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Original Article

Risk factors for the severity and mortality of pneumococcal pneumonia: Importance of premorbid patients' performance status

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ABSTRACT

Comorbidity is known to be associated with the severity and mortality of pneumonia. The severity of each underlying disease varies, and performance status, which is known to be a prognostic factor of malignant diseases, reflects the overall patient condition as affected by his/her comorbidity and underlying diseases of various severity. We investigated whether premorbid patients' performance status is associated with the severity and mortality of pneumococcal pneumonia. This retrospective study assessed these factors in hospitalized patients suffering from pneumococcal pneumonia from 2002 to 2015. We included 424 patients aged 68.9 ± 14.1 years in the study, of which 68.9% were men. A multivariate analysis found that advanced age (≥65 years), diabetes mellitus, and poor performance status were independent factors associated with severity, whereas old pulmonary tuberculosis, poor performance status, pneumococcal bacteremia, and severe pneumonia were independent factors that were associated with non-survival. Poor performance status was associated with the severity and mortality of pneumococcal pneumonia.

1. Introduction

Pneumonia is a common infection that is potentially life threatening, especially in older adults and those with comorbid disease. Pneumonia was the 3rd most common cause of death in Japan in 2013 and the leading cause of death from infectious disease. Among the etiologies of pneumonia, *Streptococcus pneumoniae* is known as the most common causative pathogen in overall cases, severe cases, and non-survivors of both community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP) [1]. To establish better management practices for pneumococcal pneumonia, the factors which contribute to severe pneumonia and pneumonia-associated mortality should be clarified. Several studies have assessed these factors in adult pneumococcal pneumonia patients; however, most of these studies only investigated patients with invasive pneumococcal pneumonia (IPP) [2–5]. As many as 90% of adult pneumococcal pneumonia cases are not classified as IPP [6]. Given that IPP accounts for such a limited subpopulation of pneumococcal pneumonia patients, it is possible that analyses which only include IPP cases may not reflect the exact clinical features of pneumococcal pneumonia. Only two studies have investigated the factors contributing to severity and mortality in pneumococcal pneumonia in a population that included patients with non-invasive pneumonia [6,7]. Further investigation of these factors may yield useful information for treatment and prevention strategies.

Comorbidity is known to be associated with severity and mortality in pneumonia; however, the degree of each comorbidity differs among patients. Functional assessment of patients' daily living is also a prognostic factor [8]. Performance status (PS), which describes patients' level of functioning in terms of their ability to care for themselves, daily activity, and physical ability, reflects their comorbidities and has prognostic significance, especially in advanced cancer. Only a limited number of reports have shown the usefulness of PS as a prognostic factor of pneumonia in several settings [9–13]. Thus, we hypothesized that PS might be associated with the severity and mortality of pneumococcal pneumonia. Therefore, we investigated the risk factors associated with severity

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and mortality in pneumococcal pneumonia in a study population that included patients with invasive and non-invasive disease with a special focus on PS.

2. Patients and methods

We performed a retrospective study of 424 patients who were hospitalized with pneumococcal pneumonia (CAP and HCAP) at our institution in Saitama, Japan, from January 2002 to 2015. The study protocol was approved by the Ethics Committee of Saitama Cardiovascular and Respiratory Center (approved December 14, 2015. No. 2015034). Pneumonia was diagnosed on the basis of symptoms suggestive of lower respiratory tract infection and the development of infiltration on chest X-ray films. CAP and HCAP were defined according to the Infectious Disease Society of America (IDSA)/American Thoracic Society (ATS) consensus guidelines [14,15]. Severe pneumonia was defined when at least one major criterion or three minor criteria of the IDSA/ATS guidelines [14] were present. The premorbid PS was recorded on admission based on anamnesis from the patients and the patients' families and classified based on the criteria suggested by the Eastern Cooperative Oncology Group [16]. The criteria of PS are as follows: Grade 0: fully active, able to carry on all pre-disease performance without restriction; Grade 1: restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (e.g., light housework, office work); Grade 2: ambulatory and capable of all self-care but unable to carry out any work activity up and about more than 50% of waking hours; Grade 3: capable of only limited self-care, confined to bed or chair more than 50% of waking hours; Grade 4: completely disabled, unable to carry on any self-care, totally confined to bed or chair; Grade 5: dead. Patients with acquired immunodeficiency syndrome, tuberculosis, non-resected lung cancer, or an alternative diagnosis that was confirmed until the end of the follow-up period were excluded from the present study. The diagnosis of causative microorganisms was based on the results of semi-quantitative cultures of respiratory samples or blood, paired sera, urinary antigen tests (UATs) for *S. pneumoniae* and *Legionella pneumophila*, and nasopharyngeal swabs for influenza virus, as reported previously [17,18]. Colony morphologies were distinguished by viewing them with oblique transmitted light on transparent agar surfaces.

