International Journal of Infectious Diseases 84 (2019) 89–96

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Efficacy and accuracy of qSOFA and SOFA scores as prognostic tools for community-acquired and healthcare-associated pneumonia

Nobuhiro Asai[a,b], Hiroki Watanabe[a,b], Arufumi Shiota[a,b], Hideo Kato[a,b], Daisuke Sakanashi[b], Mao Hagihara[a,b], Yusuke Koizumi[a,b], Yuka Yamagishi[a,b], Hiroyuki Suematsu[b], Hiroshige Mikamo[a,b,*]

[a] Department of Clinical Infectious Diseases, Aichi Medical University Hospital, Aichi, Japan
[b] Department of Infection Control and Prevention, Aichi Medical University Hospital, Aichi, Japan

ARTICLE INFO

Article history:
Received 24 October 2018
Received in revised form 14 April 2019
Accepted 18 April 2019
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keyword:
qSOFA
SOFA score
Community-acquired pneumonia
Healthcare-associated pneumonia

ABSTRACT

Background: The Japanese Respiratory Society recently updated its prognostic guidelines for pneumonia, recommending that pneumonia severity be evaluated using the sequential organ failure assessment (SOFA) and quick SOFA (qSOFA) scoring systems in a therapeutic strategy flowchart. However, the efficacy and accuracy of these tools are still unknown.
Methods: All patients with community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP) who were admitted to the study institution between 2014 and 2017 were enrolled in this study. Pneumonia severity on admission was evaluated by A-DROP, CURB-65, PSI, I-ROAD, qSOFA, and SOFA scoring systems. Prognostic factors for 30-day mortality were also analyzed.
Results: This study included 406 patients, 257 male (63%) and 149 female (37%). The median age was 79 years (range 19–103 years). The 30-day and in-hospital mortality rates were both 5%. With respect to the diagnostic value of the predictive assessments for 30-day mortality, the area under the receiver operating characteristic curve (AUROC) value for the SOFA score was 0.769 for CAP patients and 0.774 for HCAP patients. Further, the AUROC values for the SOFA score in CAP and HCAP patients with a qSOFA score ≥2 were 0.829 and 0.784, respectively, for 30-day mortality.
Conclusions: qSOFA and SOFA scores were able to correctly evaluate the severity of CAP and HCAP.

Introduction

Pneumonia is one of the most common reasons for hospital admission in Japan and is a leading cause of death worldwide (WHO Global Health Observatory (GHO), 2018). The mortality rate of pneumonia has not changed over the past several decades, despite advancements in technical methods such as multiplex PCR and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), as well as the development of many effective antibiotics (Venditti et al., 2009). In Japan's aging society, the number of elderly patients with pneumonia is increasing every year. Therefore, not only specialists, but every hospital physician should be well-practiced in the treatment of pneumonia in the hospital setting.

To aid physicians who do not specialize in respiratory infections, several prognostic tools have been developed since 2000, including A-DROP (Miyashita et al., 2006), CURB-65 (British Thoracic Society Standards of Care Committee, 2001), PSI (Niederman et al., 2001), I-ROAD (Japanese Respiratory Society, 2009; Seki et al., 2008), and SMART-COP (Charles et al., 2008). The Japanese Respiratory Society updated its prognostic guidelines for pneumonia in 2017. The most dramatic change in the newly published guidelines is the suggestion that pneumonia severity be evaluated using the sequential organ failure assessment (SOFA) and the quick SOFA (qSOFA) scoring systems as part of a published flowchart of the therapeutic strategy (Figure 1).

It has been shown that the SOFA and qSOFA assessments are useful diagnostic tools for predicting hospital mortality among

* Corresponding author at: Department of Clinical Infectious Diseases, Aichi Medical University, School of Medicine, 1-1 Yazakokarimata, Nagakute, Aichi, 480-1195, Japan.
E-mail addresses: asai.nobuhiro.039@mail.aichi-med-u.ac.jp (N. Asai), watanabe.hiroki.769@mail.aichi-med-u.ac.jp (H. Watanabe), shiota@aichi-med-u.ac.jp (A. Shiota), katou.hideo.233@mail.aichi-med-u.ac.jp (H. Kato), saka74d@aichi-med-u.ac.jp (D. Sakanashi), hagimao@aichi-med-u.ac.jp (M. Hagihara), ykoizumi@aichi-med-u.ac.jp (Y. Koizumi), y.yamagishi@mac.com (Y. Yamagishi), hsuemat@aichi-med-u.ac.jp (H. Suematsu), mikamo@aichi-med-u.ac.jp (H. Mikamo).

https://doi.org/10.1016/j.ijid.2019.04.020

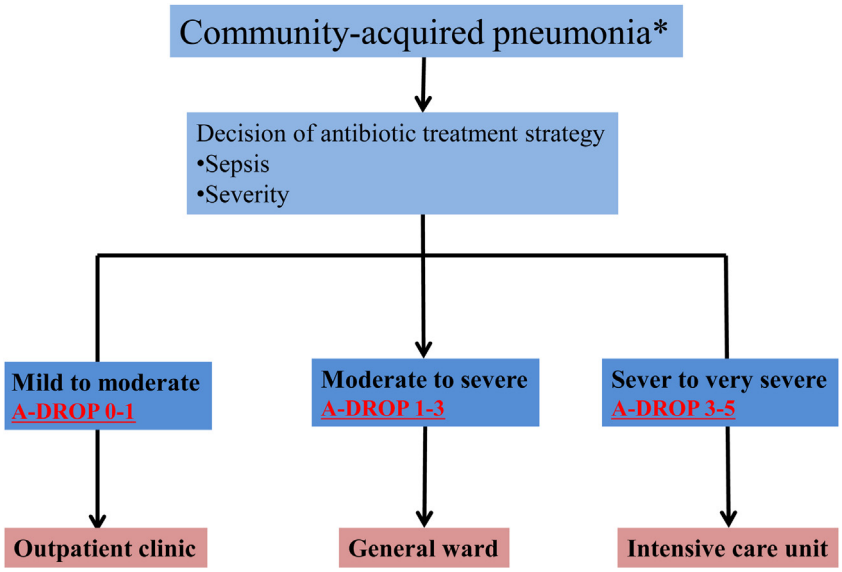

Figure 1. Flowcharts of the therapeutic strategy for (A) community-acquired pneumonia (CAP) patients, and (B) healthcare-associated pneumonia (HCAP) patients.

