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Importance of Functional Assessment in the Management of Community-acquired and Healthcare-associated Pneumonia

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Abstract

Objective In Japan, the number of elderly people who have difficulties performing the activities of daily living (ADLs) is increasing. The objective of this study was to assess the relationship between ADL and the clinical characteristics of pneumonia.

Methods We conducted a retrospective study of 219 adult patients hospitalized due to pneumonia [151 patients with community-acquired pneumonia (CAP) and 68 patients with healthcare-associated pneumonia (HCAP)]. CAP, HCAP, and all the patients were stratified into two groups using a modified version of the Katz index of five ADLs as follows: independent in all ADLs or dependent in one to three ADLs (CAP-A, HCAP-A, and All-A groups) and dependent in four or five ADLs (CAP-B, HCAP-B, and All-B groups). Disease severity, microbiological findings, and mortality were compared between the groups.

Results As the ability to perform ADLs declined, A-DROP scores (the CAP severity measurement index) increased significantly in CAP (CAP-A: 1.1±1.1, CAP-B: 2.6±1.1), HCAP (HCAP-A: 2.0±1.0, HCAP-B: 2.8±1.0), and all patients (All-A: 1.3±1.1, All-B: 2.8±1.0). Thirty-day mortality was higher in the CAP-B (23.1%) and All-B (19.2%) groups than in the CAP-A (0.7%) and All-A (1.8%) groups, respectively. A multivariate Cox proportional hazards analysis showed an ADL score ≥ four to be a significant predictor of 30-day mortality in CAP patients [hazard ratio (HR), 19.057; 95% confidence interval (CI), 1.930-188.130] and in all patients (HR, 8.180; 95% CI, 1.998-33.494).

Conclusion A functional assessment using a modified version of the Katz index is useful for the management of CAP and HCAP patients.

Key words: activities of daily living, respiratory tract infections, frail elderly, mortality, healthcare

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Introduction

In Japan and other developed countries, the number of elderly people who have difficulties and require supports in their activities of daily living (ADLs) is growing (1, 2). To manage patients with pneumonia who have frequent or chronic contact with the healthcare system and are found to be at risk of having drug-resistant pathogens with high mortality, healthcare-associated pneumonia (HCAP) that requires broad-spectrum antimicrobial drugs was included as a category of pneumonia according to the 2005 American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines (3).

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However, the HCAP population is heterogeneous and overlaps with that of community-acquired pneumonia (CAP) in the elderly (4-6). Additionally, physical functional status is not included in the HCAP definition, even though it is a crucial predictor of drug-resistant pathogens and patient outcome (4, 7, 8).

El Solh et al. previously analyzed 88 patients with culture-positive, severe nursing home-acquired pneumonia (NHAP) and reported that the degree of ADL decline was one of the important predictors of drug-resistant pathogens (9). In addition, Lim et al. evaluated 437 patients with NHAP and CAP in the UK and found that NHAP patients had greater mortality related to poor functional status (10).

It is conceivable that ADLs are an important factor in the management of elderly patients with pneumonia. Nevertheless, few studies have evaluated the relationship between ADLs and the clinical characteristics of CAP and HCAP in Japan. The objective of this study was to evaluate differences in the clinical characteristics of pneumonia among patients classified by stratification of ADL before admission and to determine how ADL is related to clinical outcome in CAP and HCAP patients.

Materials and Methods

Study design, subjects, and definitions

We conducted a retrospective study of 219 patients with pneumonia who were hospitalized at Nijigaoka Hospital (a 150-bed community hospital in Nagasaki, Japan) between July 2009 and March 2012.

All patients were divided into CAP and HCAP groups based on the 2005 ATS/IDSA guidelines. Briefly, a patient with HCAP was defined as any patient with pneumonia who satisfied one of the following criteria: (1) hospitalization for two or more days in the preceding 90 days, (2) residence in a nursing home or extended care facility, (3) home infusion therapy (including antibiotics), (4) chronic dialysis within 30 days, or (5) home wound care (3). Long-term care facilities (LTCFs) included nursing homes, homes with more medical services, chronic-care hospitals, and psychiatric hospitals.