The treatment prescribed during the first 24 h of hospitalization was considered to be the initial treatment. Concordant CAP therapy was defined according to the established IDSA/ATS guidelines [14].

The variables that were assessed in association with severe pneumonia and which were considered to be possible risk factors for 30-day mortality included the patient's demographic factors, the presence of comorbid diseases, PS, the previous administration of antibiotics by a local physician, mixed infection, the disease severity on admission, and the antibiotics that were used in the initial treatment.

2.1. Statistical analysis

The results are presented as numbers and percentages or means ± standard deviation unless otherwise indicated. Risk factors for severity on admission and mortality due to pneumococcal pneumonia were evaluated by univariate and multivariate logistic regression analyses. Variables that were found to be significant by univariate analysis were included in the multivariate logistic regression analysis. In all instances, a 2-tailed P value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

3. Results

3.1. Patient characteristics

Overall, 424 patients with pneumococcal pneumonia were investigated. The characteristics of the patients are shown in Table 1. The patients were 68.9 ± 14.1 years of age and 292 (68.9%) were men. Thirty-five patients had a poor PS (PS 3 or 4) before admission, whereas the PS could not be determined in 58 patients because of difficulty in anamnesis on admission due to the patient's severe general condition or because the information was not included in the patient's medical records. The methods for diagnosing the causative microorganisms and the results obtained are listed in Table 2. *S. pneumoniae* cultures were positive in 164 (38.7%) patients (blood, 17 of 277 [6.1%]; sputum, 152 of 381 [39.9%]; bronchial washing, 2 of 4 [50.0%]; and bronchoalveolar lavage fluid, 3 of 6 [50.0%]; the sum exceeds 164 because multiple samples were positive in some patients). Seventeen patients (3.9%) had received a 23-valent pneumococcal polysaccharide vaccine within the previous 5 years, but none had received a pneumococcal conjugated vaccine. Twenty-seven patients had received an influenza virus vaccination within the previous year. Respiratory failure on admission was present in 192 patients, and 81 (19.1%) were classified as having severe pneumonia. After admission, guideline-

Table 1
Patients characteristics.

Characteristic		Value
Age (years)		68.9 ± 14.1
Male sex		292 (68.9)
Smoking history		268 (63.2)
Vaccination history		
23-valent polysaccharide vaccine (within 5 years)		17 (4.0)
Influenza vaccine (within one year)		27 (6.4)
CAP/HCAP		286/138
Comorbidity		
Chronic pulmonary disease		229 (54.0)
Chronic obstructive pulmonary disease		102 (24.1)
Asthma		59 (13.9)
Bronchiectasis		20 (4.7)
Nontuberculous mycobacteriosis		18 (4.2)
Old pulmonary tuberculosis		22 (5.2)
Chronic pulmonary aspergillosis		7 (1.7)
Interstitial pneumonia		28 (6.6)
Post lung cancer operation		9 (2.1)
Hypertension		58 (12.7)
Chronic cardiac disease		58 (13.7)
Congestive heart failure		26 (6.1)
Ischemic heart disease		19 (4.5)
Valvular heart disease		6 (1.4)
Arrhythmia		25 (5.9)
Diabetes mellitus		42 (9.9)
Post surgery of upper digestive system		12 (2.8)
Chronic liver disease		12 (2.8)
Connective tissue disease		14 (3.3)
Psychiatric disease		10 (1.0)
Malignancy		7 (1.7)
Alcoholism		2 (0.5)
Steroid or immunosuppressant use		28 (6.6)
Chronic kidney disease		7 (1.7)
Neurological disorders		35 (8.3)
Performance status	0–2	331 (78.1)
	3–4	35 (8.3)
	Unknown	58 (13.7)
Severe		81 (19.1)
Mortality		22 (5.2)

The data presented as means ± standard deviation or n (%). CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia.
Some patients had more than one comorbidity.