adults with suspected infection in the intensive care unit (Raith et al., 2017). Further, it has been shown that these assessments are useful prognostic tools for community-acquired pneumonia (CAP), urinary tract infections, and sepsis (Ranzani et al., 2017). However, whether qSOFA and SOFA scores are able to correctly evaluate the severity and prognosis of healthcare-associated pneumonia (HCAP) has yet to be determined. Additionally, although Matsunuma et al. (Matsunuma et al., 2014) reported that I-ROAD was useful in evaluating HCAP severity, its prognostic value for HCAP is still unknown. In a recent pilot study, we reported that the SOFA score was able to evaluate the severity and prognosis of HCAP more accurately than A-DROP, CURB-65, PSI, or I-ROAD (Asai et al., 2018). We have since continued to examine the validity of qSOFA and SOFA scores in the management of CAP and HCAP.

Patients and methods

Study population and patient inclusion criteria

This retrospective study was conducted between 2014 and 2017 at the Aichi Medical University Hospital, which is a 900-bed tertiary hospital in the Aichi Prefecture in Japan. Patients with CAP and HCAP who were admitted to the hospital were included in this study. Patients with hospital-associated pneumonia were excluded. Pneumonia was diagnosed according to previously published international guidelines (American Thoracic Society and Infectious Diseases Society of America, 2005; Mandell et al., 2007). Patient characteristics (age, sex, coexisting illness, etc.), symptoms, laboratory data, radiological findings, initial antibiotic regimen, pneumonia severity, clinical outcome, and pathogens isolated by sputum culture and blood culture at the time of admission were evaluated. This study was approved by the Institutional Review Board of Aichi Medical University Hospital (IRB number 17-H106).

Evaluation of comorbidities

Comorbidities were evaluated using the Charlson comorbidity index (CCI). This index predicts the 10-year mortality for 22 different comorbid conditions, including heart disease, AIDS, and cancer. Each condition is assigned a score of 1, 2, 3, or 6 depending on the risk of dying. For each patient, the sum of these scores is used as the total score to predict mortality. As patients are often unaware of the severity of their conditions, each patient's chart was reviewed to determine the appropriate comorbid conditions and the resulting CCI score (Charlson et al., 1987; de Groot et al., 2003).

Severity of pneumonia

Pneumonia severity on admission was evaluated by A-DROP, CURB-65, PSI, I-ROAD, qSOFA, and SOFA scores. The use of vasopressor agents, use of mechanical ventilation, and the existence of do-not-resuscitate orders were also examined during admission.

Microbiological evaluation

A sputum sample and two sets of blood were collected from each patient for microbiological examination. Serological tests were performed to detect antibodies against *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae* (Ishida et al., 1998; Miyashita et al., 2008). Additionally, *Legionella pneumophila* serogroup 1 antigen in urine was tested by immunochromatography. The antimicrobial susceptibility of isolated bacterial pathogens was assessed on the basis of the minimum inhibitory concentration according to the Clinical and Laboratory Standards Institute guidelines (Clinical and Laboratory Standards Institute, 2011). Methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and extended-spectrum β-lactamase-producing organisms were defined as potentially drug-resistant (PDR) pathogens based on the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines (American Thoracic Society and Infectious Diseases Society of America, 2005).

Definition of appropriate and inappropriate treatment

Antibiotic treatment was classified as appropriate or inappropriate according to whether the pathogens identified were sensitive or resistant, respectively, to the initial prescribed antibiotics.

Analysis of prognostic factors for 30-day mortality

All of the patients were examined at the time of admission to the hospital. For CAP patients, clinical factors involving continuous

Table 1
Patient characteristics.

