The impact of pneumonia on hospital stay among patients hospitalized for acute stroke

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ABSTRACT

الأهداف: دراسة أثر الالتهاب الرئوي على مدة العلاج والبقاء في المستشفى للمرضى المصابين بالسكتة الدماغية الحادة.

الطريقة: هذه الدراسة عبارة عن دراسة موضعية على 368 مريضاً مصاب بالسكتة الدماغية الحادة والذين يخضعون للعلاج في مستشفى ابن سينا من يناير 2010م إلى مارس 2011م. تم تحديد الخصائص الديموغرافية والمضاعفات الثانوية أثناء الإقامة في المستشفى، ومن ثم تم تحديد تأثير كل متغير من خلال تحليل الانحدار اللوجستي واختبار السجل الرتبي.

النتائج: بلغت مدة إقامة المرضى المصابين بالالتهاب الرئوي بين المرضى المصابين بالسكتة الدماغية الحادة (11.5±6.4 يوماً) مقارنة مع المرضى الآخرين (7.2±4.1 يوماً) يعني (p=0.0005). وأظهرت نتائج تحليل الانحدار اللوجستي وجود علاقة وثيقة بين طول الإقامة في المستشفى والتهاب المسالك البولية (p=0.001)، واستهلاك الستيرويد (p=0.028)، ومؤشر شدة السكتة الدماغية (p=0.039) والالتهاب الرئوي (p=0.042) واضطراب البلع (p=0.048).

الخاتمة: نظراً لتأثير ذات الرئة على مدة الإقامة الطويلة في المشفى ينصح باتباع أنشطة الوقاية والتشخيص السريع لمرض الالتهاب الرئوي والتي قد تحسن من النتائج وتخفض من التكاليف للمصابين بالسكتة الدماغية الحادة.

Objectives: To determine the impact of pneumonia on length of hospital stay in cases of acute stroke.

Methods: This was a retrospective cross-sectional study on 368 stroke patients admitted with a diagnosis of stroke at the Avicenna Hospital, Qazvin, Iran between January 2010 and March 2011. By reviewing the hospital patient records, the demographic characteristics, stroke characteristics, and complications of stroke in these patients were determined during their hospital stay. In surviving patients, the impact of each variable on length of hospital stay was calculated by logistic regression analysis and the Log-Rank test.

Results: Patients with pneumonia during the post stroke period had an increased length of hospital stay (11.5±6.4 days), compared with other patients (7.2± 4.1 days), (p=0.0005). Multiple logistic regression analysis showed a significant association between length of hospital stay and urinary tract infection (p=0.001), steroid consumption (p=0.028), index of stroke severity (p=0.039), pneumonia (p=0.042), and swallowing disorder (p=0.048).

Conclusion: Considering the impact of pneumonia on the length of hospital stay and its consequences, prophylactic activities, rapid diagnosis, and treatment of pneumonia may improve outcome and reduce costs in stroke patients.

Neurosciences 2014; Vol. 19 (2): 118-123

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Received 5th November 2013. Accepted 4th March 2014.

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Stroke is today considered the third cause of death in the world,[1] with some authorities believing it is the second cause of death worldwide.[2] Complications are one of the most important factors determining prognosis following stroke.[3] These complications not only cause prolonged hospital stay and impose enormous costs,[4] but also are effective in the final functional status of patients.[5] Infectious complications are an important disadvantage of stroke, and in addition to causing mortality and morbidity, even after discharge, can be the main reason for hospital readmission.[1] Pneumonia is an important

Disclosure. The authors declare no conflicting interests, support or funding from any drug company.

factor for mortality after stroke and generally occurs in bedridden patients, and patients with impaired cough reflex or swallowing disorders.[6] The risk of pneumonia in the acute phase of stroke is higher and increases the mortality rate up to 10%.[3,7] In most previous studies, pneumonia was associated with increased length of hospital stay in acute stroke patients,[7,8] but some studies did not find significant associations even in univariate analysis.[9] In all these studies, the length of hospital stay was calculated in surviving and dead patients and the confounding effect of early mortality on hospital stay in critically ill patients was not considered. The aim of this study was to determine the impact of pneumonia with correction of the confounding effect of early mortality on duration of hospital stay.

