leading cause of death in industrialized countries[1]. The incidence of stroke has decreased over the past 50 years but the lifetime risk has not declined to the same degree, perhaps due to improved life expectancy[2].

Pneumonia is among the most common medical complications after stroke, with an estimated incidence ranging from 2.4% to 47%[2,3,4,5,6,7]. Katzan et al.[6] showed that pneumonia has been associated with a relative risk of 3.0 for mortality in a study including 14,293 patients with stroke.

Despite the well-documented association of stroke-associated infections with increased mortality and worse long-term outcome[6], as yet there are only limited data available on independent predictors of pneumonia in acute stroke patients[8,9] treated in the emergency unit. The identification of early predictors is of paramount importance for clinicians, so that specific therapies and management strategies can be applied to patients at high risk of dying.

In the present study the objective was to evaluate risk factors and comorbid conditions associated with the diagnosis of pneumonia and to determine the independent predictors of pneumonia in patients with acute stroke.

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METHOD

Study population

This is an exploratory, retrospective cohort study. All patients admitted from July to December 2011 with a diagnosis of stroke in an Emergency Unit of an Academic Medical Center were included. Some patients were transferred to the intensive care unit or neurology ward, depending on the severity and availability of the wards. The diagnosis of stroke was based on clinical characteristics and imaging studies. Patients with symptoms that had completely resolved within 24 hours were excluded as well as those with subarachnoid hemorrhage and secondary intracerebral hemorrhage.

The study was approved by the Committee on Ethics of the Faculty of Medical Sciences at the *Universidade Estadual de Campinas* in accordance with the Regional Health Counsel's resolution 196/96 (Protocol 1038/2011).

Data collection

We review all the medical charts and extracted information using a structured questionnaire. The questionnaire included demographics (age, sex, discharge destination), vascular risk factors (hypertension, diabetes, dyslipidemia, smoking, alcohol, previous vascular disease, with coronary artery disease and atrial fibrillation). Stroke severity was assessed on admission using the National Institute of Health Stroke Scale (NIHSS)[10] and level of consciousness was assessed using the Glasgow Coma Score (GCS) scale[11], type (ischemic *vs.* hemorrhagic) and localization of stroke (anterior *vs.* posterior circulation); use of thrombolytic therapy; and time use of mechanical ventilation were also collected.

Pneumonia was diagnosed based on clinical, laboratory and radiological data by the treating physician and registered on the medical chart.

Statistical analysis

Categorical variables are expressed as proportions and continuous variables are expressed as mean ± standard deviation (SD) and median (IQR). Univariable analysis comparing demographics, vascular risk factors, stroke severity, level of consciousness, type of stroke, localization, use of thrombolytic and use of mechanical ventilation between patients with and without a diagnosis of pneumonia was performed. Proportions were analyzed with the Fisher's exact test. Continuous variables were analyzed with the Man-Whitney U test. Variables selected a priori (age, sex, NIHSS, type of stroke) and those with p-value < 0.1 in the bivariate analysis were included in a logistic regression model to assess the independent predictors for a diagnosis of pneumonia. All p-values are double-sided, and the level of statistical significance was set at $p < 0.05$. All statistical analyses were performed with SPSS 20.0 for Windows.

RESULTS

Study population and stroke characteristics

A total of 159 patients (92 men and 67 women, mean age 63.4 ± 13.4 years) with acute stroke were included. Most patients were discharged home (115, 72.3%), and others died (25, 15.7%) or were transferred to other hospital (19, 11.9%). Ischemic and hemorrhagic stroke were diagnosed in (129, 81.1%) and (30, 18.9%) patients, respectively. Anterior circulation stroke was documented in (132, 83.01%) patients, followed by posterior circulation (27, 16.9%). The location of the lesion was left hemisphere (80, 50.3%) patients; in (64, 40.3%) was right hemisphere and (14, 8.9%) was posterior circulation. Thrombolytic therapy was administered in (29, 18.2%) patients. Pneumonia was diagnosed in (51, 32%) of the patients.

Main outcome measures

Table 1 represents baseline characteristics in patients with and without pneumonia. No significant differences were observed regarding demographic data, site and localization of stroke or use of the thrombolytic therapy. Higher rate of pneumonia was observed among patients with hemorrhagic stroke (odds ratio (OR): 4.36, 95%CI: 1.9-10.0).

Table 2 shows the frequency of pneumonia in stroke patients adjusted by age, NIHSS, Glasgow Coma Score, length of stay in hospital and time use of mechanical ventilation (in days). Pneumonia was most common in those with higher NIHSS ($p = 0.047$) and lower Glasgow Coma Score ($p < 0.0001$).

Patients with longer hospital stay more frequently developed pneumonia, the mean hospital stay length was 13.4 days compared with 5.2 days in group without pneumonia ($p < 0.0001$).