The ADL dependency of all hospitalized patients was routinely evaluated by nurses according to a uniform format used in Nijigaoka Hospital. ADL decline was defined as the need for personal assistance in performing one or more ADLs. The physical functional status was measured using a simplified and modified version of the Katz index of five ADLs: bathing, dressing, moving from a bed to a chair, using a toilet, and eating (11). CAP patients, HCAP patients, and all patients were divided into two groups according to their level of dependence on assistance to perform ADLs before admission as follows: patients with pneumonia who were independent in all ADLs or dependent in one to three ADLs (CAP-A, HCAP-A, and All-A groups) and those who were dependent in four or five ADLs (CAP-B, HCAP-B, and All-B groups).

We compared the baseline characteristics, identified pathogens, and clinical outcomes between the groups. The study was approved by the institutional review board of Nijigaoka Hospital. Informed consent was not required because the study was retrospective and the data were obtained within the context of normal daily practice. Pneumonia was defined as the appearance of a new infiltrate on chest images that was accompanied by clinical symptoms, such as cough, sputum and fever, or inflammatory reactions (e.g., leukocytosis, leukopenia, or increased C-reactive protein levels) on laboratory tests. Patients who were diagnosed with hospital-acquired pneumonia (HAP), lung cancer-associated obstructive pneumonia, interstitial pneumonia, organizing pneumonia, or eosinophilic pneumonia were excluded. Probable aspiration was defined as aspiration witnessed, confirmed by the water-drinking test on hospital admission, or strongly suspected based on the patient's clinical course (12). The outcome measures were 30-day mortality and initial treatment failure. Initial treatment failure was defined as death during initial treatment or change of therapeutic agents from initial agents to others due to clinical ineffectiveness (e.g., lack of response or worsening of fever pattern, respiratory condition, and/or radiographic findings). Therapy was deemed inappropriate if the identified pathogens were resistant to the initially prescribed antibiotics based on in vitro susceptibility testing or if the initially administered antibiotics were not recommended for treatment of the identified pathogens according to the Japanese CAP and HAP guidelines (13, 14).

Severity evaluation

Pneumonia severity was evaluated using the predictive rule of a five-point scoring system for CAP: the A-DROP [age, dehydration, respiratory failure, orientation disturbances, and low blood pressure (BP)], which was proposed by the Japanese Respiratory Society (13). These are basically modified versions of the CURB-65 (13, 15, 16).

Microbiological evaluation

Pathogens in samples obtained from sputum, blood, or other body fluids were investigated using standard microbiological procedures. The results of blood cultures were accepted as an etiological diagnosis if no other source could be identified for the positive culture. Sputum samples were cultured in a quantitative manner, and positive bacterial culture results for sputum were documented from medical records. Serologic methods using single sera were used to detect immunoglobulin (Ig)M antibodies against *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*. Rapid immunochromatographic assays were used to detect the influenza virus antigen in nasopharyngeal swabs, *Streptococcus pneumoniae* in urine and *Legionella pneumophila* serogroup 1 antigen in urine. These examinations were ordered by attending physicians as needed for each patient. Methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas* species, *Acinetobacter* species, and extended-spectrum beta-

