ORIGINAL PAPER

Nagoya J. Med. Sci. **84**. 247–259, 2022
doi:10.18999/nagjms.84.2.247

Clinical characteristics and risk factors for mortality in patients with community-acquired staphylococcal pneumonia

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ABSTRACT

Staphylococcus aureus (*S. aureus*) is increasing in prevalence as a causative pathogen of community-acquired pneumonia (CAP). However, reports on the clinical features and mortality risk factors for *S. aureus* CAP are limited. We therefore aimed to identify the clinical characteristics and risk factors for mortality in these patients. We performed a post hoc and multivariate analysis of a multicenter prospective observational study that included adult hospitalized patients with *S. aureus* CAP. To elucidate the features of *S. aureus* CAP, we comparatively analyzed pneumococcal CAP (PCAP). We analyzed 196 patients with *S. aureus* CAP and 198 patients with PCAP. *S. aureus* CAP had a 30-day mortality of 16% (31/196) and a higher frequency of factors such as advanced age, comorbidities, poor functional ability, altered mental status, hypoalbuminemia, hyponatremia/hypernatremia, acidemia, and hypoxemia. In the multivariate analysis, the significant risk factors for mortality in *S. aureus* CAP were PaO_2/FiO_2 ≤250 [adjusted odds ratio (AOR), 3.29; 95% confidence interval (CI), 1.20–9.04] and albumin <3.0 g/dL (AOR, 2.41; 95% CI, 1.01–5.83). Non-ambulatory status tended to increase the risk (AOR, 2.40; 95% CI, 0.93–6.17). Methicillin resistance was not associated with mortality. In PCAP, hypoalbuminemia and non-ambulatory status affected mortality but hypoxemia did not. In conclusion, patients with *S. aureus* CAP have distinct clinical features, and their mortality risk factors can include hypoxemia and hypoalbuminemia. Physicians should recognize that the factors influencing mortality might differ somewhat among causative pathogens, and appropriate management should be performed after obtaining information on the causative pathogen.

Keywords: *Staphylococcus aureus*, community-acquired pneumonia, pneumococcal pneumonia, clinical characteristics, mortality

Abbreviations:
S. aureus: *Staphylococcus aureus*
CAP: community-acquired pneumonia

Received: April 5, 2021; accepted: July 21, 2021
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MRSA: methicillin-resistant *Staphylococcus aureus*
MSSA: methicillin-susceptible *Staphylococcus aureus*
HCAP: healthcare-associated pneumonia
PSI: Pneumonia Severity Index
BUN: blood urea nitrogen
BP: blood pressure
PVL: Panton-Valentine leukocidin
TSST-1: toxic shock syndrome toxin-1
SCC*mec*: Staphylococcal Cassette Chromosome *mec*
CI: confidence interval
AOR: adjusted odds ratio
CNS: central nervous system
GCS: Glasgow Coma Scale

INTRODUCTION

Pneumonia is one of the leading causes of death worldwide.[1] *Staphylococcus aureus* (*S. aureus*), one of the causative pathogens of community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP), is increasing in prevalence.[2] Several reports have shown the emergence of *S. aureus* CAP as one of the causes of severe pneumonia leading to critical illness and death.[2-7] To provide better management practices for patients with *S. aureus* CAP, their clinical characteristics and factors contributing to mortality should be clarified.

The initial step in managing patients with CAP is to assess pneumonia severity to determine site-of-care. In recent decades, scoring systems have been developed such as the Pneumonia Severity Index (PSI) and CURB-65 [confusion, blood urea nitrogen (BUN) > 7 mmol/L (20 mg/dL), respiratory rate ≥ 30 bpm, low blood pressure (BP) (diastolic BP ≤ 60 mm Hg or systolic BP < 90 mm Hg), and age ≥ 65 years].[8,9] These scoring systems help physicians distinguish patients with CAP at low mortality risk from those at high risk at the diagnosis of pneumonia. However, these scoring systems consist of findings observed at diagnosis, and the microbiological test results usually obtained after diagnosis are not included in the systems. Furthermore, the microbial etiology of CAP has been demonstrated to be a mortality risk factor.[10] Thus, the types and weight of risk factors for adverse outcomes might differ among patients with CAP according to the causative organisms. Studies on patients with pneumococcal pneumonia have revealed various prognostic factors.[11,12]

However, studies to date on the risk factors for poor outcomes in *S. aureus* CAP have been scarce and have focused on identifying the microbial risk factors for poor outcomes, especially in methicillin-resistant *Staphylococcus aureus* (MRSA), such as the Panton-Valentine leukocidin (PVL) gene, the toxic shock syndrome toxin-1 (TSST-1) gene, arginine dysfunction, and Staphylococcal Cassette Chromosome *mec* (SCC*mec*) types.[13,14] To our knowledge, host factors for mortality in *S. aureus* CAP have not been clarified. We therefore designed this post hoc analysis study to investigate the clinical characteristics and mortality risk factors for *S. aureus* CAP using a dataset from a prospective multicenter observational study.