Predictors of stroke-associated pneumonia

In the multivariable analysis the NIHSS was the only factor associated ($p = 0.002$) with pneumonia (Table 3). Ages, gender, type of stroke were not associated with pneumonia.

DISCUSSION

In this study, pneumonia frequency was higher in patients with hemorrhagic stroke, more common in those with higher NIHSS and lower GCS scores. Patients with longer hospital stay more frequently developed pneumonia. Logistic regression analysis identified only the NIHSS as an independent predictor of pneumonia.

A variety of neurological and medical complications may occur post-stroke, such as pneumonia, urinary tract infections, malnutrition or volume depletion. Many of those complications are potentially preventable with the improvement of stroke care. This is best done in a dedicated stroke unit with

Table 1. Demographic and clinical data in 159 patients stroke with pneumonia and without pneumonia that have been treated in an Emergency Unit.

Patient Characteristics	Pneumonia (n = 51)*	Non-pneumonia (n = 108)*	OR	95%CI	p-value
Demographic data					
Sex male	29 (56.9)	63 (58.3)	1.06	0.54-2.08	p = 0.497[1]
Hypertension	42 (82.4)	84 (77.8)	0.75	0.32-1.75	p = 0.329[1]
Diabetes	15 (29.4)	32 (29.9)	0.97	0.49-2.12	p = 0.552[1]
Dyslipidemia	8 (15.7)	18 (16.7)	0.93	0.43-2.66	p = 0.537[1]
Previous vascular disease	28 (54.9)	51 (47.2)	1.36	0.37-1.43	p = 0.232[1]
Smoking					p = 0.806[2]
Non-smoker	26 (51)	54 (50)	Reference		
Current	14 (27.5)	26 (24.1)	1.036	0.43-2.46	
Past-smoker	11 (21.6)	28 (25.9)	0.858	0.34-2.11	
Alcohol					p = 0.490[2]
Non-alcohol	36 (70.6)	82 (75.9)	Reference		
Current	8 (15.7)	10 (9.3)	2.027	0.65-6.32	
Past-alcohol	7 (13.7)	16 (14.8)	1.189	0.40-3.46	
Type of stroke					
Ischemic	33 (64.7)	96 (88.9)	Reference	1.90-10.01	p < 0.0001[1]
Hemorrhagic	18 (35.3)	12 (11.1)	4.36		
Site of stroke					p = 0.284[2]
Right	18 (35.3)	46 (43)	0.39	0.11-1.29	
Left	26 (51)	54 (50.5)	0.46	0.14-1.48	
Posterior	7 (13.7)	7 (6.5)	Reference		
Localization of stroke					
Anterior circulation	42 (82.4)	90 (83.3)	1.07	0.44-2.58	p = 0.522[1]
Posterior circulation	9 (17.6)	18 (16.7)	Reference		p = 0.522[1]
Thrombolysis	7 (13.7)	22 (20.4)	0.62	0.24-1.56	p = 0.216[1]

*: Data given as total number (percentage proportion) of all stroke patients in that group; [1]: Fisher´s exact test; [2]: X^2 test. OR: Odds ratio; CI: Confidence interval.

Table 2. Variables associated with pneumonia in stroke patients.

	Pneumonia (N = 51)		Non-pneumonia (N = 108)		p-value*
	Median	IQR	Median	IQR	
Age	67	55-74	64.5	53.25-72	0.245
NIH stroke scale	15.5	8-19	8	3-14	0.047
GCS scale	11.5	10-14	15	14-15	< 0.0001
Length of stay in hospital	7	4-18	3	1-6	< 0.0001
Duration of MV (days) use	6.5	3.5-8	4	2-7.5	0.499

NIHSS: National Institute of Health Stroke Scale; GCS: Glasgow coma score; MV: Mechanical ventilation; IQR: Interquartile range.
*: Man-Whitney U Test (significant values of p < 0.05).

experienced staff and early mobilization[12,13,14]. Pneumonia is the leading cause of death in the post-acute phase of stroke[6]. The majority of the pneumonias are caused by aspiration but there are other reasons that include hypostatic pneumonia due to poor caring and immobilization. Frequent changes of the patient position in bed and pulmonary physical therapy may prevent this type of infection[14]. Thus, a better understanding of the risk factors and comorbid conditions may guide the implementation of strategies in organized stroke care provision[15].

Chen et al.[16] referred that ischemic stroke could be a predictor for the lower occurrence of general infections in all

Table 3. Risk factors of stroke associated pneumonia using multivariable logistic model.

	OR	95%CI		p-value*
		Lower	Upper	
Age	1.034	0.996	1.073	0.083
Sex	1.286	0.502	3.294	0.600
NIHSS	1.143	1.049	1.246	0.002
Type of Stroke	0.662	0.186	2.357	0.525

NIHSS: National Institute of Health Stroke Scale; OR: odds ratio; CI: confidence interval; *: Multivariable logistic model.

stroke patients, based on findings showing that hemorrhagic stroke patients showed a higher frequency of general infections. Our cohort showed the relationship between pneumonia and hemorrhagic stroke, probably because these patients had more complications during the hospitalization and more deaths than ischemic group.