	All patients (n = 406)	CAP patients (n = 177)	HCAP patients (n = 229)	*p*-Value[a]
Age, years, mean ± SD	75.4 ± 14.8	71.9 ± 18.4	78.1 ± 10.6	<0.001
Age, years, median (range)	79 (19–103)	76 (19–103)	80 (42–99)	
Sex, male (%)	257 (63)	109 (62)	148 (65)	0.535
Smoking history (%)				
Current	36 (9)	26 (15)	10 (4)	<0.001
Ex	205 (51)	82 (46)	123 (54)	0.161
Never	135 (33)	61 (34)	74 (32)	0.672
Unknown	30 (7)	8 (5)	22 (10)	0.057
Condition				
Altered state (GCS<15)	167 (41)	55 (31)	112 (49)	<0.001
Shock state (SBP<100 mmHg)	55 (14)	19 (11)	36 (16)	0.188
RR>22/min	172 (42)	55 (31)	117 (51)	<0.001
qSOFA≥2	146 (36)	36 (20)	110 (48)	<0.001
SIRS	214 (53)	82 (46)	132 (58)	0.028
Outcome (%)				
30-day mortality	19 (5)	3 (2)	16 (7)	0.02
In-hospital mortality	21 (5)	4 (2)	17 (7)	0.023
Healthcare-associated factors				
Attendance at hospital within the past 90 days	81 (20)	0	81 (35)	ND
Use of antibiotics within the past 90 days	84 (21)	0	84 (37)	ND
Nursing home resident	64 (16)	0	64 (28)	ND
Hemodialysis	18 (4)	0	18 (8)	ND
Chemotherapy	25 (6)	0	25 (11)	ND
Immunosuppression	44 (11)	0	44 (19)	ND
Tube feeding	20 (5)	0	20 (9)	ND
Severity of pneumonia (%)				
A-DROP				
0–1	150 (37)	84 (47)	66 (29)	<0.001
2	106 (26)	42 (24)	64 (28)	0.363
3	100 (25)	40 (23)	60 (26)	0.419
4–5	50 (12)	11 (6)	39 (17)	0.001
CURB-65				
0–1	163 (40)	96 (54)	67 (29)	<0.001
2	132 (33)	48 (27)	84 (37)	0.043
3	88 (22)	28 (16)	60 (26)	0.015
4–5	23 (6)	5 (3)	18 (8)	0.031
PSI				
I–II	68 (17)	50 (28)	18 (8)	<0.001
III	68 (17)	38 (21)	30 (13)	0.032
IV–V	270 (67)	89 (50)	181 (79)	<0.001
I-ROAD				
A	136 (33)	87 (49)	49 (21)	<0.001
B	86 (21)	34 (19)	52 (23)	0.463
C	184 (45)	56 (32)	128 (56)	<0.001
SOFA				
0–1	118 (29)	64 (36)	54 (24)	0.006
2–3	172 (42)	81 (46)	91 (40)	0.226
4–5	78 (19)	26 (15)	52 (23)	0.043
≥6	38 (9)	6 (3)	32 (14)	<0.001
Comorbidity (%)				
Cerebrovascular disease	100 (25)	28 (16)	72 (31)	<0.001
Chronic pulmonary disease	174 (43)	63 (36)	111 (48)	0.011
Diabetes mellitus	60 (15)	31 (18)	29 (13)	0.204
Heart disease	125 (31)	51 (29)	74 (32)	0.516
Malignancy	74 (18)	10 (6)	64 (28)	<0.001
Chronic liver disease	15 (4)	4 (2)	11 (5)	0.198
Chronic kidney disease	51 (13)	14 (8)	37 (16)	0.105
Collagen vascular disease	41 (10)	1 (1)	40 (17)	<0.001
Dementia	74 (18)	23 (13)	51 (22)	0.019
Gastroesophageal reflux disease	13 (3)	4 (2)	9 (4)	0.405
Use of a proton pump inhibitor	121 (30)	37 (21)	84 (37)	<0.001
Use of sleeping agents	59 (15)	22 (13)	36 (16)	0.48
CCI (mean ± SD)	2.1 ± 1.8	1.2 ± 1.1	2.7 ± 2.0	<0.001
Antibiotics initially used				
Penicillin alone	196 (48)	70 (40)	126 (55)	0.003
Cephems alone	58 (14)	30 (17)	28 (12)	0.199
Carbapenems alone	77 (19)	26 (15)	51 (22)	0.057
Quinolones alone	26 (6)	22 (12)	4 (2)	<0.001
Macrolides alone	0	0	0	ND
β-lactams with macrolides	11 (3)	7 (4)	4 (2)	0.222
β-lactams with quinolones	22 (5)	16 (9)	6 (3)	0.007
Other	17 (4)	6 (3)	11 (5)	0.619
Anti-MRSA agents	5 (1)	0	5 (2)	0.071
Anti-pseudomonal regimen	248 (61)	93 (53)	155 (68)	0.002
Other factors (%)				

Table 1 (*Continued*)

	All patients (n = 406)	CAP patients (n = 177)	HCAP patients (n = 229)	*p*-Value[a]
Initial treatment failure	27 (7)	10 (6)	17 (7)	0.55
Inappropriate antibiotic treatment	43/196 (22)	5/71 (7)	38/125 (30)	<0.001
Detection of PDR pathogens	59 (15)	10 (6)	49 (21)	<0.001
Bacteremia	26/232 (11)	9/107 (8)	17/125 (14)	0.297
DNAR order	75 (18)	21 (12)	54 (24)	0.003
Mechanical ventilation	19 (5)	7 (4)	12 (5)	0.639
Use of vasopressor agent	11 (3)	4 (2)	7 (3)	0.763

CAP, community-acquired pneumonia; CCI, Charlson comorbidity index; DNAR, do not attempt resuscitate; GCS, Glasgow coma scale; HCAP, healthcare-associated pneumonia; MRSA, methicillin-resistant *Staphylococcus aureus*; ND, not done; SD, standard deviation; SIRS, systemic inflammatory response syndrome; SOFA, sequential organ failure assessment; qSOFA, quick SOFA; RR, respiratory rate; PDR, potentially drug resistant; DNAR, do-not attempt resuscitation.

[a] Fisher's exact tests were performed to compare CAP and HCAP groups for all variables except age. The difference in the mean age between the two groups was analyzed using a *t*-test.

variables were divided into two categories as follows: age (<76, ≥76 years); white blood cell count (<4 and >9, ≥4 and ≤9×10^9 cells/l); hemoglobin (<10, ≥10g/dl); hematocrit (<30, ≥30); platelets (<150, ≥150×10^9 cells/l); sodium (<130, ≥130 mEq/l); total bilirubin (<1.2, ≥1.2 mg/dl); C-reactive protein (CRP) (<11, ≥11 mg/dl); blood urea nitrogen (<20, ≥20 mg/dl); creatinine (<1.2, ≥1.2 mg/dl); albumin (Alb) (<3.3, ≥3.3 g/dl), pH (<7.3 or >7.4, 7.3–7.4).