Methods. *Study design.* A retrospective cross-sectional study was conducted between January 2010 and March 2011 at the Avicenna Hospital (the only tertiary care hospital for neurological diseases in Qazvin province, Iran). All patients with a diagnosis of stroke admitted to hospital during this time interval were included in the study. The only exclusion criterion was fever or prominent infection when the patient was admitted to the hospital. Stroke was diagnosed by neurologists based on history, physical examination, and neurological imaging, including CT scan or MRI of the brain. Demographic characteristics such as gender, race, age, and marital status of patients was noted on a checklist. Differentiation between hemorrhagic and ischemic strokes was based on imaging (CT scan or MRI) findings. Strokes in the field of anterior and middle cerebral arteries and their branches were defined as strokes in the anterior territory, and strokes in vertebral, basilar, and posterior cerebral arteries and their branches were defined as posterior territory strokes. Small ischemic areas with diameters between 0.5-1.5 centimeters were defined as lacunar infarctions. Stroke severity was calculated by the cumulative number of these signs: loss of consciousness, weakness or paralysis of extremities, aphasia, and dysarthria.[10]

Pneumonia was diagnosed by an internist or infectious diseases specialist based on the presence of at least 3 of these criteria: fever (core body temperature >38° centigrade), purulent cough, abnormal respiratory signs (tachypnea, tachycardia, inspiratory crackles), abnormal chest radiographic findings, hypoxemia (arterial oxygen tension <70 mm Hg or arterial oxygen saturation <94%), and detection of microorganisms on tracheal direct smear.[11] A diagnosis of urinary tract infection (UTI) was based on the detection of more than 10 leukocytes per microscopic field (1000x) of centrifuged urine or positive urine culture for urinary pathogens (>10^5 colony forming units/ml). The hospital stay was defined as the days from hospital admittance to discharge or death. A swallowing disorder was defined as choking, coughing, or a wet voice after swallowing of 5 milliliters of water on more than one occasion out of 3 attempts.[12]

The data was recorded in checklists for each patient individually for statistical analysis. The Ethical Committee of Qazvin University of Medical Sciences approved the study.

Statistical analysis. The data were analyzed using statistical tests, including t-test, chi-squared, Fisher exact, logistic regression, Kaplan-Meier survival curves and the log-rank test using the Statistical Package for Social Sciences version 16 (SPSS Inc., Chicago, IL, USA).

Results. During the study period, 368 patients were admitted with stroke. Their mean age was 69.45±13.3 years. One hundred and ninety-eight (53.8%) were men, and 170 (46.2%) were women. Habits and underlying diseases of the patients are summarized in **Table 1**.

Table 2 denotes stroke subtypes and the complications during hospitalization in surviving and non-surviving patients. Among the studied patients, 47 (12.8%) died, and 321 (87.2%) survived. The incidence of pneumonia was 9.3% in surviving patients, and 68.1% in deceased patients (odds ratio [OR]=20.7; confidence interval [CI]: 10.1-42.5; p=0.000). The mean length of hospital stay in surviving patients was 7.6±4.5 days. In this group, the mean length of stay for pneumonic patients was 11.5±6.4, and for other patients was 7.2±4.1 days (p=0.0005). Among patients admitted to the ICU,

Table 1 - Habits and underlying disorders of stroke patients admitted to hospital with a diagnosis of stroke.

Habits and underlying disorders	Frequency (%)	
Hypertension	227	(61.7)
Coronary artery disease	137	(37.2)
Smoking	127	(34.5)
Previous stroke	118	(32.1)
Hyperlipidemia	107	(29.1)
Diabetes	79	(21.5)
Heart failure	79	(21.5)
Systemic steroid use	56	(15.2)
Atrial fibrillation	45	(12.2)
Renal failure	12	(3.3)
Dementia	11	(3.0)
Known cancer	7	(1.9)
Cirrhosis	6	(1.6)

the mean length of stay for pneumonic patients was 10.6±9.2, and for other patients was 7.0±3.0 days (p=0.529). Of 321 patients who were discharged from hospital, 252 (78.5%) stayed in hospital for at most 10 days, and 69 (21.5%) stayed at least 11 days.