Table 1. Baseline Characteristics of Patients with Pneumonia

	CAP (n = 151)		p value	HCAP (n = 68)		p value	All patients (n = 219)		p value
	CAP-A n = 138	CAP-B n = 13		HCAP-A n = 29	HCAP-B n = 39		All-A n = 167	All-B n = 52	
Age (years)	67.6 ± 18.9	88.0 ± 8.3	<0.001	79.8 ± 9.7	82.7 ± 12.5	0.076	69.7 ± 18.2	84.0 ± 11.7	<0.001
Sex (male / female)	77/61 (55.8)	5/8 (38.5)	0.257	17/12 (58.6)	15/24 (38.5)	0.141	94/73 (56.3)	20/32 (38.5)	0.027
Tube feeding	0 (0.0)	1 (7.7)	0.086	0 (0.0)	6 (15.4)	0.034	0 (0.0)	7 (13.5)	<0.001
Antibiotic use within 90 days	0 (0.0)	0 (0.0)	-	10 (34.5)	5 (12.8)	0.042	10 (6.0)	5 (9.6)	0.357
Use of gastric acid-suppressants[a]	40 (29.0)	5 (38.5)	0.530	19 (65.5)	20 (51.3)	0.323	59 (35.3)	25 (48.1)	0.105
Probable aspiration	10 (7.2)	6 (46.2)	0.005	9 (31.0)	25 (64.1)	0.014	19 (11.4)	31 (59.6)	<0.001
Comorbidities									
Cerebrovascular disease	11 (8.0)	5 (38.5)	0.005	5 (17.2)	16 (41.0)	0.040	16 (9.6)	21 (40.4)	<0.001
Chronic pulmonary disease	42 (30.4)	3 (23.1)	0.756	15 (51.7)	5 (12.8)	0.001	57 (34.1)	8 (15.4)	0.009
Congestive heart failure	14 (10.1)	4 (30.8)	0.051	2 (6.9)	7 (17.9)	0.282	16 (9.6)	11 (21.2)	0.050
Chronic renal dysfunction	4 (2.9)	1 (7.7)	0.367	2 (6.9)	8 (20.5)	0.171	6 (3.6)	9 (17.3)	0.002
Chronic liver disease	7 (5.1)	2 (15.4)	0.174	3 (10.3)	2 (5.1)	0.644	10 (6.0)	4 (7.7)	0.746
Diabetes mellitus	22 (15.9)	2 (15.4)	1.000	4 (13.8)	10 (25.6)	0.364	26 (15.6)	12 (23.1)	0.215
Gastrectomy	5 (3.6)	0 (0.0)	1.000	3 (10.3)	2 (5.1)	0.644	8 (4.8)	2 (3.8)	1.000
Malignancy	6 (4.3)	2 (15.4)	0.143	5 (17.2)	3 (7.7)	0.272	11 (6.6)	5 (9.6)	0.541
Immunosuppression[b]	9 (6.5)	0 (0.0)	1.000	0 (0.0)	6 (15.4)	0.034	9 (5.4)	6 (11.5)	0.204

Values are expressed as mean ± standard deviation or the number (%).
CAP: community-acquired pneumonia, HCAP: healthcare-associated pneumonia
[a] Gastric acid-suppressants included histamine H_2-receptor blockers or proton pump inhibitors.
[b] Immunosuppression was defined as administration of corticosteroids (5 mg/day or more) or other immunosuppressive agents.

lactamase (ESBL) producing *Enterobacteriaceae* were considered as multidrug-resistant (MDR) pathogens (3, 17).

Statistical analysis

Continuous variables are expressed as mean ± standard deviation, and differences between groups were statistically analyzed by Student's *t*-tests when variables were normally distributed and Mann-Whitney U tests when variables were not normally distributed. Fisher's exact tests were used to compare categorical data between the groups. Survival rates within 30 days were estimated using the Kaplan-Meier method and compared between the groups with log-rank tests. We conducted univariate and multivariate analyses using a Cox proportional hazards model. Variables with p values <0.2 in univariate analysis were selected and adjusted by forward stepwise selection in multivariate analysis to identify the predictors of 30-day mortality. The data were analyzed using SPSS 16.0J for Windows (SPSS Inc., Chicago, USA), and p values of 0.05 were considered statistically significant.

