

Aspiration pneumonia is an independent risk factor associated with long-term hospital stay: a prospective cohort study

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Abstract

Background

Long-term hospital stay is associated with functional decline in patients with pneumonia especially in the elderly. Among elderly patients with pneumonia, aspiration pneumonia is a major disease category. It is still not clear whether long-term hospital stay is due to aspiration pneumonia itself caused by underlying oropharyngeal dysfunction or simply due to functional decline in elderly patients with multiple comorbidities during acute infection. The observational study aim is to identify whether aspiration pneumonia itself was associated with long-term hospital stay.

Methods

A prospective observational study focused on community-acquired or healthcare-associated pneumonia (HCAP) was carried out from January 2012 through January 2014. Patients at risk for aspiration pneumonia were identified as those who experienced documented episodes of aspiration, chronic disturbances of consciousness and/or chronic neuromuscular diseases. We defined thirty-day hospital stay as long-term hospital stay and compared thirty-day hospital stay between aspiration pneumonia group and the other pneumonia group with logistic regression analysis. Potential confounding factors included age, gender, diagnosis of HCAP, CURB criteria, body mass index, long-term bed-ridden state, heart failure, cerebrovascular disorders, dementia, use of antipsychotics, and use of hypnotics. In a sub-analysis, we also explored factors associated with long-term hospital stay in patients with aspiration pneumonia.

Results

Our study enrolled 2,795 patients; 878 (31.4%) were at risk for developing aspiration pneumonia. After adjusting potential confounders, the aspiration pneumonia is a risk factor of long-term hospital stay (adjusted odds ratio 1.43; 95% confidence interval 1.09 - 1.88, $p < 0.01$). Higher age, male gender, high CURB score, diagnosis of HCAP, low BMI, heart failure, cerebrovascular disease and use of antipsychotics were suggested to be the risk of long-term hospital stay. Sub-analysis revealed factors associated with long-term hospital stay in aspiration pneumonia group that included higher age, male gender, high CURB score, multi-lobar chest X-ray involvement and use of antipsychotic drugs.

Conclusions

Aspiration pneumonia itself was independently associated with long-term hospital stay. This result can lead to move specific rehabilitation strategies for pneumonia patients with underlying oropharyngeal dysfunction.

Background

Pneumonia is one of the most common clinical syndromes and an important public health issue with serious personal and economic ramifications. Pneumonia is currently the third leading cause of mortality in Japan. There are several clinical classifications of pneumonia based on setting, clinical characteristics, causative microbes, and prognosis [1]. Aspiration pneumonia is a distinct and clinically useful category of this disease. This condition is defined as an acute lung infection that develops in response to significant aspiration of oropharyngeal or upper gastrointestinal contents [2]. However, it is sometimes difficult to prove the evidence of aspiration in patients with pneumonia. One previous study used the definition of aspiration pneumonia as pneumonia associated with either witnessed aspiration or risk factors for aspiration and showed that as many as 23% of community-acquired pneumonia (CAP) were aspiration pneumonia [3]. Likewise, another study used the definition as pneumonia in patients with a predisposition to aspiration and indicated that up to 60% of hospitalized patients with CAP were found to be aspiration pneumonia [4]. Therefore, aspiration pneumonia is often clinically defined as pneumonia occurring in patients with risk factors for aspiration as well as that occurring after witnessed aspiration episode [5]. As a result, aspiration pneumonia is a familiar condition to most clinicians.

In recent years, hospitalization costs associated with aspiration pneumonia have been increasing in the United States [6]. Previous studies have revealed that a single episode of acute illness involving hospitalization can be accompanied by functional decline, deterioration in performance of activities of daily living (ADLs), and the need for long-term care [7–12]. A decline in capacity to perform ADLs was particularly notable for elderly patients who were hospitalized due to lower respiratory infections [13]. Long-term hospital stay has been associated with functional decline [14] and can lead to a substantial decrease in quality of life (QOL) [15, 16]. In this way, long-term hospital stay with aspiration pneumonia may also cause a large amount of medical expenses and lower the ADLs and QOL of hospitalized patients.

It is still not clear whether long-term hospital stay is simply due to functional decline in elderly patients with acute infection or rather due to pneumonia in patients with underlying oropharyngeal dysfunctions, which are the risk factors for aspiration. The answer to this question can provide a better focus on specific rehabilitation strategies. The goal of our study is to clarify whether or not aspiration pneumonia per se represents an independent risk factor associated with long-term hospital stay. We conducted a prospective cohort study to identify the relationship between aspiration pneumonia and long-term hospital stay among patients with CAP or healthcare-associated pneumonia (HCAP). As a sub-analysis, we explored the potential risk factors that might be independently associated with long-term hospital stay in the group of patients with aspiration pneumonia.