Univariate analysis demonstrated a significant association between duration of hospital stay and a history of steroid consumption. During the hospital admission period, index of stroke severity, swallowing disorder, impaired cough reflex, pneumonia, UTI, urinary incontinence, loss of consciousness, debilitation, and hemorrhagic infarct were associated with a prolonged hospital stay. In univariate analysis, lacunar infarct was found as a protective factor compared with other types of stroke in prolonged hospital stay in surviving patients (**Tables 3** & 4). Multiple logistic regression analysis with all the above variables, showed a significant association between length of hospital stay (at most 10 days, and at least 11 days) and UTI, steroid consumption, index of stroke severity, pneumonia, and swallowing disorder during hospital admission (**Table 5**). Cumulative survival distribution function and log rank test also show that the pneumonic patients had a significantly longer length of hospital stay than other patients (p=0.000, **Figure 1**).

Table 2 - Complications and stroke characteristics during hospital stay in patients admitted with a diagnosis of stroke.

Complications during hospital stay	Frequency (%)	
Index of stroke severity:		
0-1	195	(53.0)
2	80	(21.7)
3	44	(12.0)
4	49	(13.3)
Hemorrhagic infarct	52	(14.1)
Ischemic infarct	312	(84.8)
Anterior circulation	318	(86.4)
Posterior circulation	111	(30.2)
Lacunar infarct	157	(42.7)
Right side hemiplegia	169	(45.9)
Debilitation	236	(64.1)
Swallowing disorder	121	(32.9)
Loss of consciousness	77	(20.9)
Incontinence	71	(19.3)
Impaired cough reflex	62	(16.8)
Pneumonia	62	(16.8)
Urinary tract infection	58	(15.8)

Table 3 - Association between stroke characteristics with prolonged hospital stay in univariate analysis in surviving stroke patients.

Underlying disorders and hospital complications	Odds ratio (95% confidence interval)	*P*-value
Index of stroke severity:		
0-1	1.00 (Reference)	
2	2.62 (1.34-5.13)	
3	9.20 (3.93-21.57)	0.000
4	7.48 (2.81-19.90)	
Lacunar infarct	0.47 (0.27-0.82)	0.007
Hemorrhagic infarct	2.42 (1.20-4.87)	0.012
Ischemic infarct	0.63 (0.31-1.27)	0.193
Posterior circulation	1.38 (0.78-2.45)	0.296
Anterior circulation	1.58 (0.63-3.95)	0.322
Right side hemiplegia	1.17 (0.69-2.00)	0.567

Discussion. Pneumonia is the most common cause of fever during the first 48 hours of hospitalization, and the first medical complication in the first weeks following

Table 4 - Association between underlying disorders and hospital complications with prolonged hospital stay in univariate analysis in surviving patients.

Underlying disorders and hospital complications	Odds ratio (95% confidence interval)	*P*-value
Swallowing disorder	6.69 (3.73-12.01)	0.000
Impaired cough reflex	6.42 (2.51-16.44)	0.000
Pneumonia	5.13 (2.36-11.16)	0.000
Urinary tract infection	4.75 (2.47-9.13)	0.000
Incontinence	4.25 (2.21-8.17)	0.000
Loss of consciousness	4.17 (1.98-8.79)	0.000
Systemic steroid use	3.07 (1.57-6.02)	0.001
Debilitation	2.27 (1.25-4.01)	0.006
A previous stroke	1.67 (0.96-2.91)	0.066
Atrial fibrillation	1.98 (0.91-4.32)	0.081
Renal failure	3.04 (0.79-11.64)	0.104
Cirrhosis	7.49 (0.67-83.86)	0.118
Heart failure	1.57 (0.85-2.91)	0.145
Smoking	0.65 (0.36-1.17)	0.150
Female gender	0.674 (0.39-1.16)	0.153
Coronary artery disease	1.46 (0.85-2.51)	0.171
Age over 70 years	1.35 (0.79-2.32)	0.272
Dementia	2.48 (0.41-15.13)	0.293
Hyperlipidemia	1.33 (0.76-2.35)	0.318
Anterior circulation	1.58 (0.63-3.95)	0.322
Hypertension	1.21 (0.70-2.12)	0.495
Known cancer	0.912 (0.10-8.29)	0.707
Diabetes	0.93 (0.48-1.81)	0.837

Table 5 - Logistic regression analysis of underlying disorders and hospital complications with prolonged hospital stay in surviving patients.