Results

Patient characteristics

The characteristics of the 219 patients enrolled in the study are presented in Table 1. The mean age was significantly higher in the CAP-B and All-B groups than in CAP-A and All-A groups. All patients who received tube feeding were included in the reduced ADL group. As inactivity advanced, the proportion of aspiration pneumonia increased. About 40% of CAP-B and HCAP-B patients had cerebrovascular disease as a comorbidity. Immunosuppression was significantly higher in the HCAP-B group compared to the HCAP-A group. Conversely, the incidence of chronic lung disease was lower in the HCAP-B and All-B groups than in the HCAP-A and All-A groups. Chronic renal dysfunction was higher in the All-B group compared to the All-A group.

Regarding ADL dependency, a total of 75.5% of CAP patients and 27.9% of HCAP patients were independent in all ADLs. Conversely, 7.3% of CAP and 44.1% of HCAP patients needed support in all five ADLs.

HCAP-A patients were previously administered antibiotics within 90 days more frequently than HCAP-B patients. Gastric acid-suppressants were similarly prescribed between the groups.

Symptoms, clinical, laboratory, and radiographic findings

Cough was the most common symptom in CAP patients (CAP-A group: 80.4%, CAP-B group: 61.5%, p=0.150), with a lower frequency in HCAP patients with declined ADL (HCAP-A group: 69.0%, HCAP-B group: 43.6%, p=0.050). In contrast, the percentage of disoriented patients significantly increased along with ADL decline in CAP (6.5% in CAP-A group, 53.8% in CAP-B group, p<0.001) and HCAP patients (10.3% in HCAP-A group, 56.4% in HCAP-B group, p<0.001).

Table 2 shows the physical findings and laboratory data of the study subjects. Hypoxia was observed in 53.8% of the CAP-B group but only 23.9% of the CAP-A group. More than 60% of HCAP patients had hypoxia, which was similar for the HCAP-A and B groups. The frequency of low BP was higher in the HCAP-B group compared to the HCAP-A group.

The laboratory data indicated that serum albumin decreased with worsening physical function in CAP and