PATIENTS AND METHODS

Study design and setting

This study employed prospectively collected data from an observational multicenter study of patients with pneumonia, which was conducted from March 15 to December 22, 2010 at 10 medical institutions in Japan[15] that were members of the Central Japan Lung Study Group. This study was approved by the institutional review boards of the medical institutions. The study protocol adhered to the Japanese Ethical Guidelines for Epidemiological Studies. Although informed consent was not required from the study participants, the study information was disclosed to the target patients through the Internet, brochures, and bulletin boards at the participating institutions to give the candidates the opportunity to decline participation. This study was registered with the University Medical Information Network in Japan (number UMIN000003306).

Patients

All adult patients (aged ≥ 20 years) hospitalized with CAP or HCAP were enrolled. The definitions of pneumonia, CAP, and HCAP followed the international guidelines.[16] *S. aureus* CAP was defined as the detection of *S. aureus* in cultures from sputum samples, tracheobronchial aspirates, bronchoalveolar lavage fluid, pleural fluid, and blood. The *S. aureus* CAP group included MRSA and methicillin-susceptible *Staphylococcus aureus* (MSSA). Pneumococcal CAP was defined when *S. pneumoniae* was detected in the cultures from the samples mentioned above. Patients in whom *S. pneumoniae* and other pathogens were co-detected were not included in the pneumococcal CAP group. Patients with co-detection of *S. aureus* and *S. pneumoniae* were included in the *S. aureus* CAP group. Details on the inclusion and exclusion criteria are described elsewhere.[15]

Procedure and data collection

Details on the definition of variables, procedures, data collection, and micro bacteriological assessment in the prospective study were described previously.[15] Antibiotic treatment was classified as appropriate initial antibiotics when identified pathogens were susceptible to the initially prescribed antibiotics.

Endpoint

The primary endpoint in this study was 30-day all-cause mortality, which was defined as death within 30 days of the pneumonia diagnosis.

Statistical analysis

We performed statistical analyses with SPSS (version 25). All tests were two-tailed, and a p-value < 0.05 was considered significant. We employed Pearson's chi-squared test or the Mantel extension test for trends in the analysis of discrete variables. For the analysis of risk factors for 30-day mortality in *S. aureus* CAP, we performed univariable and multivariate analyses. The univariate analysis employed the following variables: sex, age, comorbidities, non-ambulatory status, physical findings, laboratory findings and radiographic findings, variables decided *a priori* by referring to previous reports.[8,9,17-22] When determining the cutoff values of the continuous variables, we considered the values from previous studies and performed histograms for each variable in this study.

We performed a multivariate logistic regression analysis using a forced entry selection method with variables that had significant p-value in the univariate analysis ($p \leq 0.05$) in addition to the following variables: age, sex, and presence of methicillin resistance. We calculated the adjusted odds ratios (AORs) and corresponding 95% confidence intervals (CIs).

Subgroup analyses of the patients with pneumococcal pneumonia were performed to compare the risk and risk factors for 30-day mortality between the *S. aureus* and pneumococcal CAP groups.

RESULTS

Patient flow and characteristics

In total, 1413 of the 1742 assessed patients with pneumonia were identified as eligible, 526 of whom had HCAP. Of the eligible patients, 196 (14%) were identified with *S. aureus* CAP, and 198 had pneumococcal CAP (14%). The *S. aureus* CAP group included 119 patients (61%) with MSSA and 77 patients (39%) with MRSA and had a 30-day mortality of 16% (31 deaths) (Figure 1). Table 1 shows the characteristics of the two CAP groups; the pneumococcal CAP patients are shown as a reference. Certain clinical characteristics were more prevalent in the *S. aureus* CAP group, including age ≥ 80 years, central nervous system (CNS) disorder, non-ambulatory