Method

Design and setting / study population

This research was performed as a part of a multicenter prospective study of adult pneumonia by Adult Pneumonia Study Group-Japan (APSG-J) [17]. The APSG-J study enrolled patients from four community-

based hospitals in Japan from September 2011 to January 2014. We collected information from the medical records of patients diagnosed with CAP and HCAP including age, gender, diagnosis of aspiration pneumonia, laboratory data, comorbidities, and measures of disease severity. Hospital physicians provided a clinical diagnosis that included the presence or absence of aspiration as indicated on the patient data form.

All hospitalized patients and outpatients aged 15 years or older were screened by hospital physicians; patients who met the standard case definition were identified. Patients who fulfilled all the following criteria were enrolled in the study: (1) age ≥ 15 years, (2) symptoms indicative of pneumonia (e.g., fever, cough, sputum, pleuritic chest pain, and dyspnea), and (3) evidence of new-onset pulmonary infiltrates on chest radiography and/or computed tomography scan films that were consistent with this diagnosis. All the enrolled cases were classified as CAP or HCAP according to the definitions in the American Thoracic Society (ATS) / Infectious Diseases Society of America guidelines [18, 19]. Patients diagnosed with HCAP were those who were hospitalized for ≥ 2 days in the preceding 90 days, who were residents of a nursing home or extend-care facility, those receiving home infusion therapy (including antibiotics) or who underwent chronic dialysis within 30 days of diagnosis, and those treated with home wound care or who have a family member diagnosed with multi-resistant pathogens. Patients who developed signs and symptoms within 48 hours after admission were diagnosed with hospital-acquired pneumonia patients; these patients were excluded from this research study. Likewise, repeated episodes of pneumonia in a single patient within 2-week period were regarded as a single episode.

Exposure

Aspiration pneumonia was defined as a pneumonia that develops in patients at high risk for aspiration. Patients at high risk for aspiration were those who experienced previous episodes of aspiration, those with chronic disturbances of consciousness or chronic neuromuscular diseases [20–22]. As confounding factors for long-term hospital stay, we selected age, gender, a diagnosis of HCAP, CURB score, body mass index (BMI), long-term bed-ridden state, heart failure, cerebrovascular disorders, dementia, use of antipsychotic and use of hypnotic drugs. The confounding factors were selected as variables associated with both exposure and outcome based on the previous studies and medical findings. Age is included in CURB65 [23], a severity classification of pneumonia, and is known to be associated with risk of mortality [24]. Male gender was shown to be associated with high mortality among pneumonia patients [25]. We used the CURB criteria [26] excluding the age factor from CURB65 in order to adjust more accurately the effect of age. CURB criteria is also known as the severity of pneumonia [26]. The HCAP [19, 27], BMI [28] and ADL [29] have been associated with pneumonia-associated mortality; as such, we included these factors as potential confounders as a way to adjust for patient disease severity. The HCAP classification has recently been deleted from the guidelines; however, we considered this classification as a simple indicator for estimating disease severity. A long-term bed ridden was adopted as a surrogate index for ADL. In comorbidity and drug, heart failure was shown to be risk of mortality in CAP patients [30] and

cerebrovascular disorder [31], dementia [32], use of antipsychotic drugs [33], and use of hypnotic drugs [34] have all been associated with aspiration pneumonia in previous studies.

For sub-analysis, we sought to identify independent variables associated with long-term hospital stay due to aspiration pneumonia. We selected potential risk factors for long-term hospital stay that showed a significant difference in the univariate analysis between the aspiration pneumonia group and the other pneumonia group. For this analysis, the aforementioned factors were evaluated as potential independent variables, and long-term hospital stay was introduced as the dependent variable.

Outcomes

The primary outcome was long-term hospital stay. We defined the long-term hospital stay as thirty-day or longer hospitalization. The term, thirty-day, was often used as the standard criteria regarding with mortality and readmission in various studies.

In the sub-analysis, we aimed to explore the potential independent factors associated with long-term hospital stay in patients with aspiration pneumonia.