Table 2. Physical Examinations and Laboratory Findings of the Patients

	CAP (n = 151)		p value	HCAP (n = 68)		p value	All patients (n = 219)		p value
	CAP-A n = 138	CAP-B n = 13		HCAP-A n = 29	HCAP-B n = 39		All-A n = 167	All-B n = 52	
Clinical parameters									
Temperature (°C)	38.4 ± 1.0	37.9 ± 1.1	0.201	38.2 ± 0.8	38.3 ± 0.7	0.610	38.3 ± 1.0	38.2 ± 0.9	0.458
Pulse rate (/min)	88.5 ± 16.6	78.3 ± 15.3	0.035	85.4 ± 18.7	89.4 ± 18.4	0.378	87.9 ± 16.9	86.6 ± 18.2	0.636
Systolic BP ≤ 90 mmHg	1 (0.7)	0 (0.0)	1.000	1 (3.4)	9 (23.1)	0.036	2 (1.2)	9 (17.3)	<0.001
SpO_2 ≤ 90%	33 (23.9)	7 (53.8)	0.042	18 (62.1)	25 (64.1)	1.000	51 (30.5)	32 (61.5)	<0.001
Laboratory data									
White blood cell (/μL)	10,891.3 ± 5,301.4	10,092.3 ± 3,929.7	0.779	12,073.4 ± 5,111.8	11,723.1 ± 5,422.0	0.788	11,096.6 ± 5,273.0	11,315.4 ± 5,103.3	0.609
Red blood cell ($\times 10^4$/μL)	402.2 ± 53.1	387.5 ± 45.8	0.336	378.6 ± 43.2	369.8 ± 61.7	0.204	398.1 ± 52.2	374.2 ± 58.2	0.006
Platelets ($\times 10^4$/μL)	21.6 ± 8.0	24.1 ± 6.3	0.162	21.2 ± 9.9	20.6 ± 9.4	0.968	21.5 ± 8.3	21.5 ± 8.8	0.987
Total protein (g/dL)[a]	6.9 ± 0.6	6.6 ± 0.7	0.135	6.5 ± 0.8	6.3 ± 0.7	0.055	6.8 ± 0.7	6.3 ± 0.7	<0.001
Albumin (g/dL)[a]	3.6 ± 0.6	3.0 ± 0.4	0.002	3.1 ± 0.6	2.8 ± 0.5	0.037	3.5 ± 0.6	2.8 ± 0.5	<0.001
BUN (mg/dL)	16.2 ± 8.5	23.3 ± 6.9	<0.001	20.3 ± 10.4	27.3 ± 25.5	0.611	16.9 ± 9.0	26.3 ± 22.3	<0.001
Creatinine (mg/dL)	0.9 ± 0.4	1.0 ± 0.4	0.399	0.9 ± 0.4	1.1 ± 0.6	0.802	0.9 ± 0.4	1.0 ± 0.6	0.396
Na (mEq/L)	136.6 ± 3.9	132.1 ± 7.4	0.013	137.7 ± 4.6	136.4 ± 6.1	0.329	136.8 ± 4.0	135.3 ± 6.6	0.188
K (mEq/L)	3.9 ± 0.5	4.4 ± 0.9	0.053	4.0 ± 0.6	4.2 ± 1.0	0.424	3.9 ± 0.5	4.3 ± 1.0	0.024
Cl (mEq/L)	99.3 ± 4.4	94.5 ± 8.4	0.035	100.6 ± 4.7	100.5 ± 6.1	0.937	99.5 ± 4.5	99.0 ± 7.2	0.843
CRP (mg/dL)	12.0 ± 9.3	9.1 ± 5.8	0.427	9.7 ± 8.6	10.5 ± 8.7	0.522	11.6 ± 9.2	10.2 ± 8.1	0.457

Values are expressed as mean ± standard deviation or the number (%).

CAP: community-acquired pneumonia, HCAP: healthcare-associated pneumonia, BP: blood pressure, SpO_2: pulse oximetric oxygen saturation, BUN: blood urea nitrogen, CRP: C-reactive protein

[a] Serum total protein and albumin were measured in 79.5% and 82.2% of all patients, respectively.

HCAP patients. High levels of blood urea nitrogen (BUN) and hyponatremia were observed in the CAP-B group compared to the CAP-A group. A significant difference in potassium levels was seen between All-A and All-B patients.

Radiography demonstrated that the incidence of bilateral involvement was similar between the groups in CAP (CAP-A group: 31.9%, CAP-B group: 30.8%, p=1.000), HCAP (HCAP-A group: 51.7%, HCAP-B group: 56.4%, p=0.807), and all patients (All-A group: 35.3%, All-B group: 50.0%, p=0.073). Pleural effusion tended to occur more frequently in ADL-declined groups in CAP (CAP-A group: 26.1%, CAP-B group: 53.8%, p=0.051), HCAP (HCAP-A group: 27.6%, HCAP-B group: 46.2%, p=0.138), and all patients (All-A group: 26.3%, All-B group: 48.1%, p=0.006).

Distribution of identified pathogens

Streptococcus pneumoniae was the most frequently isolated pathogen in all patients, and the isolation rate was similar between the CAP (20.5%) and HCAP groups (23.5%). *Mycoplasma pneumoniae* was the second most commonly detected pathogen in the CAP (12.6%) and HCAP (14.7%) groups.

The microbes identified in each group are shown in Table 3. MRSA was significantly more frequently identified in the All-B group (13.5%) compared to the All-A group (3.0%). An inter-group comparison indicated no significant differences between the groups in terms of the numbers of identified pathogens.

Among patients with identified pathogens, MDR pathogens were identified more frequently in the All-B group (36.0%, nine of 25 patients) than the All-A group (13.4%, nine of 67 patients) (p=0.035).