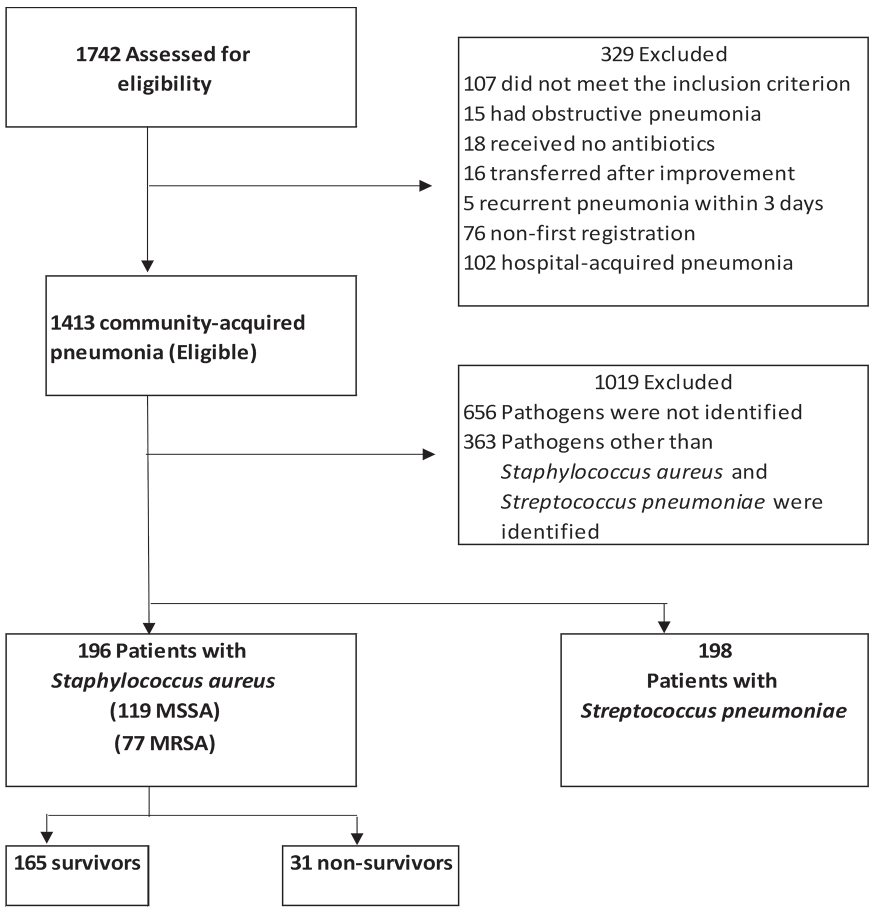

Fig. 1 Patient flow

MRSA: methicillin-resistant *Staphylococcus aureus*
MSSA: methicillin-susceptible *Staphylococcus aureus*

status, Glasgow Coma Scale (GCS) ≤ 12, albumin < 3.0 g/dL, sodium levels < 130 or ≥ 150 mEq/L, pH < 7.35, ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO_2/FiO_2) ≤ 250, and bilateral lung involvement. Eighty-eight percent of the *S. aureus* CAP group were classified into more severe PSI classes (IV and V).

Table 1 Patient characteristics

Variables	All CAP (n = 1413)	*Staphylococcus aureus* (n = 196)	*Pneumococcus* (n = 198)
Age ≥80 years	572 (40.5)	91 (46.4)	62 (31.3)
Sex, male	915 (64.8)	124 (63.3)	122 (61.6)
Comorbidities			
Neoplastic diseases	208 (14.7)	27 (13.8)	24 (12.1)
Chronic lung diseases	470 (33.3)	71 (36.2)	53 (26.8)
Congestive heart failure	183 (13.0)	32 (16.3)	15 (7.6)
Chronic renal diseases	113 (8.0)	14 (7.1)	15 (7.6)
Chronic liver diseases	53 (3.8)	6 (3.1)	8 (4.0)
Central nervous system disorders	304 (21.5)	64 (32.7)	25 (12.6)
Diabetes	258 (18.3)	31 (15.8)	35 (17.7)
Immunosuppression	129 (9.1)	14 (7.1)	22 (11.1)
Non-ambulatory status	338 (23.9)	82 (41.8)	35 (17.7)
Physical findings			
Glasgow Coma Scale ≤12	249 (17.6)	61 (31.1)	21 (10.6)
Pulse rate ≥125 beats per min	140 (9.9)	24 (12.2)	20 (10.1)
Systolic blood pressure <90 mm Hg	81 (5.5)	22 (11.2)	14 (7.1)
Respiration rate ≥30 breaths per min	314 (22.2)	48 (24.5)	43 (21.7)
Laboratory findings			
Hematocrit <0.3	213 (15.1)	33 (16.8)	24 (12.1)
Platelet count <120,000/mm^3	115 (8.1)	18 (9.2)	14 (7.1)
Albumin <3.0 g/dL	478 (33.8)	96 (49.0)	57 (28.8)
Glucose ≤60 or ≥300 mg/dL	69 (4.9)	14 (7.1)	11 (5.6)
Blood urea nitrogen ≥30 mg/dL	310 (21.9)	56 (28.6)	44 (22.2)
Na <130 or ≥150 mEq/L	118 (8.4)	28 (14.3)	14 (7.1)
Creatinine ≥1.2	290 (20.5)	36 (18.4)	43 (21.7)
pH <7.35	149 (10.5)	27 (13.8)	14 (7.1)
PaO_2/FiO_2 ≤250	531 (37.6)	104 (53.1)	63 (31.8)
Radiographic findings			
Bilateral lung involvement	649 (45.9)	110 (56.1)	84 (42.4)
Pleural effusion	344 (24.3)	53 (27.0)	37 (18.7)
Pneumonia Severity Index class			
I–III	441 (31.2)	35 (17.9)	81 (40.9)
IV	534 (37.8)	86 (43.9)	74 (37.4)
V	372 (26.3)	67 (34.2)	37 (18.7)