Statistical analysis

Baseline characteristics were presented using standard descriptive statistics, including means for age and laboratory data, median for length of hospital stay and percentages for categorical variables. For the primary outcome, adjusted odds ratios (AORs) and 95% confidence intervals (CIs) for likelihood of having long-term hospital stay were estimated using a multiple logistic regression model. In the logistic regression model, we adjusted for the clinically relevant potential confounding factors. As we could not feasibly neglect missing values for certain variables, we encoded these missing values as "unknown states" and included them in the analysis. This facilitated inclusion of all patients in the primary analysis. For the sub-analysis, we performed logistic analysis in order to identify significant risk factors associated with long-term hospital stay in the aspiration pneumonia patient cohort. A p -value of < 0.05 was considered to be statistically significant. All analyses were performed with SPSS version 22.0 for Windows (SPSS Inc, Chicago, IL, USA).

Ethical consideration

The study was conducted in accordance with the Guideline for Ethical Aspects in Epidemiological Study (Ministry of Health, Labour and Welfare, Japan 2008). This study was approved by the Institutional Review Board of the Tropical Medicine at Nagasaki University and the institutional review board of each participating hospitals; Ebetsu City Hospital, Kameda Medical Centre, Chikamori Hospital, and Juzenkai Hospital. We used a standardized questionnaire form to provide patients and their guardians with necessary information. Written informed consent to participate in this study was obtained from

participants or their guardians. Investigators maintain all patient-related datasets in password-protected systems and present the data in this manuscript while maintaining the anonymity of the study participants.

Results

Baseline Characteristics

The original cohort study included 3,020 patients. Of these, 225 patients were excluded; 114 patients did not meet the inclusion criteria, 100 patients lacked the information of aspiration risk factors, and 11 patients lacked outcome data. As such, we enrolled 2,795 patients with diagnoses of CAP or HCAP in this study (Figure 1). Of this group, 878 patients were included in the aspiration pneumonia group (31.4%); 703 of these patients had documented episodes of aspiration, 151 had chronic disturbances of consciousness, and 179 were diagnosed with chronic neuromuscular diseases that did not include previous stroke or dementia. Some patient cases included more than one risk factor. Patient characteristics are summarized in Table 1. Median (interquartile range; IQR) for age was 78 (66–85) years; 59.5% of the participants were males. 95.7% of aspiration pneumonia patients were hospitalized, and the median length of hospital stay was 19 days (IQR 12-31 days).

Primary Outcome

We estimated AORs of long-term hospital stay associated with aspiration pneumonia (Table 2). After adjusting potential confounders, the aspiration pneumonia is independently a risk factor of long-term hospital stay (AORs 1.43; 95% CIs 1.09 - 1.88, $p < 0.01$). Higher age (AORs 1.01; 95% CIs 1.002 - 1.02, $p < 0.05$), male gender (AORs 1.38; 95% CIs 1.06 - 1.80, $p < 0.05$), high CURB score (AORs 1.29; 95% CIs 1.13 - 1.47, $p < 0.01$), diagnosis of HCAP (AORs 1.47; 95% CIs 1.11 - 1.94, $p < 0.01$), low BMI (AORs 0.95; 95% CIs 0.92 - 0.98, $p < 0.01$), heart failure (AORs 1.40; 95% CIs 1.03 - 1.92, $p < 0.01$), cerebrovascular disease (AORs 1.34; 95% CIs 1.01 - 1.76, $p < 0.01$) and use of antipsychotics (AORs 1.51; 95% CIs 1.06 - 2.16, $p < 0.05$) were suggested to be the risk of long-term hospital stay.

Sub analysis

Of the 878 patients diagnosed with aspiration pneumonia, 229 (26.1%) were among those who experienced a long-term hospital stay. In univariate analysis, there was a significant difference in male gender, CURB ($3 \leq$), multi-lobar chest X-ray involvement, hypoalbuminemia ($< 3\text{g/dl}$), liver disease, kidney disease and use of antipsychotics between two groups (supplemental table 1). We added variable related to age to these factors and we set them as confounding factors.

In this sub-analysis, we found that higher age (≥ 75) (AORs 1.81; 95% CIs 1.18–2.79, $p < 0.01$), male gender (AORs 1.54; 95% CIs 1.08–2.21, $p < 0.05$), high CURB score ($3 \leq$) (AORs 2.29; 95% CIs 1.38–3.79, $p < 0.01$), multi-lobar involvement chest X-ray involvement (AORs 1.50; 95% CIs 1.05–2.21, $p < 0.05$) and use of antipsychotic drugs (AORs 1.60; 95% CIs 1.02–2.52, $p < 0.05$) were among the independent risk

factors associated with a longer hospital stay among patients diagnosed with aspiration pneumonia (Table 3).