Disease severity, antibiotic treatment, and clinical outcome

Pneumonia severity and the clinical outcomes are presented in Table 4. As physical function diminished, the A-DROP score increased, with statistically significant differences between groups. The 30-day mortality was higher in the CAP-B and All-B groups compared to the CAP-A and All-A groups. A similar was observed in the comparison of the HCAP-A and B groups, although the difference was not significant.

Initial treatment failure occurred more frequently in the CAP-B group than in the CAP-A group, and the duration of antibiotic therapy and length of hospital stay were much longer in the CAP-B and All-B groups than in CAP-A and All-A groups.

No significant differences were seen between the groups in terms of overall antimicrobial therapy by monotherapy in CAP patients (CAP-A group: 55.8% and CAP-B group: 69.2%, p=0.396) or in HCAP patients (HCAP-A group: 58.6% and HCAP-B group: 71.8%, p=0.305). A total of 67.3% of patients in the All-B group received monotherapy with beta-lactams. In particular, carbapenem was administered to 13.5% of patients in All-B and only 3.6% of the All-A group (p=0.015). Conversely, combination therapy with beta-lactams plus tetracyclines was administered to 17.4% of patients in the All-A group and 3.8% of patients in the All-B group (p=0.012).

In the All-A group, 11 of 67 patients with at least one identified pathogen received inappropriate therapy. Initial treatment failure occurred in five of 56 patients (8.9%) who received appropriate therapy, while four of 11 patients (36.4%) in the All-A group received inappropriate therapy (p=0.034). In the All-B group, nine of 25 patients with iden-

Table 3. Pathogens Identified in Patients with Pneumonia

	CAP (n = 151)		p value	HCAP (n = 68)		p value	All patients (n = 219)		p value
	CAP-A n = 138	CAP-B n = 13		HCAP-A n = 29	HCAP-B n = 39		All-A n = 167	All-B n = 52	
Gram-positive pathogens									
Streptococcus pneumoniae	30 (21.7)	1 (7.7)	0.306	6 (20.7)	10 (25.6)	0.775	36 (21.6)	11 (21.2)	1.000
Staphylococcus aureus	8 (5.8)	1 (7.7)	0.566	3 (10.3)	7 (17.9)	0.498	11 (6.6)	8 (15.4)	0.085
MSSA	5 (3.6)	0 (0.0)	1.000	1 (3.4)	1 (2.6)	1.000	6 (3.6)	1 (1.9)	1.000
MRSA	3 (2.2)	1 (7.7)	0.305	2 (6.9)	6 (15.4)	0.451	5 (3.0)	7 (13.5)	0.009
Gram-negative pathogens									
Haemophilus Influenzae	11 (8.0)	0 (0.0)	0.600	2 (6.9)	1 (2.6)	0.571	13 (7.8)	1 (1.9)	0.196
Klebsiella pneumoniae	2 (1.4)	0 (0.0)	1.000	2 (6.9)	4 (10.3)	1.000	4 (2.4)	4 (7.7)	0.093
Pseudomonas aeruginosa	1 (0.7)	1 (7.7)	0.165	1 (3.4)	2 (5.1)	1.000	2 (1.2)	3 (5.8)	0.088
Escherichia coli	1 (0.7)	0 (0.0)	1.000	0 (0.0)	2 (5.1)	0.504	1 (0.6)	2 (3.8)	0.141
Acinetobacter baumannii	0 (0.0)	0 (0.0)	-	2 (6.9)	0 (0.0)	0.178	2 (1.2)	0 (0.0)	1.000
Moraxella catarrhalis	1 (0.7)	0 (0.0)	1.000	0 (0)	0 (0)	-	1 (0.6)	0 (0.0)	1.000
Other gram negative pathogens	1 (0.7)	0 (0.0)	1.000	0 (0.0)	1 (2.6)	1.000	1 (0.6)	1 (1.9)	0.419
MDR pathogens	5 (3.6)	2 (15.4)	0.112	4 (13.8)	7 (17.9)	0.747	9 (5.4)	9 (17.3)	0.016
Atypical pathogens									
Mycoplasma pneumoniae	17 (12.3)	2 (15.4)	0.669	6 (20.7)	4 (10.3)	0.305	23 (13.8)	6 (11.5)	0.817
Chlamydophila pneumoniae	1 (0.7)	1 (7.7)	0.165	1 (3.4)	0 (0.0)	0.426	2 (1.2)	1 (1.9)	0.558
Legionella pneumophila	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0)	-	0 (0.0)	0 (0.0)	-
Influenza virus	2 (1.4)	0 (0.0)	1.000	0 (0.0)	0 (0.0)	-	2 (1.2)	0 (0.0)	1.000
The number of identified pathogens									
At least one	52 (37.7)	5 (38.5)	1.000	15 (51.7)	20 (51.3)	1.000	67 (40.1)	25 (48.1)	0.337
Single	32 (23.2)	4 (30.8)	0.510	9 (31.0)	13 (33.3)	1.000	41 (24.6)	17 (32.7)	0.281
Double	16 (11.6)	1 (7.7)	1.000	4 (13.8)	3 (7.7)	0.449	20 (12.0)	4 (7.7)	0.458
Triple	4 (2.9)	0 (0.0)	1.000	2 (6.9)	4 (10.3)	1.000	6 (3.6)	4 (7.7)	0.253