For HCAP patients, continuous variables were divided into two categories using the same cut-offs as were used for the CAP patients, but with the following changes: age (<80, ≥80 years); CRP (<8.7, ≥8.7 mg/dl); Alb (<3.0, ≥3.0 g/dl). The cut-off points for white blood cell count, hemoglobin, hematocrit, platelets, sodium, total bilirubin, blood urea nitrogen, creatinine, pH, systolic blood pressure, and PaO_2/FiO_2 ratio were set at values to assess normal vs. abnormal ranges, whereas age, Alb, and CRP were based on the median values of the patient groups.

Statistical analysis

The data for categorical variables were expressed as percentages, while continuous variables were recorded as the mean ± standard deviation (SD). The Chi-square test or Fisher's exact test (two-tailed) was used to compare categorical variables, and the unpaired Student *t*-test or Mann–Whitney *U*-test was used to compare continuous variables. Logistic regression analysis was used to identify independent risk factors associated with 30-day mortality of patients with CAP or HCAP. Variables with a *p*-value of less than 0.10 from the univariate analysis were entered into the multivariable model. All tests were calculated using IBM SPSS Statistics version 23 for Windows (IBM Corp., Armonk, NY, USA). Variables that showed a *p*-value of less than 0.05 were considered statistically significant.

Results

Patient characteristics

Patient characteristics are shown in Table 1. A total of 406 patients were enrolled in this study: 257 male (63%) and 149 female (37%). The median age was 79 years (range 19–103 years). Two hundred and forty-one patients (59%) were current or ex-smokers, while the smoking status was unknown for 30 patients (7%).

Outcomes

The 30-day and in-hospital mortality rates were both 5%. Initial treatment failure was seen in 27/409 patients (7%) and inappropriate antibiotic treatment in 43/196 patients (22%) (Table 1). PDR pathogens were detected in 59/409 patients (15%). Vasopressors and mechanical ventilation were used in four (2%) and seven (4%)

Table 2
Microorganisms identified by sputum culture.

Microorganism, *n* (%)	All patients	CAP patients	HCAP patients	*p*-Value
Gram-positive	120	41	79	
Streptococcus pneumoniae	32 (9)	19 (13)	13 (7)	0.061
Streptococcus non-pneumonia	19	5 (3)	14 (7)	0.156
Staphylococcus aureus	30	11 (8)	19 (10)	0.563
MRSA	35	6 (4)	29 (15)	0.001
Coagulase-negative staphylococci	1	0	1 (1)	1.000
Corynebacterium species	2	0	2 (1)	1.000
Enterococcus species	1	0	1 (1)	1.000
Gram-negative	122	42	80	
Haemophilus influenzae	21	12 (8)	9 (5)	0.255
Escherichia coli	17	4 (3)	13 (7)	0.131
Pseudomonas aeruginosa	15	2	13 (7)	0.017
Klebsiella pneumoniae	26	7 (5)	19 (10)	0.1
Klebsiella oxytoca	4	2 (1)	2 (1)	1.000
Moraxella catarrhalis	11	4 (3)	7 (4)	0.763
Serratia marcescens	5	2 (1)	3 (2)	1.000
Acinetobacter species	3	0	3 (2)	0.262
Proteus mirabilis	4	1 (1)	3 (2)	0.637
Stenotrophomonas maltophilia	2	0	2 (1)	1.000
Legionella pneumoniae	1	1 (1)	0	1.000
Enterobacteriaceae	13	7 (5)	6 (3)	0.57

CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; MRSA, methicillin-resistant *Staphylococcus aureus*.

Table 3
(a) Correlations between qSOFA and other pneumonia assessments among CAP patients. (b) Correlations between qSOFA and other pneumonia assessments among HCAP patients.

(a)

	qSOFA ≥2 (n = 37)	qSOFA <2 (n = 140)	*p*-value
A-DROP (mean ± SD)	2.9 ± 1.0	1.2 ± 1.1	<0.001
CURB-65 (mean ± SD)	2.8 ± 1.0	1.3 ± 0.9	<0.001
PSI (mean ± SD)	125.3 ± 36.0	79.1 ± 44.1	<0.001
I-ROAD (mean ± SD)	2.6 ± 0.6	1.6 ± 0.8	<0.001
SOFA (mean ± SD)	3.6 ± 1.4	1.8 ± 1.2	<0.001

(b)

	qSOFA ≥2 (n = 80)	qSOFA <2 (n = 149)	*p*-value
A-DROP (mean ± SD)	3.2 ± 1.1	1.8 ± 1.1	<0.001
CURB-65 (mean ± SD)	2.8 ± 0.9	1.7 ± 0.9	<0.001
PSI (mean ± SD)	137.3 ± 29.7	108.7 ± 33.0	<0.001
I-ROAD (mean ± SD)	2.7 ± 0.6	2.1 ± 0.9	<0.001
SOFA (mean ± SD)	4.2 ± 2.2	2.6 ± 1.9	<0.001

CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; SD, standard deviation; SOFA, sequential organ failure assessment; qSOFA, quick SOFA.

of the CAP patients and in seven (3%) and 12 (5%) of the HCAP patients, respectively. Do-not-resuscitate orders were confirmed for 21 CAP patients (12%) and 54 HCAP patients (24%).