CAP: community-acquired pneumonia
PaO_2/FiO_2: ratio of arterial oxygen partial pressure to fractional inspired oxygen
Data are present as number and percentage.
Immunosuppression included any immunosuppressive diseases such as congenital and acquired immunodeficiency, hematological diseases, and neutropenia (<1000/mm^3); treatment with immunosuppressive drugs within the previous 30 days; and corticosteroids dosages of at least 10 mg/day of a prednisone equivalent for more than 2 weeks.
Non-ambulatory status was defined as being bedridden or using a wheelchair because of difficulty walking.

Table 2 lists the characteristics of the survivors and non-survivors in the *S. aureus* CAP group. Many of the patients who died had the following physical and laboratory findings: non-ambulatory status (68%), GCS ≤ 12 (52%), albumin <3.0 g/dL (65%), pH < 7.35 (26%) and PaO_2/FiO_2 ≤ 250 (81%) (Table 2).

Table 2 Staphylococcal community-acquired pneumonia (survivors and non-survivors)

Variables	Survivors (n = 165)	Non-survivors (n = 31)	*P* value
Age ≥80 years	75 (45.5)	16 (51.6)	0.528
Sex, male	105 (63.6)	19 (61.3)	0.804
Comorbidities			
Neoplastic diseases	22 (13.3)	5 (16.1)	0.776
Chronic lung diseases	54 (32.7)	17 (54.8)	0.263
Congestive heart failure	26 (15.8)	6 (19.4)	0.602
Chronic renal diseases	12 (7.3)	2 (6.5)	0.999
Chronic liver diseases	5 (3.0)	1 (3.2)	0.999
Central nervous system disorders	52 (31.5)	12 (38.7)	0.433
Diabetes	27 (16.4)	4 (12.9)	0.791
Immunosuppression	11 (6.7)	3 (9.7)	0.468
Non-ambulatory status	61 (37.0)	21 (67.7)	0.001
Physical findings			
Glasgow Coma Scale ≤12	45 (27.3)	16 (51.6)	0.007
Pulse rate ≥125 beats per min	19 (11.5)	5 (16.1)	0.549
Systolic blood pressure <90 mm Hg	17 (10.3)	5 (16.1)	0.355
Respiration rate ≥30 breaths per min	36 (21.8)	12 (38.7)	0.072
Laboratory findings			
Hematocrit <0.3	28 (17.0)	5 (16.1)	0.999
Platelet count <120,000/mm^3	14 (8.5)	4 (12.9)	0.495
Albumin <3.0 g/dL	76 (46.1)	20 (64.5)	0.015
Glucose ≤60 or ≥300 mg/dL	10 (6.1)	4 (12.9)	0.244
Blood urea nitrogen ≥30 mg/dL	43 (26.1)	13 (41.9)	0.073
Na <130 or ≥150 mEq/L	21 (12.7)	7 (22.6)	0.164

Creatinine ≥1.2	30 (18.2)	6 (19.4)	0.806
pH <7.35	19 (11.5)	8 (25.8)	0.046
PaO_2/FiO_2 ≤250	79 (47.9)	25 (80.7)	0.001
Radiographic findings			
Bilateral lung involvement	90 (54.6)	20 (64.5)	0.305
Pleural effusion	43 (26.1)	10 (32.3)	0.476
Pneumonia Severity Index class			0.013
I–III	34 (20.6)	1 (3.2)	
IV	73 (44.2)	13 (41.9)	
V	50 (30.3)	17 (54.8)	