Values are expressed as the number (%).
CAP: community-acquired pneumonia, HCAP: healthcare-associated pneumonia, MSSA: methicillin-susceptible *Staphylococcus aureus*, MRSA: methicillin-resistant *Staphylococcus aureus*, MDR: multidrug-resistant

Table 4. Disease Severity according to the A-DROP Scoring System, and Clinical Outcomes

	CAP (n = 151)		p value	HCAP (n = 68)		p value	All patients (n = 219)		p value
	CAP-A n = 138	CAP-B n = 13		HCAP-A n = 29	HCAP-B n = 39		All-A n = 167	All-B n = 52	
Severity evaluation									
A-DROP score	1.1 ± 1.1	2.6 ± 1.1	<0.001	2.0 ± 1.0	2.8 ± 1.0	0.002	1.3 ± 1.1	2.8 ± 1.0	<0.001
Outcome									
Initial treatment failure	8 (5.8)	5 (38.5)	0.002	5 (17.2)	4 (10.3)	0.481	13 (7.8)	9 (17.3)	0.063
30-day mortality	1 (0.7)	3 (23.1)	0.002	2 (6.9)	7 (17.9)	0.282	3 (1.8)	10 (19.2)	<0.001
Duration of intravenous antibiotics (days)	6.6 ± 3.5	10.0 ± 5.7	0.013	6.5 ± 2.7	8.6 ± 4.3	0.064	6.6 ± 3.3	8.9 ± 4.7	0.001
Hospitalization (days)	14.7 ± 19.5	21.8 ± 16.9	0.008	20.5 ± 18.0	29.8 ± 24.0	0.061	15.7 ± 19.3	27.8 ± 22.5	<0.001

Values are expressed as mean ± standard deviation or the number (%).
CAP: community-acquired pneumonia, HCAP: healthcare-associated pneumonia, A-DROP: age, dehydration, respiratory failure, orientation disturbances and low blood pressure

tified pathogens received inappropriate therapy. The frequencies of initial treatment failure were similar in patients with appropriate therapy (two of 16 patients, 12.5%) and those with inappropriate therapy (one of nine patients, 11.1%) (p= 1.000) in the All-B group.

Survival analysis and independent prognostic factors in CAP and HCAP patients

Kaplan-Meier curves showed that survival rates in the CAP-B and All-B groups were significantly lower than those in the CAP-A and All-A groups (Figure a, c). These trends were similar for the HCAP group (Figure b), although the difference was not significant.