Microorganisms identified

Sputum cultures were performed in 337/406 patients (83%). Microorganisms were confirmed in 242 of these patients (72%; Table 2). Blood cultures were performed in 232/407 patients (107 CAP patients and 125 HCAP patients). Of these, 26 (11%) showed positive cultures: nine CAP patients (8%) and 17 HCAP patients (14%).

Correlation between qSOFA score and other pneumonia severity scores

The qSOFA scores were compared with other pneumonia severity scores for patients with qSOFA scores of 0 or 1 and for patients with qSOFA scores of ≥2. It was found that the other pneumonia severity scores were much higher in the group of patients with a qSOFA of ≥2 compared to those with scores of 0 or 1 in both the CAP group (Table 3a) and the HCAP group (Table 3b).

Prognostic accuracy of the predictive values for 30-day mortality

To evaluate the prognostic accuracy of the predictive values, the following cut-off points were set for the assessment of 30-day mortality among pneumonia patients, in accordance with previous studies: A-DROP ≥4, CURB-65 ≥ 3, PSI ≥ IV, and I-ROAD C (Matsunuma et al., 2014; Shindo et al., 2009). Table 4 reports the prognostic accuracy of the SOFA and qSOFA scores for 30-day mortality. A combination of qSOFA ≥2, or ≥4, or ≥6 and SOFA scorepoor prognostic factor showed higher sensitivity and specificity than A-DROP, CURB-65, PSI, or I-ROAD in both CAP and HCAP patients.

Receiver operating characteristic curves for 30-day mortality in the CAP and HCAP groups

The ability of the various prognostic assessments included in this study to predict 30-day mortality was also assessed. For all patients, the area under the receiver operating characteristic curve (AUROC) for A-DROP, CURB-65, PSI, I-ROAD, and SOFA scores was

Table 4
(a) Comparison of predictive assessments for 30-day mortality among all pneumonia patients. (b) Comparison of predictive assessments for 30-day mortality among CAP patients. (c) Comparison of predictive assessments for 30-day mortality among HCAP patients.

(a)

Predictive rules	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
A-DROP ≥4	47.4	89.1	17.6	97.2
CURB-65 ≥ 3	47.4	73.6	8.1	96.6
PSI ≥IV	89.5	34.6	6.3	98.5
I-ROAD C	68.4	56.1	7.1	97.3
qSOFA ≥2 and SOFA ≥2	63.2	74.9	11	97.6
qSOFA ≥2 and SOFA ≥4	57.9	85.2	16.2	98.2
qSOFA ≥2 and SOFA ≥6	42.1	96.9	40	95.6

(b)

Predictive rules	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
A-DROP ≥4	33.3	93.7	8.3	98.8
CURB-65 ≥ 3	33.3	81.6	3	98.6
PSI ≥IV	100	50.6	3.4	100
I-ROAD C	66.7	70.1	3.7	99.2
qSOFA ≥2 and SOFA ≥2	66.7	81	5.7	99.3
qSOFA ≥2 and SOFA ≥4	66.7	89.1	9.5	99.4
qSOFA ≥2 and SOFA ≥6	33.3	98.3	25	98.8

(c)

Predictive rules	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
A-DROP ≥4	50	85	20.5	95.8
CURB-65 ≥ 3	50	67.1	10.3	94.7
PSI ≥IV	87.5	21.6	7.7	95.8
I-ROAD C	68.8	45.1	8.6	95
qSOFA ≥2 and SOFA ≥2	62.5	70	13.5	96.1
qSOFA ≥2 and SOFA ≥4	56.3	82.2	19.1	96.2
qSOFA ≥2 and SOFA ≥6	43.8	94.4	36.8	95.7

CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; NPV, negative predictive value; PPV, positive predictive value; SOFA, sequential organ failure assessment; qSOFA, quick SOFA.

0.798, 0.714, 0.692, 0.651, and 0.803, respectively. Among CAP patients, the AUROC values for A-DROP, CURB-65, PSI, I-ROAD, and SOFA scores were 0.800, 0.784, 0.812, 0.769, and 0.804, respectively (Figure 2A). For HCAP patients, the AUROC values for A-DROP, CURB-65, PSI, I-ROAD, and SOFA scores were 0.773, 0.66, 0.614, 0.573, and 0.774, respectively (Figure 2C). Of note, the SOFA score had the highest diagnostic value for both CAP and HCAP patients (0.804 and 0.774, respectively). AUROC values for CAP and HCAP patients with qSOFA scores of ≥2 are shown in Figure 2B and Figure 2D, respectively.

With regard to the other scores, the AUROC values of the qSOFA score and SIRS criteria for 30-day mortality among all patients, CAP patients, and HCAP patients were 0.726 ($p = 0.001$, 95% confidence interval (CI) 0.618–0.835) and 0.470 ($p = 0.66$, 95% CI 0.357–0.583), 0.667 ($p = 0.323$, 95% CI 0.281–1.000) and 0.197 ($p = 0.073$, 95% CI 0.069–0.325), and 0.701 ($p = 0.007$, 95% CI 0.584–0.818) and 0.525 ($p = 0.736$, 95% CI 0.409–0.642), respectively (Table 4).

Prognostic factors of 30-day mortality among the CAP and HCAP groups

Several potential prognostic factors for 30-day mortality in both CAP (**Supplementary Material**, S1) and HCAP (**Supplementary Material**, S2) patients were analyzed. Using univariate analysis, it was found that the combination of a qSOFA score ≥2 and a SOFA score ≥4, as well as the presence of pleural effusion, were both factors indicating a poor prognosis for 30-day mortality ($p = 0.038$ and $p = 0.006$, respectively; Table 5). Further, logistic regression analysis showed that the combination of a qSOFA score ≥2 and a SOFA score ≥4 was an independent poor prognostic factor among CAP patients (odds ratio (OR) 18.0, 95% CI 1.2–262.7; $p = 0.035$).

