Stroke-Associated Pneumonia in Thrombolyzed Patients: Incidence and Outcome

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Background: Stroke-associated pneumonia often negatively influences the prognosis of stroke patients. The aims of this study were to determine the frequency of pneumonia and to investigate the correlation between pneumonia and prognosis in stroke patients receiving intravenous thrombolysis with recombinant tissue plasminogen activator (IV thrombolysis). *Methods:* Between 2008 and 2013, 538 consecutive stroke patients (mean age, 72 ± 13 years; 50.4% women) receiving IV thrombolysis at the Department of Neurology, University of Lübeck, were investigated. *Results:* Pneumonia occurred among 122 patients (23%; 95% confidence interval [CI], 19.1-26.2). Pneumonia patients were older (76 versus 71 years; $P < .001$), more severely affected at admission (National Institutes of Health Stroke Scale [NIHSS] score, 13 versus 9; $P < .001$), and more likely to have atrial fibrillation (54% versus 42%; $P = .02$) than patients without pneumonia. They had also a longer hospitalization (15 versus 10 days; $P < .001$). Using logistic regression analysis, the occurrence of pneumonia was associated with male sex (odds ratio [OR], 1.9; 95% CI, 1.2-3.1; $P = .006$), neurologic deficit severity (NIHSS score ≥10; OR, 4.4; 95% CI, 2.5-7.4; $P < .0019$), previous stroke (OR, 1.5; 95% CI, 1.0-2.2; $P = .06$), and occurrence of symptomatic intracerebral hemorrhage (OR, 1.6; 95% CI, 1.0-3.2; $P = .048$). Mortality rates (in-hospital mortality [18.9% versus 7.0; $P < .0019$]; 3-month mortality [34.3% versus 10.6%; $P < .001$], and 12-month mortality [53.6% versus 19.6%; $P < .001$]) were higher in pneumonia patients than those without. A favorable outcome (modified Rankin Scale score ≤2) was more likely in patients without pneumonia than those with pneumonia (42% versus 7%; $P < .001$). *Conclusion:* Pneumonia was correlated with increased age, male sex, neurologic deficit severity, and a less favorable prognosis. **Key Words:** Stroke—thrombolysis—pneumonia—complication—outcome.

Systemic thrombolysis with recombinant tissue plasminogen activator (rt-PA) is the only proven medicamentous therapy for acute ischemic stroke (AIS) that improves functional outcome.[1] The prognosis for AIS is often negatively influenced by complications like pneumonia.[2] In 21% to 65% of cases, stroke patients also experience infectious complications.[3] Several terminologies regarding diagnosing of stroke-related pneumonia exist in the literature.[4-6]

The incidence of stroke-related pneumonia depends on the setting. Research studies have shown that it varies between 10% and 57% for patients treated in intensive care units and between 4% and 12% for patients treated exclusively in stroke units, whereas the number of hospital-acquired pneumonia merely amounts to 1%.[5-11]

Pneumonia is the most common cause of mortality following acute stroke and is also associated with poor functional outcome.[2,10]

Hilker et al[12] found that stroke-associated pneumonia patients had significantly more severe neurologic deficits

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compared with stroke patients without infections. Traditionally, stroke-associated pneumonia is considered to be secondary to aspiration.[3,4,6,7,13-15] During the past decade, major advances have been obtained in understanding the pathophysiological mechanisms of stroke-associated pneumonia, and some studies have provided evidence for stroke-induced immunodepression.[15-18]

The aims of the present study were to determine the frequency of pneumonia and to investigate the correlation between pneumonia and prognosis after AIS in patients who had received thrombolysis.

Methods

Study Design

All consecutive AIS patients who had received IV thrombolysis to treat AIS at our institution (n = 538; mean age, 72 ± 13 years; 50.4% women; mean National Institutes of Health Stroke Scale [NIHSS] score at admission, 11.3 points) between October 2008 and November 2013 were included and analyzed. Data of patients were collected prospectively. The data acquisition was a part of the stroke register in the Department of Neurology at the University of Lübeck. Approval for the study was obtained from the Ethics Committee of the University of Lübeck. A physician (T.B.) who was not involved in the treatment of patients with AIS at the University of Lübeck retrieved the data. Baseline and sociodemographic characteristics such as gender, age, comorbid conditions, neurologic deficits (NIHSS) on admission, incident complications, clinical findings, and radiologic and laboratory data were identified from clinical records and the hospital information system and are presented in Table 1.