Underlying disorders and hospital complications	Odds ratio (95% confidence interval)	*P*-value
Urinary tract infection	3.77 (1.77-8.03)	0.001
Systemic steroid use	4.72 (1.19-18.78)	0.028
Index of stroke severity	1.75 (1.03-2.96)	0.039
Pneumonia	2.70 (1.02-7.02)	0.042
Swallowing disorder	2.41 (1.01-5.74)	0.048
Loss of consciousness	0.30 (0.08-1.15)	0.079
Incontinence	1.73 (0.77-3.88)	0.182
Hemorrhagic infarct	0.46 (0.11-2.02)	0.313
Impaired cough reflex	1.33 (0.35-4.99)	0.672
Lacunar infarction	0.88 (0.43-1.78)	0.713
Debilitation	0.99 (0.46-2.12)	0.981

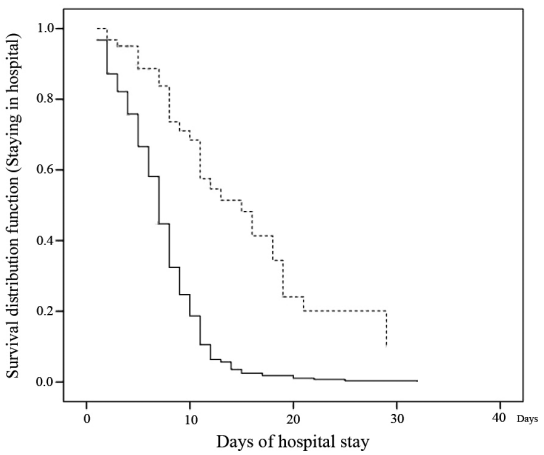

Figure 1 - Cumulative survival distribution function of length of hospital stay for pneumonic patients (dashed line) and other patients (solid line).

stroke.[13] Animal studies have shown the role of stroke induced immunodeficiency in susceptibility to bacterial infections leading to septicemia and pneumonia. Prass and colleagues[14] demonstrated that cerebral ischemia in mice has caused cell mediated immune deficiency (inactivation of monocytes, lymphopenia, and impaired function of natural killer cells) and impaired the production of gamma interferon. On the other hand, all severe inflammatory responses, including pneumonia can induce neuronal injury. This is suggested by the evidence that inhibition of the inflammatory response can improve prognosis of stroke in animal models.[15]

In the present study almost one in every 6 patients with the diagnosis of stroke, acquired pneumonia during the hospitalization period. In other studies, prevalence ranging between 4-23% was reported due to different inclusion criteria and study populations.[5,16] In addition to high prevalence, in some studies, pneumonia is the most important cause of hospital mortality after stroke.[10] Up to 35% of stroke mortality is attributed to pneumonia.[17] Due to the importance of this complication, the occurrence of fever after stroke makes it necessary to investigate signs of pneumonia.[18] In addition to increasing mortality in stroke, similar to other infectious complications, pneumonia may also increase the length of hospital stay. Spratt et al,[19] in a study of 257 acute stroke patients reported that age over 65, diabetes, infections, and disability were associated with a prolonged hospital stay.[19] Al-Eithan et al[20] demonstrated that right sided stroke, diabetes mellitus, and hypertension were associated with a more prolonged hospital stay in Saudi Arabia.[20] Saxena et al[9] in a study on 200 stroke patients in rehabilitating hospitals in Singapore reported that the difference between the length of hospital stay in patients with post stroke aspiration pneumonia and other patients was not statistically significant. The difference between this study and the present study was the study population (patients admitted to a general hospital in our study, and rehabilitation hospital in Saxena et al's study), and inclusion of all kinds of pneumonia in our study and inclusion of only post stroke aspiration pneumonia in Saxena et al's study.