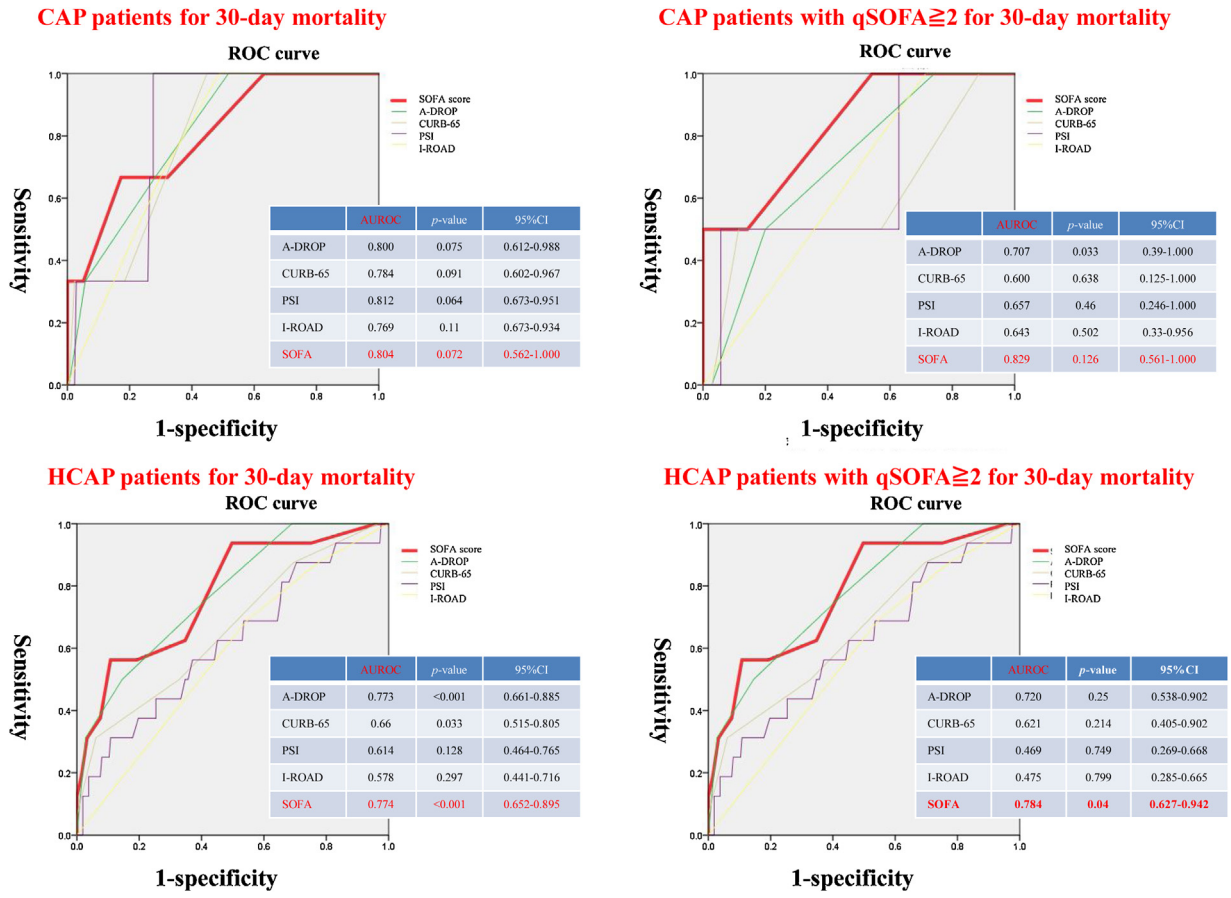

Figure 2. Receiver operating characteristic curves for A-DROP, CURB-65, PSI, I-ROAD, and SOFA scores for 30-day mortality in (A) CAP patients, (B) CAP patients with qSOFA scores ≥2, (C) HCAP patients, and (D) HCAP patients with qSOFA scores ≥2.

Table 5
Significant predictors of 30-day mortality among CAP and HCAP patients by univariate and multivariate analysis.

CAP						
	Univariate analysis			Multivariate analysis		
Variable	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
qSOFA ≥2 and SOFA score ≥4	16.3	1.4–188.6	0.038	18.0	1.2–262.7	0.035
Pleural effusion	33.2	1.7–658.7	0.006			
HCAP						
	Univariate analysis			Multivariate analysis		
Variables	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
qSOFA ≥2 and SOFA score ≥6	13.3	4.1–41.0	<0.001	21.5	1.8–254.1	0.015
A-DROP ≥4	5.9	2.1–16.8	0.002			
Initial treatment failure	27.1	8.4–87.6	<0.001	10.3	2.0–53.2	0.005
Chronic pulmonary diseases	5.1	1.4–18.4	0.008			
Alb <3.0 mg/dl	11.0	2.4–49.5	<0.001	16.3	2.3–115.2	0.005
CRP ≥8.7 mg/dl	3.3	1.0–10.7	0.039			
Residence of nursing home	0.2	0–1.2	0.046			
Home oxygen therapy	3.8	1.2–11.8	0.032			
Male sex	4.1	0.9–18.6	0.058			

Alb, albumin; CAP, community-acquired pneumonia; CRP, C-reactive protein; CI, confidence interval; HCAP, healthcare-associated pneumonia; OR, odds ratio; SOFA, sequential organ failure assessment; qSOFA, quick SOFA.