PaO_2/FiO_2: ratio of arterial oxygen partial pressure to fractional inspired oxygen

Microbiological findings and appropriateness of antibiotics

Table 3 presents the microbiological findings of the survivors and non-survivors. In *S. aureus* CAP, we identified a high rate of co-infection (approximately 72%, n=142), especially Gram-negative pathogens, which were detected in 99 patients (51%). The 30-day mortality rates were 21% (16/77) for the patients with MRSA and 13% (19/142) for those with *S. aureus* and other co-infected pathogens, respectively. The most detected Gram-negative pathogens were *Klebsiella pneumoniae*, followed by *Pseudomonas aeruginosa* and *Haemophilus influenzae*. In contrast, we identified Gram-positive pathogen co-infections in only 43 patients (22%). In this study, only one patient with *S. aureus* CAP was identified as co-infected with the influenza virus.

Table 3 Microbiological findings in the staphylococcal community-acquired pneumonia group

Variables	Total (n = 196)	Survivors (n = 165)	Non-survivors (n = 31)
Methicillin-resistant *Staphylococcus aureus*	77 (39.3)	61 (37.0)	16 (51.6)
All co-detection	142 (72.4)	123 (74.5)	19 (61.3)
Gram-positive pathogens	43 (21.9)	38 (23.0)	5 (16.1)
Streptococcus pneumoniae	29 (14.8)	27 (16.4)	2 (6.5)
Gram-negative pathogens	99 (50.5)	85 (51.5)	14 (45.2)
Klebsiella pneumoniae	30 (15.3)	25 (15.2)	5 (16.1)
Pseudomonas aeruginosa	16 (8.2)	12 (7.3)	4 (12.9)
Haemophilus influenzae	12 (6.1)	12 (7.3)	0
Influenza virus	1 (0.5)	1 (0.6)	1 (3.2)
Bacteremia	13 (6.6)	9 (5.4)	4 (12.9)

The appropriateness of antibiotics was assessed in 193 of the 196 patients; 77 (39%) received inappropriate initial antibiotics, and 116 (60%) received appropriate initial antibiotics. Anti-MRSA antibiotics were administered to only 6 patients (6/196); only 8% (6 /77) of the patients with MRSA received appropriate antibiotics.

Risk factors for 30-day mortality

We performed a univariate analysis using the 26 baseline characteristics shown in Table 2. The results showed five variables with *p*-values ≤0.05. These variables were non-ambulatory status, GCS ≤ 12, albumin < 3.0 g/dL, pH < 7.35 and PaO_2/FiO_2 ≤ 250 (Table 4).

Table 4 Risk factors for 30-day mortality in the *S. aureus* community-acquired pneumonia group

	Univariate analysis			Multivariate analysis		
Variables	Crude OR	95 % CI	*P* value	Adjusted OR	95 % CI	*P* value
Sex, male	1.11	(0.50–2.43)	0.804	0.89	(0.36–2.16)	0.788
Age ≥80 years	1.28	(0.59–2.76)	0.528	0.79	(0.33–1.92)	0.608
Non-ambulatory status	3.58	(1.58–8.10)	0.001	2.40	(0.93–6.17)	0.070
GCS ≤12	2.84	(1.30–6.23)	0.007	1.40	(0.56–3.47)	0.469
Albumin <3.0 g/dL	2.63	(1.18–5.85)	0.015	2.41	(1.01–5.83)	0.047
pH <7.35	2.58	(1.01–6.58)	0.046	2.19	(0.78–6.17)	0.140
PaO_2/FiO_2 ≤250	4.27	(1.66–10.97)	0.001	3.29	(1.20–9.04)	0.021
Methicillin resistance	1.82	(0.84–3.94)	0.126	1.17	(0.49–2.74)	0.727

OR: odds ratio
CI: confidence interval
GCS: Glasgow Coma Scale
PaO_2/FiO_2: ratio of arterial oxygen partial pressure to fractional inspired oxygen

To identify the mortality risk factors for patients with *S. aureus* CAP, we performed a multivariate analysis using the 5 significant variables in addition to age, sex, and presence of methicillin resistance. Table 4 shows the independent risk factors for 30-day mortality including PaO_2/FiO_2 ≤ 250 (adjusted odds ratio [AOR], 3.29; 95% confidence interval [CI] 1.20–9.04; $p = 0.021$) and albumin < 3.0 g/dL (AOR, 2.41; 95% CI 1.01–5.83; $p = 0.047$). Non-ambulatory status (AOR, 2.40; 95% CI 0.93–6.17; $p = 0.070$) tended to increase the mortality risk, although it was not statistically significant. The presence of methicillin resistance (AOR, 1.17; 95% CI 0.50–2.74; $p = 0.727$) was not detected as a significant risk factor.