In the study of Hilker et al[7] on 124 patients admitted to the neurological intensive care unit (NICU) with a diagnosis of stroke, the mean length of NICU stay was 6 days longer in patients with pneumonia compared with other patients. In the present study, the increase in length of hospital stay attributed to pneumonia was 4.3 days for all patients, and 3.6 days for patients admitted to the ICU. In the latter group, the difference was not statistically significant probably due to the low number of patients in this group (13 patients).

Ovbiagele and his colleagues[8] in the United States, in 2 consecutive 3-month periods in 2002 and 2003, showed that pneumonia in stroke patients increased hospital stay by 9 days. In their study, 663 patients who were admitted in 11 hospitals in California due to ischemic stroke were evaluated for pneumonia and UTI. According to their results, the incidence of pneumonia was 10%, and the incidence UTI was 13%. In our study, the prevalence of pneumonia calculated as 16.8% did not differ greatly from the mentioned study. Ovbiagele et al's study[8] showed pneumonia not only increased hospital stay time, but also, caused

more mortality during admission periods, and hospital mortality for patients with pneumonia was 6 times greater than the others.

There have been limited studies on the influence of pneumonia on the length of hospital stay in the Middle East region. Hassan et al,[16] at Shafa hospital in Islamabad, Pakistan, over a 4-year period, showed the hospital stay time in patients who had infiltration in chest x-rays was 7 days, and in patients with positive tracheal culture was 9 days more than other patients. In their study, both of these situations were known as independent factors of increasing length of hospital stay.[16] The difference between the present study and that of Hassan et al's is that they excluded patients who had previous neurological problems or were admitted in ICUs, while in the present study they were included. In all studies mentioned above, the length of hospital stay was calculated in all patients. Since in critically ill patients who died in hospital, a decrease in hospital stay does not necessarily indicate a better condition of the patient, and confounds the results, we therefore omitted these patients from the analysis of variables influencing the length of hospital stay.

In addition to pneumonia, in our study, a swallowing disorder was associated with increased length of hospital stay. It is interesting that dysphagia by itself was associated with pneumonia in previous studies. Langdon et al[6] showed dysphagia increased the rate of pneumonia in acute stroke patients in 2 and 7 days after stroke. In Langdon et al's study, dysphagia was also associated with a prolonged hospital stay.[6] Numerous studies have been carried on the cost of hospital stay. For instance, in a study in the United States in 2001,[21] pneumonia increased the average total costs for ischemic stroke care at training hospitals from $17,700 to $29,652. We did not consider cost analysis in the present study, but our results showed 4.3 days longer hospital stay time due to pneumonia (11.5 versus 7.2 days). Clearly, despite the low cost of hospital services in the Middle East, it is not logical to waste health resources by increasing the length of hospital stay. As an important factor for cost saving is reducing unnecessary hospital utilization,[22] it is important to control preventable causes of increased hospital stay. Even ignoring the financial problems, increasing length of hospital stay may lead to nosocomial complications and morbidity in stroke patients.

By considering the high incidence of pneumonia and its complications, and the cost of prolonged hospitalization, numerous studies have evaluated the value of prophylactic antibiotic therapy in patients with ischemic stroke. In a double blinded clinical trial, in Germany between 2003-2006,[23] prophylactic use of "moxifloxacin" decreased infectious complications; however, it did not show any significant effect in neurological complications and mortality, probably due to insufficient sample size, according to the researchers' concept. Although, we cannot suggest prophylactic use of antibiotics in ischemic stroke, the importance of preventional activities for infectious complications is highlighted.

The retrospective design and reliance on medical file contents are the main limitations of this study.

In conclusion, according to the results, and considering the probability of other complications due to prolonged hospital stay, timely diagnosis, and treatment of pneumonia in the acute phase of ischemic stroke is important. Complementary studies for cost analysis and evaluating contributing factors for pneumonia are important and could be interesting topics for further research. Interventional studies exploring the role of prophylactic measures such as antibiotic prophylaxis in acute stroke patients may show acceptable results.

Acknowledgments. *This study was conducted as a General Medicine thesis project in the Medical Faculty of the Qazvin University of Medical Sciences. We thank the staff of the Avicenna Hospital for their help in this study.*

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