For HCAP patients, 11 prognostic factors were evaluated by univariate analysis (Table 5). Logistic regression showed that a combination of qSOFA ≥2 and a SOFA score ≥6 (OR 21.5, 95% CI 1.8–254.1; $p = 0.015$), initial treatment failure (OR 10.3, 95% CI 2.0–53.2; $p = 0.005$), and Alb <3.0 mg/dl (OR 2.3, 95% CI 2.3–115.2; $p = 0.005$) were independent factors indicating a poor prognosis for 30-day mortality.

Discussion

This study showed that a combination of qSOFA and SOFA scores was the best indicator of both pneumonia severity and prognosis. The qSOFA is determined by three vital signs: respiratory rate, systolic pressure, and altered consciousness, and qSOFA and SOFA scores are very easy to obtain compared to the other predictive assessments for pneumonia. These scores could thus help any physician to make the decision regarding where a patient should be admitted (to a general ward or an intensive care unit), as well as which antibiotic therapy should be employed. In this study, it was found that pneumonia severity was greater in CAP and HCAP patients with qSOFA scores of ≥2 than in those with scores of 0 or 1. A previous study demonstrated that the qSOFA score could evaluate the state of sepsis accurately with equivalence to the SIRS criteria (Raith et al., 2017). Thus, a qSOFA score ≥2 could be correlated with the severity of pneumonia by any predictive values. Indeed, a comparison of AUROC values for 30-day mortality among CAP patients revealed that all of the predictive assessments for pneumonia appeared to be equally good prognostic tools. The present study results also suggest that tachypnea, hypotension, and altered consciousness might be factors indicating a poor prognosis for patients with pneumonia.

It was observed that the predictive ability of the SOFA score was superior to other predictive assessments for CAP patients with a qSOFA score ≥2. For HCAP patients, A-DROP and SOFA scores both showed a higher AUROC value compared to CURB-65, PSI, or I-ROAD. In HCAP patients with a qSOFA score ≥2, the AUROC value for SOFA score was higher than all other predictive assessments. These results suggest that a combination of qSOFA and SOFA scores might be the best method to assess the prognosis in CAP and HCAP. Matsunuma et al. (Matsunuma et al., 2014) reported that I-ROAD was the best predictive assessment for 30-day mortality in HCAP patients. However, the present study did not reproduce this result. This discrepancy may be due to differences in the variables assessed, the patient group, and the study design.

In this study, the clinical profiles of the HCAP patients were quite different from those of the CAP patients. In particular, the HCAP patients showed a greater number of comorbidities than the CAP patients. Additionally, the HCAP patients in this study were more likely to be treated with anti-pseudomonal antibiotic therapy than the CAP patients. The HCAP group patients also showed higher 30-day and in-hospital mortality rates than the CAP group patients, consistent with the results of previous studies (Matsunuma et al., 2014; Shindo et al., 2009; Ugajin et al., 2014). However, the 30-day and in-hospital mortality rates for the HCAP patients in the current study were lower than those reported previously (5% in the current study vs. 13.7–18.9% in previous studies). This study also found a small proportion of severe HCAP patients compared with previous studies, with 37% of patients showing an A-DROP score of 4–5, 73% of patients showing a CURB-65 score of 4–5, and 67% of patients showing a PSI score of IV–V. The differences in severity are likely related to the differences in mortality rates between the present study and previous studies. There were fewer severe/very severe pneumonia patients and more mild/moderate pneumonia patients due to the location of the study institution. In particular, patients living in nursing homes tended to present early to the hospital even if they were not very ill. This is because such patients cannot be cared for in a nursing home in Japan.

With regard to the CAP patients in this study, the sample of patients was not large enough to identify differences between this study and previous studies.

The mean age of patients in this study was 75.4 years, which seems to represent the elderly population in developed countries. The mean age in this study was higher than that reported in previous studies. The study institution is located in a rural area and there is no municipal hospital in the city. This institute works not only as a university hospital but also as a municipal hospital. These special factors could reflect the very high mean age of the cohort.

Previously, Maruyama et al. (Maruyama et al., 2013) reported that initial treatment failure and hypoalbuminemia were unfavorable prognostic factors for 30-day mortality in HCAP patients. In contrast, another study reported that inappropriate antibiotic therapy was not a poor prognostic factor for 30-day mortality (Matsunuma et al., 2014). In support of these results, it was observed in the present study that neither inappropriate antibiotic therapy nor the detection of PDR pathogens was correlated with a poor outcome among either HCAP or CAP patients. Although the reasons for these results are unclear, it is possible that PDR pathogens are not always associated with pneumonia but rather may colonize the bronchial tracts or the lungs. Thus, CAP-related pathogens should be covered as an initial treatment. The overuse of broad-spectrum antibiotics does not contribute to improved outcomes among CAP and HCAP. Rather, it may lead to the occurrence of *Clostridium difficile* infections or the emergence of PDR pathogens, both of which could result in an increased risk of in-hospital mortality.

There are several limitations to the present study. First, the study employed a retrospective design and only included a relatively small number of patients from one hospital. A large-scale multicenter study is thus necessary to assess the efficacy and accuracy of the qSOFA and SOFA scores as prognostic tools for 30-day mortality among CAP and HCAP patients. Second, this study had a lower proportion of severe HCAP patients compared with previous studies. This difference in severity may explain the lower mortality rate seen in the present study compared to previous studies (Matsunuma et al., 2014; Shindo et al., 2009; Ugajin et al., 2014).