Symptomatic intracerebral hemorrhage (sICH) was diagnosed according to the definition put forth by ECASS II as any bleeding signs in computed tomography scan after IV thrombolysis with a deterioration of 4 or more points in the NIHSS score.[19]

The diagnosis of pneumonia used in our study is made in accordance with the Centers for Disease Control and Prevention criteria. These criteria require the presence of a new and persistent infiltrate or consolidation on at least 1 chest X-ray—or at least 2 serial chest X-rays in cases of underlying lung disease—combined with one of the following clinical signs: fever, leukopenia, or leukocytosis, and altered mental status in individuals who are older than 70 years (in the absence of other causes). These signs should be added to 2 of the following signs: new onset of purulent sputum or change in the characteristics of the sputum, new onset or worsening cough, rales, and worsening of gas exchange.

All stroke patients treated with rt-PA underwent a dysphagia screening as part of the thrombolysis protocol before feeding or oral drug administrations.

Outcome measures were assessed with the modified Rankin Scale (mRS; assessment score for disability and functional status in stroke, range 0 [no symptoms] to 6 points [dead]). Mortality was evaluated at discharge from hospital and after 3 and 12 months. These parameters were acquired by telephone interview with patients, relatives, or family doctors. All patients included in the study were admitted to the Stroke Unit of the Department of Neurology at the University of Lübeck and were treated by stroke neurologists.

Statistics

We used the Statistical Product and Service Solutions (SPSS, IBM Corporation, Armonk, New York, USA) program (version 22) to analyze the data. The data were described with mean and standard deviation values for continuous variables, median and interquartile range values for scores, and absolute numbers and percentages for nominal and categorical variables. We performed a chi-square test to determine the correlation between categorical variables, a *t* test between continuous variables, and a Mann–Whitney test between scores. Adjusted logistic regression was carried out to estimate the odds ratios (ORs). All variables with a P value less than .1 were entered into the logistic regression model. A P value less than .05 was considered as significant.

Results

During hospitalization (average length, 10 days), 122 thrombolyzed AIS patients (22.7%; 95% confidence interval [CI], 19.1-26.2) experienced pneumonia. Patients with pneumonia were older than those without pneumonia (76 versus 71 years, respectively; $P < .001$). In addition, patients with pneumonia were more severely affected than those without pneumonia (NIHSS score, 13 versus 9, respectively; $P < .001$). Patients with atrial fibrillation were more likely to develop pneumonia than those without atrial fibrillation (54% versus 42%, respectively; $P = .02$). An association was not found between pneumonia and hypertension, nor between pneumonia and diabetes mellitus (Table 1). Patients with pneumonia also had longer hospital stays than those without pneumonia (15 versus 10 days, respectively; $P < .001$), The logistic regression (see Table 2) showed associations between pneumonia and the following: male sex (OR, 1.9; 95% CI, 1.2-3.1; $P = .006$), the severity of neurologic deficits (NIHSS score ≥10; OR, 4.4; 95% CI, 2.5-7.4; $P < .0019$), previous stroke (OR, 1.6; 95% CI, 1.0-2.4; $P = .04$), and the incidence of sICH (OR, 1.6; 95% CI, 1.0-3.2; $P = .048$).

Fifty-three of all 538 patients and 23 of all 122 patients with pneumonia died in hospital (9.9 versus 18.9, respectively; $P < .001$). After 3 months, the mortality rates for patients without pneumonia and for those with pneumonia were 10.6% and 34.3% ($P < .001$), respectively, and after 12 months, these rates were 19.6% and 53.6% ($P < .001$), respectively (see Fig 1). A favorable outcome (mRS ≤2) was more likely to occur in patients without pneumonia