Discussion

We identified aspiration pneumonia itself as an independent risk factor associated with long-term hospital stays. We also identified that higher age, male gender, high CURB score, multi-lobar chest X-ray involvement and use of antipsychotic drugs were associated with long-term hospital stay among patients with aspiration pneumonia in an exploratory sub-analysis.

The reason why aspiration pneumonia itself is associated with long-term hospital stay may be that dysphagia in pneumonia patients is an inhibitory factor of discharge from hospital. Previous studies also revealed that aspiration pneumonia was associated with an increase in recurrent pneumonia [35]. This condition may result from repeated aspiration, either silent or in evidence, which may result in long-term hospital stay even when the pneumonia itself is adequately treated. Therefore, both pre-, in-, and post-hospital interventions are important.

The most important pre-hospital intervention may be disease prevention. Implementation of preventive measures, including drug therapy, vaccination and/or rehabilitation, is a critical intervention, notably in patients with risk factors for aspiration. As an in-hospital intervention, in addition to adequate antibiotic therapy, early rehabilitation and physical therapy have been shown to shorten the length of hospital stay in patients with dysphagia[36]. Follow-up management strategies such as newer rehabilitation approaches of stimulation techniques for patients with aspiration pneumonia due to dysphagia have already been recommended [37].

In addition to aspiration pneumonia itself, our study also suggests that higher age, male gender, high CURB score, diagnosis of HCAP, low BMI, heart failure, cerebrovascular disease and use of antipsychotics are also independently associated with long-term hospital stay. Higher age, male gender, high CURB score, diagnosis of HCAP, and low BMI may indicate the severity of the disease. The presence of heart failure, cerebrovascular disease may prolong the care of pneumonia itself or prolong the time required for rehabilitation. Use of antipsychotics may cause an impaired consciousness and delirium which may extend the length of hospital stay.

In the sub-analysis, we identified that higher age, male gender, high CURB score, multi-lobar involvement as revealed by chest radiography and use of antipsychotic drugs were the risks of long-term hospital stay in the aspiration pneumonia group. As mentioned above, higher age, male gender, and high CURB score were shown to be associated with mortality. In some studies, multi-lobar chest X-ray involvement [38, 39] were used as a tool for prediction of the need for hospitalization among patients diagnose with pneumonia. Use of antipsychotic drugs may affect the patient's oropharyngeal function [33]. It is necessary of further research whether the length of hospital stay for aspiration pneumonia can be shortened by discontinuing use of antipsychotics. The sub-analysis outcomes might be used to predict the risk of a long-term hospital stay among those patients diagnosed with aspiration pneumonia.

Antipsychotic drug use can be a modifiable factor for inhibiting long term hospital stay in patients with aspiration pneumonia.

Our study has some limitations. The first limitation relates to the functional and morphological definition of aspiration pneumonia. In this study, we did not confirm the dysphagia using a laryngeal endoscopic procedure. Thus, the definition of aspiration pneumonia does not include the confirmation of functional abnormalities. However, in real clinical practice, we do not always use laryngeal endoscopy to diagnose aspiration pneumonia. Therefore, we used the clinical definition, pneumonia occurring in patients with risk factors for aspiration.

Next, we selected potential confounding factors when generating adjustments in the multivariate analysis. However, there is a possibility that unmeasured confounding factors influence the outcomes. Especially, social factors, such as annual income and public support, can affect the length of hospital stay. However, thanks to the universal healthcare insurance system of Japan, financial factors for medical care may minimally affect the length of hospital stay in Japan.

Finally, we note that the relationship between aspiration pneumonia and the primary outcome was represented by the AORs 1.43 with 95% CIs of 1.09–1.88. The magnitude of aspiration pneumonia itself as a factor for long term hospital stay was not very outstanding. Comprehensive management including those for other modifiable factors is necessary to prevent long-term hospital stay in patients with aspiration pneumonia.

Conclusions

In this observational cohort study, we found that aspiration pneumonia itself was an independent risk factor associated with long-term hospital stays. We also identified that higher age, male gender, high CURB score, multi-lobar involvement as revealed by chest radiography and use of antipsychotic drugs were associated with long-term hospital stay among patients with aspiration pneumonia.

Abbreviations

AOR

Adjusted odds ratio

BMI

Body mass index

CAP

Community-acquired pneumonia

CI

Confidence interval

CURB65

Confusion, elevated blood urea nitrogen, tachypnea, hypotension, and age ≥ 65

HCAP
Healthcare-associated pneumonia
HR
Hazard ratio
QOL
quality of life

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Guideline for Ethical Aspects in Epidemiological Study (Ministry of Health, Labour and Welfare, Japan 2008). This study was approved by the Institutional Review Board of the Tropical Medicine at Nagasaki University and the institutional review board of each participating hospitals; Ebetsu City Hospital, Kameda Medical Centre, Chikamori Hospital, and Juzenkai Hospital. We used a standardized questionnaire form to provide patients and their guardians with necessary information. Written informed consent to participate in this study was obtained from participants or their guardians. Investigators maintain all patient-related datasets in password-protected systems and present the data in this manuscript while maintaining the anonymity of the study participants.