Subgroup analyses

To compare the mortality risk factors between the *S. aureus* and pneumococcal CAP groups, we performed a further analysis to assess the risk factors for 30-day mortality in pneumococcal CAP (Supplemental Table 1). We identified 198 patients with pneumococcal CAP, with a 30-day mortality of 7.1% (14 of 198 patients). When performing the analysis of mortality risk factors for the pneumococcal CAP patients, we assessed the same 26 variables employed for the *S. aureus* CAP patients. The univariate analysis results showed that the variables (age ≥ 80 years, non-ambulatory status, GCS ≤ 12, albumin < 3.0 g/dL, neoplastic diseases, congestive heart failure, chronic renal diseases, glucose ≤ 60 or ≥ 300 mg/dL, blood urea nitrogen ≥ 30 mg/dL, and pleural effusion) had significant *p*-values ($p \leq 0.05$). Using these variables, we performed a multivariate logistic analysis to compare mortality risk factors between the two pathogen groups. The following host factors were identified as associated with 30-day mortality in pneumococcal CAP: non-ambulatory status (AOR, 16.1; 95% CI 2.6–98.9; $p = 0.003$), albumin < 3.0 g/dL

(AOR, 10.2; 95% CI 1.8–55.8, $p = 0.007$) and age ≥ 80 years (AOR, 4.9; 95% CI 0.98–24.6; $p = 0.052$).

DISCUSSION

In this post hoc analysis of a multicenter prospective observational study, we identified two potential risk factors (respiratory failure [$PaO_2/FiO_2 \leq 250$] and hypoalbuminemia [albumin < 3.0 g/dL]) associated with 30-day mortality in patients with *S. aureus* CAP. A non-ambulatory status also tended to increase the mortality risk. This study also implied the differences in types of risk factors for 30-day mortality between the *S. aureus* and pneumococcal CAP groups. Hypoalbuminemia and non-ambulatory status had similar trends to increase the mortality risk in both groups. However, effects of advanced age and respiratory failure differed between the two groups.

As for clinical characteristics, the patients with *S. aureus* CAP in our study had distinct clinical features compared with the patients with pneumococcal CAP, which included advanced age, CNS disorders, poor functional ability, altered mental status, hypoalbuminemia, hyponatremia/hypernatremia, acidemia, hypoxemia, and bilateral lung involvement. These are well-known risk factors for mortality in all patients with CAP.[9,17,18,21,22] Regarding the microbiological findings, we noted that the rate of co-infections in the *S. aureus* CAP group was surprisingly high (72%). The most detected co-infective organisms were Gram-negative pathogens, including *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae*. Physicians should recognize these co-infections and consider using appropriate antibiotics for these co-infection pathogens.

To develop predictive rules, several prior studies have emphasized the potential mortality risk factors in CAP. The two most representative rules are the Pneumonia Severity Index[8] and CURB-65.[9] Assessing the severity at the pneumonia diagnosis is useful for determining the initial site of care. The current predictive scoring systems were developed using data from time points where information on the causative pathogens was not available in many cases. However, the patient care strategy might need modifications several days after the pneumonia diagnosis and once information on the causative pathogen has been obtained. Furthermore, the types and weight of risk factors for adverse outcomes might differ among patients with CAP according to the causative organisms. A previous study revealed that the microbial etiology of pneumonia was a mortality risk factor.[10] Self et al compared the clinical outcomes of *S. aureus* CAP with those of pneumococcal CAP and reported more severe clinical outcomes for MRSA CAP than for pneumococcal CAP.[23] In fact, this study showed a higher patient mortality proportion (16%) in *S. aureus* CAP than in pneumococcal CAP (7%), with MRSA mortality proportion of 20%, which suggests the importance of the pathogens identified in the patients. In this study, we focused on *S. aureus* because the prevalence of this organism is increasing as a causative pathogen in CAP.[2,24,25]

Our study revealed the mortality risk factors for patients with *S. aureus* CAP, which include respiratory failure and hypoalbuminemia. Previous studies have mainly focused on MRSA, with few studies focusing on both types of *S. aureus* CAP. Our study is therefore one of the few to assess the factors associated with outcomes in *S. aureus* CAP. The existing studies, which mainly focused on MRSA, have sought to identify the association between poor outcomes and microbial factors such as PVL and SCC*mec* type.[3,13,14,26] Although several studies have shown an association between these microbial factors and mortality,[3,26] an important issue in these analyses was whether the host factors were assessed as confounders for mortality. In a previous retrospective study aimed at investigating the role of the microbial characteristics in predicting mortality in patients with MRSA, the results showed that these microbial characteristics (eg,