In conclusion, qSOFA and SOFA scores were able to accurately evaluate the severity of CAP and HCAP. These tools could thus be useful in the treatment of this condition. The study results suggest that the combination of a qSOFA score ≥2 and a SOFA score ≥4 is an independent unfavorable prognostic factor for 30-day mortality among CAP patients, while the combination of a qSOFA score ≥2 and a SOFA score ≥6 is an independent unfavorable prognostic factor for 30-day mortality among HCAP patients.

Funding source

None to declare.

Ethical approval

This study was approved by the Institutional Review Board of Aichi Medical University Hospital.

Conflict of interest

No competing interest declared.

Author contributions

NA: study design, data collection, data analysis, writing; HW: data collection; AS: data analysis; DS: supervised microbiology; HK: supervised antibiotics; MH: data analysis; YK: data analysis; YY: data analysis; HS: supervised microbiology; HM: study design and final draft.

Acknowledgements

We are grateful for the diligent and thorough critical reading of our manuscript by Dr Yoshihiro Ohkuni, Chief Physician, Taiyo and Mr John Wocher, Executive Vice President and Director, International Affairs/International Patient Services, Kameda Medical Center (Japan). We acknowledge the 12th Award in the category of Clinical Research conferred by the director of the West Japan Branch of the Japanese Society of Chemotherapy.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2019.04.020.

References

American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171(4):388–416.

Asai N, Watanabe H, Shiota A, Kato H, Sakanashi D, Hagihara M. Could qSOFA and SOFA score be correctly estimating the severity of healthcare-associated pneumonia?. J Infect Chemother 2018;24(3):228–31.

British Thoracic Society Standards of Care Committee. BTS guidelines for the management of community acquired pneumonia in adults. Thorax 2001;56 (Suppl. 4):IV1–64.

Charles PG, Wolfe R, Whitby M, Fine MJ, Fuller AJ, Stirling R, et al. SMART-COP: a tool for predicting the need for intensive respiratory or vasopressor support in community-acquired pneumonia. Clin Infect Dis 2008;47(3):375–84.

Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373–83.

Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 21st informational supplement. M 100-S21. Wayne, PA: CLSI; 2011.

de Groot V, Beckerman H, Lankhorst GJ, Bouter LM. How to measure comorbidity: a critical review of available methods. J Clin Epidemiol 2003;56(3):221–9.

Ishida T, Hashimoto T, Arita M, Ito I, Osawa M. Etiology of community-acquired pneumonia in hospitalized patients: a 3-year prospective study in Japan. Chest 1998;114(6):1588–93.

Japanese Respiratory Society. Establishment of new severity ratings based on analysis of hospital-acquired pneumonia. Respirology 2009;14(Suppl2):S4–9.

Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Suppl. 2):S27–72.

Maruyama T, Fujisawa T, Okuno M, Toyoshima H, Tsutsui K, Maeda H, et al. A new strategy for healthcare-associated pneumonia: a 2-year prospective multicenter cohort study using risk factors for multidrug-resistant pathogens to select initial empiric therapy. Clin Infect Dis 2013;57(10):1373–83.

Matsunuma R, Asai N, Ohkuni Y, Nakashima K, Iwasaki T, Misawa M, et al. I-ROAD could be efficient in predicting severity of community acquired pneumonia or Healthcare-associated-pneumonia. Singapore Med J 2014;55(6):318–24.

Miyashita N, Matsushima T, Oka M, Japanese Respiratory Society. The JRS guidelines for the management of community-acquired pneumonia in adults: an update and new recommendations. Intern Med 2006;45(7):419–28.

Miyashita N, Ouchi K, Kawasaki K, Komura H, Kawai Y, Tsumura N, et al. Comparison of serological tests for detection of immunoglobulin M antibodies to chlamydophila pneumoniae. Respirology 2008;13(3):427–31.

Niederman MS, Mandell LA, Anzueto A, Bass JB, Broughton WA, Campbell GD, et al. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. Am J Respir Crit Care Med 2001;163(7):1730–54.

Raith EP, Udy AA, Bailey M, McGloughlin S, MacIsaac C, Bellomo R, et al. Prognostic accuracy of the SOFA Score, SIRS criteria, and qsofa score for in-hospital mortality among adults with suspected infection admitted to the intensive care unit. JAMA 2017;317(3):290–300.

Ranzani OT, Prina E, Menéndez R, Ceccato A, Cilloniz C, Méndez R, et al. New Sepsis Definition (Sepsis-3) and community-acquired pneumonia mortality: a validation and clinical decision-making study. Am J Respir Crit Care Med 2017;196(10):1287–97.

Seki M, Watanabe A, Mikasa K, Kadota J, Kono S. Revision of the severity rating and classification of hospital-acquired pneumonia in the Japanese Respiratory Society guidelines. Respirology 2008;13(6):880–5.

Shindo Y, Sato S, Maruyama E, Ohashi T, Ogawa M, Hashimoto N, et al. Health-care-associated pneumonia among hospitalized patients in a Japanese community hospital. Chest 2009;135(3):633–40.

Ugajin M, Yamaki K, Hirasawa N, Kobayashi T, Yagi T. Prognostic value of severity indicators of nursing-home-acquired pneumonia versus community-acquired pneumonia in elderly patients. Clin Interv Aging 2014;9:267–74.

Venditti M, Falcone M, Corrao S, Licata G, Serra P, Study Group of the Italian Society of Internal Medicine. Outcomes of patients hospitalized with community-acquired, health care-associated, and hospital-acquired pneumonia. Ann Intern Med 2009;150(1):19–26.

WHO Global Health Observatory (GHO). Causes of death in 2008. 2018. . . [Accessed May 27, 2018] http://www.who.int/gho/mortality_burden_disease/causes_-death_2008/en/index.html.