Some studies have demonstrated that complications such as stroke progression or pneumonia adversely affect clinical outcome[6,17]. Increase risk of poor outcome in patients with pneumonia, if unadjusted, reflects not only the effect of pneumonia but the effect of other factors predisposing them to pneumonia, such as initial stroke severity or neurological complications. Ifejika-Jones et al.[18] showed the correlation between aspiration pneumonia and NIHSS, where they were more likely to require continued postacute stroke care because the lower functional status. In the actual study, it was found the relation among pneumonia and NIHSS and GCS severity. In this case, inpatients in the acute phase are more likely to develop pneumonia when they have worse consciousness level and neurological deficits. Patients with the greatest degree of impairment experienced complications most frequently.

There was a relationship between pneumonia and hospitalization time, as expected and previously shown by Chen et al.[16]. Kwan and Hand[19] reported that post-stroke infection could prolong the length of stay of patients, in the acute stroke stage. The length of stay in hospital has been influenced by the hospitals' characteristics and the organization of services within the hospital. We can't assert that the incidence of pneumonia might be the cause of the increase in length of stay in the emergency unit. However, the pneumonia group remained more time hospitalized, with an average of 13 days in the hospital compared to 5 days in the group without pneumonia. Moreover, the highest length of stay in hospital will influence the total financial costs. The marginal cost of pneumonia is up to three times higher than the group without pneumonia[20]. The pneumonia and stay in intensive care unit are independent predictors of acute treatment costs in Brazil hospitals[21].

Stroke severity on admission is a well-known predictor of mortality[8,9], but not as a predictor of pneumonia. Ruijun et al.[22] showed that age, atrial fibrillation, congestive heart failure, chronic obstructive pulmonary disease and current smoking, prestroke dependence, dysphagia, admission NIHSS and GCS scores, stroke subtype and blood glucose were independent predictors of pneumonia in ischemic stroke. Finlayson et al.[23] indicated that male sex, nonlacunar ischemic stroke, and preadmission dependency were predictors too.

Our study evaluated the predictors of pneumonia in ischemic and hemorrhagic acute stroke. After the adjustment for possible confounders, the NIHSS score was only an independent predictor of pneumonia, despite the small sample size and the reduced collection time of only 5 months. This predictor can help in the recognition of neurological impairment, including motor, sensory deficit, and aphasias. Furthermore, aspiration is frequently found in patients with reduced consciousness, impaired gag reflexes or swallowing disturbances[24]. The use of NIHSS scale could help alert the physicians to prevent pneumonia in those with increased suspicious.

Thus, it is possible an early intervention, adopting measures such as early mobilization, evaluation of swallowing and respiratory function in patients with suspect or confirmed pneumonia[25,26]. Prevention and early rehabilitation may decrease the risk of complications, reducing mortality and improving prognosis after acute ischemic stroke[27,28].

Our study further provides the differential to assess the impact of pneumonia, on the clinical outcome, after stroke, in emergency unit. We believe that the high incidence of pneumonia in this study could happen because of the lack of a specialized and trained stroke unit, where there are joint interventions of the multidisciplinary team.

All the patients should be treated in a stroke unit incorporating rehabilitation, with regular supervise about neurological status, vital functions and adequate ventilation[14]. The Brazilian Stroke Society proposed recently a classification of referral centers for diagnosis and treatment of acute stroke, including a multidisciplinary team qualified for care and management of high-complexity stroke patients[30]. Stroke unit care can act better than general ward in intervention and maintenance of physiological homeostasis, more attention to preventive measures, selective use of antipyretics, antibiotic medication and insulin, better training and greater dedication of professional staff, and emphasis on patient and family education and involvement in care[31].

Our study has the limitation of being in single-center in hospital-based study, wherever the patients with acute stroke included in the present study are not representative of the entire population. We didn't include data on some other variables that might have influence on the development of pneumonia, with pre-stroke antibiotic treatment, specific anti-inflammatory and/or immunomodulatory therapy before the index stroke. Furthermore, we didn't collected modifiable risk factors for pneumonia, e.g. subglotic aspiration, oral hygiene, raised head of bed and presence of dysphagia. Other limitations are related to a retrospective design of our study. Thus, we were not able to determine the precise date of the diagnosis of pneumonia, being possible that some assessments (e,g., time of mechanical ventilation) may have taken place before pneumonia and we could not provide data on positive cultures or timing of pneumonia after hospital admission by the lack of additional data from medical chart.

In conclusion, pneumonia was related to the severity and type of stroke and length of stay in hospital. The severity of the neurological deficit evaluated by the NIHSS was shown to be the only independent risk factor for pneumonia in acute stroke patients.

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