SCC*mec* type and PVL detection) were not significantly associated with 30-day mortality or with the duration of post-infection hospital stays after adjusting for other confounders.[13] Another study that investigated the impact of PVL on the outcome of *S. aureus* pneumonia identified no significant associations between clinical outcomes and the presence of PVL or the in vitro level of alpha-hemolysin production.[14] Our study also showed that a microbial factor, methicillin resistance, was not associated with mortality. Therefore, the microbial factors might not be the primary determinant for outcomes among patients with *S. aureus* CAP, and attention should be paid to important host factors as that could play a more significant role.

In our subanalysis, we assessed the differences in types of risk factors between the *S. aureus* and pneumococcal CAP groups. First, hypoalbuminemia and non-ambulatory status were common factors predicting mortality in both the *S. aureus* and pneumococcal CAP groups. These factors were previously reported as prognostic factors in CAP,[18] although the PSI and CURB-65 do not include these factors. Second, in pneumococcal CAP, advanced age was associated with a high mortality risk, whereas PaO_2/FiO_2 ≤250 did not significantly affect mortality. In contrast, respiratory failure was a stronger risk factor than advanced age (age ≥80 years) in *S. aureus* CAP. This finding highlights the importance of respiratory failure in predicting the prognosis of *S. aureus* CAP, regardless of patient age. Furthermore, our findings suggest that factors associated with poor outcomes might differ according to the causative pathogens, and physicians should reconsider the risk factors for poor outcomes after obtaining information on the causative pathogen.

Our study will facilitate early clinical decision making for patients with *S. aureus* CAP, especially those at high mortality risk. When *S. aureus* is suspected as the causative organism of pneumonia from Gram staining, when patients have risk factors for *S. aureus* infection, or when *S. aureus* is microbiologically proven, physicians should expect that these patients with the mentioned risk factors will have a high mortality risk. Therefore, early multidimensional therapy such as appropriate respiratory management, improving nutritional status, the use of adjunctive therapy, and appropriate antibiotic treatment for these patients should be considered to improve their outcomes.

Our study had several limitations. First, we had a limited sample size, and the number of deaths at 30 days was insufficient to accurately estimate the prognostic risk factors. Second, although numerous studies have reported high rates of *S. aureus* and influenza virus co-infection, which are associated with poor outcomes,[4,5,27,28] our study period could not include part of the influenza season because a greater than expected number of patients with pneumonia were registered. Third, the pathogens identified in this study might not have been the cause of the pneumonia. Fourth, our study did not assess microbial characteristics such as virulence and infectivity. Lastly, we could not sufficiently assess the association between mortality and the appropriateness of antimicrobial treatment. Further studies to assess the appropriateness of antibiotics are warranted.

In conclusion, patients with *S. aureus* CAP have distinct clinical features, and their most influential factors associated with mortality were respiratory failure and hypoalbuminemia. A number of potential host factors influencing mortality might be shared between *S. aureus* and pneumococcal CAP but might differ slightly. Physicians should recognize these findings and perform appropriate management strategies after obtaining information on the causative pathogen.

ACKNOWLEDGMENTS

We would like to thank Dr Daisuke Kobayashi, Dr Ryota Ito, Dr Akira Shiraki, Dr Yasuhiro Goto, Dr Yasutaka Fukui, Dr Mai Iwaki, Dr Yuka Tomita, and Dr Mitsutaka Iguchi for acquiring

the data and Dr Shigeru Yoshida and Masaki Takahashi for their advice in setting up the electronic data collection system. We are indebted to the clinical research coordinators (Kyoko Kazeto, Sumiyo Tanaka, Mika Yamauchi, Mayumi Tsuda, Junko Hisada, Yuko Okada, Tomoe Kushihara, Hideaki Sobajima, Harumi Nakano, Mieko Sakuma, and Asuka Miyake), laboratory staff (Mariko Mochizuki, Miho Saito, Yoshiko Sugaki, Yuko Asano, Tomomi Torii, Yasue Hayakawa, Yusuke Nishida, Takae Aoki, Yuki Nagata, Hideki Nishiyama, Yukie Asai, Nobuya Sakagami, and Jun Sokunaga), and all healthcare professionals who participated in the data collection.