Consent for publication

Not applicable

Availability of data and materials

The original data in the current study can be available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

Conception and design of the analysis: TW, SH, KM. Management of case enrollment and data collection: TW, SH, KM. Data analysis and interpretation: TW, SH, KM. Drafting the manuscript: TW, SH, KM. All

authors contributed to the critical revision of the manuscript and approved the final version.

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Tables

Tables 1 to 3 are available in the Supplementary Files section.

Figures

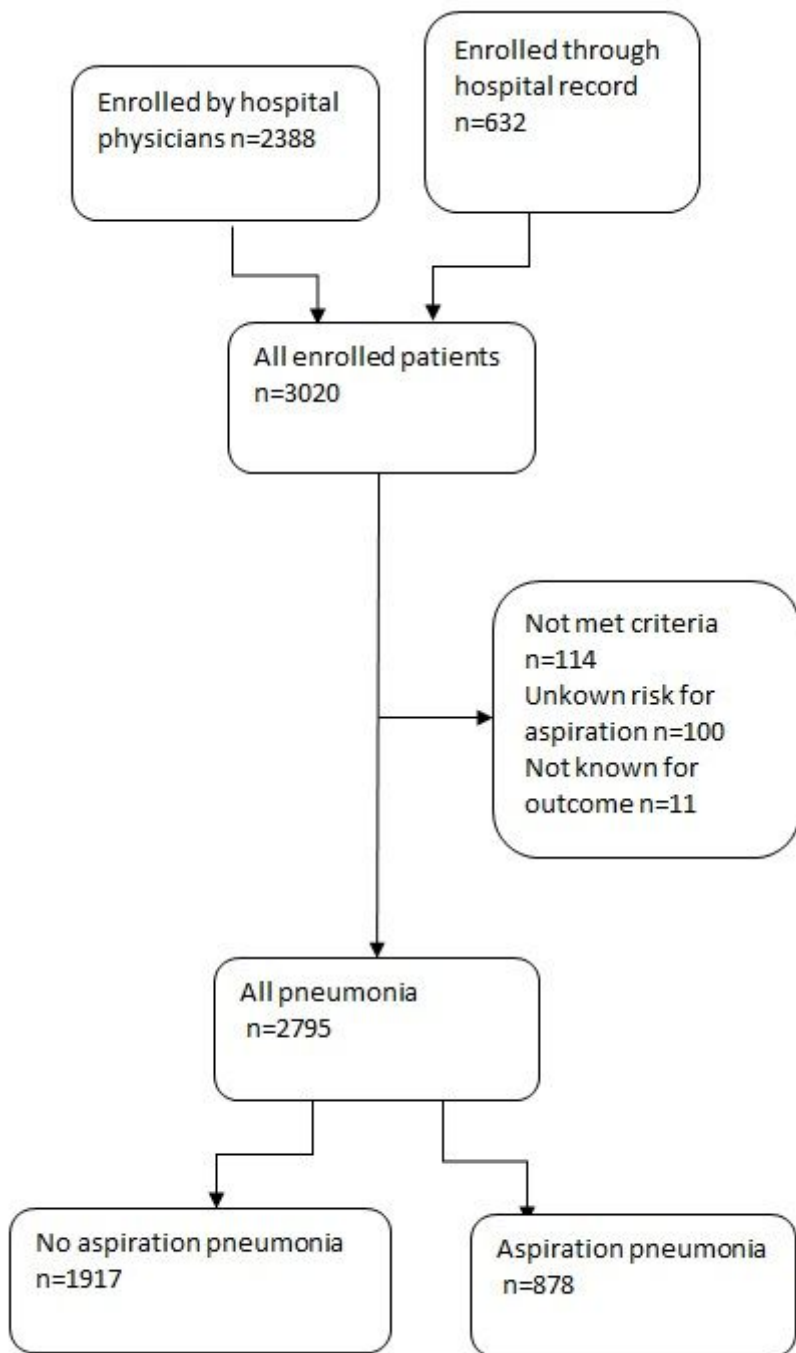


Figure 1

Selection of participants

Supplementary Files

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