CONFLICT OF INTEREST

The authors declare no conflicts of interest on this project.

FUNDING

This study was supported by the Central Japan Lung Study Group (CJLSG), a nonprofit organization supported by unrestricted donations from several pharmaceutical companies. The sponsors of CJLSG played no role in the design and conduct of the study; collection, management, analysis, and interpretation of data; and preparation of the manuscript.

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Appendix: Supplementary data

Suppl Table 1 Univariate analysis for 30-day mortality in *Staphylococcus aureus* and pneumococcal community-acquired pneumonia

	Staphylococcus aureus		*Pneumococcus*	
	Univariate analysis		Univariate analysis	
Variables	OR (95 % CI)	*P* value	OR (95 % CI)	*P* value
Age ≥80 years	1.28 (0.59–2.76)	0.528	9.56 (2.56–35.68)	<0.001
Sex, male	1.11 (0.50–2.43)	0.804	1.22 (0.41–3.67)	0.721
Comorbidities				
Neoplastic diseases	1.25 (0.43–3.60)	0.776	4.83 (1.47–15.89)	0.016
Chronic lung diseases	0.60 (0.24–1.48)	0.263	1.10 (0.33–3.68)	0.999
Congestive heart failure	1.28 (0.48–3.43)	0.602	6.29 (1.70–23.31)	0.014
Chronic renal diseases	0.88 (0.18–4.14)	0.999	6.29 (1.70–23.31)	0.014
Chronic liver diseases	1.07 (0.12–9.46)	0.999	0.93 (0.89–0.96)	0.999
Central nervous system disorders	1.37 (0.62–3.04)	0.433	3.11 (0.89–10.79)	0.082
Diabetes	0.76 (0.25–2.34)	0.791	1.30 (0.34–4.91)	0.717
Immunosuppression	1.50 (0.40–5.72)	0.468	0.92 (0.88–0.96)	0.373
Non-ambulatory status	3.58 (1.58–8.10)	0.001	24.44 (6.36–93.99)	<0.001
Physical findings				
Glasgow Coma Scale ≤12	2.84 (1.30–6.23)	0.007	5.83 (1.74–19.51)	0.009
Pulse rate ≥125 beats per min	1.48 (0.51–4.31)	0.549	2.68 (0.68–10.55)	0.155
Systolic blood pressure <90 mm Hg	1.67 (0.57–4.93)	0.355	1.01 (0.12–8.35)	0.999
Respiration rate ≥30 breaths per min	2.16 (0.96–4.86)	0.072	2.11 (0.67–6.65)	0.194
Laboratory findings				
Hematocrit <0.3	0.94 (0.33–2.66)	0.999	3.28 (0.94–11.44)	0.072
Platelet count <120,000/mm^3	1.60 (0.49–5.22)	0.495	1.01 (0.12–8.35)	0.999
Albumin <3.0 g/dL	2.63 (1.18–5.85)	0.015	18.40 (3.97–85.34)	<0.001
Glucose ≤60 or ≥300 mg/dL	2.30 (0.67–7.85)	0.244	6.00 (1.39–25.84)	0.033
Blood urea nitrogen ≥30 mg/dL	2.05 (0.93–4.53)	0.073	5.48 (1.79–16.79)	0.003
Na <130 or ≥150 mEq/L	2.00 (0.77–5.22)	0.164	4.29 (1.04–17.65)	0.064
Creatinine ≥1.2	1.08 (0.41–2.86)	0.806	2.14 (0.68–6.74)	0.190
pH <7.35	2.58 (1.01–6.58)	0.046	0.98 (0.12–8.11)	0.999
PaO_2/FiO_2 ≤250	4.27 (1.66–10.97)	0.001	3.006 (1.0–9.08)	0.071
Radiographic findings				
Bilateral lung involvement	1.52 (0.68–3.36)	0.305	2.62 (0.84–8.12)	0.086
Pleural effusion	1.35 (0.59–3.10)	0.476	10.03 (3.13–32.15)	0.001

OR: odds ratio

CI: confidence interval

PaO_2/FiO_2: ratio of arterial oxygen partial pressure to fractional inspired oxygen

Data are present as number and percentage.

Immunosuppression included any immunosuppressive diseases such as congenital and acquired immunodeficiency, hematological diseases, and neutropenia (<1000/mm^3); treatment with immunosuppressive drugs within the previous 30 days; and corticosteroids dosages of at least 10 mg/day of a prednisone equivalent for more than 2 weeks.

Non-ambulatory status was defined as being bedridden or using a wheelchair because of difficulty walking.