Table 5 shows the results of the univariate and multivariate analyses of prognostic factors for 30-day mortality in patients with CAP and HCAP. On multivariate analysis, the independent predictors of 30-day mortality were ADL score ≥ four in CAP patients, malignancy, systolic BP ≤90 mmHg, and creatinine in HCAP patients and malignancy, ADL score ≥ four, and oxygen saturation (SpO_2) ≤90% in all patients.

Discussion

The present study demonstrates the differences in baseline characteristics, identified pathogens, disease severity, and clinical outcome among patients with pneumonia divided according to their ability to perform ADLs.

In our study, A-DROP scores and the 30-day mortality

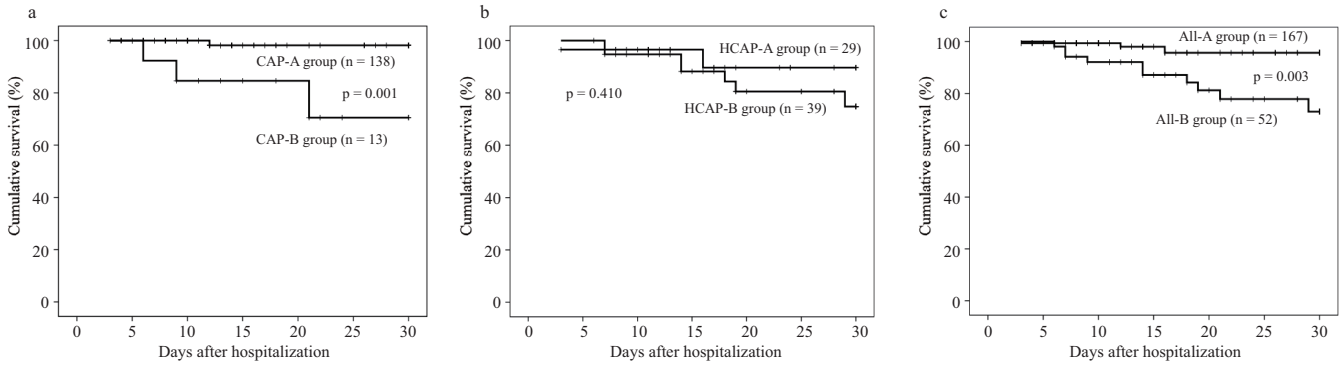

Figure. **Kaplan-Meier survival analysis of patients with pneumonia according to activities of daily living (ADLs) in community-acquired pneumonia (CAP) patients (a), healthcare-associated pneumonia (HCAP) patients (b), and all CAP and HCAP patients (c). The survival rates of the CAP-B and All-B groups were significantly lower than those in CAP-A and All-A groups, respectively. The prognosis in HCAP-B patients tended to be worse compared to HCAP-A patients, although the difference was not significant.**

Table 5. **Univariate and Multivariate Analysis of Prognostic Factors for 30-day Mortality in Patients with Community-acquired and Healthcare-associated Pneumonia**

	Univariate analysis			Multivariate analysis		
	HR	95% CI	p value	HR	95% CI	p value
CAP						
ADL score ≥ 4	19.057	1.930-188.130	0.012	19.057	1.930-188.130	0.012
Temperature (°C)	0.088	0.011-0.692	0.021			
Altered mental status	14.871	1.475-149.908	0.022			
K (mEq/L)	4.414	1.339-14.548	0.015			
Initial treatment failure	18.487	1.869-182.871	0.013			
HCAP						
Systolic BP ≤ 90 mmHg	3.159	0.789–12.648	0.104	7.762	1.567-38.450	0.012
Chronic renal dysfunction	4.315	1.152–16.159	0.030			
Malignancy	5.264	1.299-21.340	0.020	8.739	1.558-49.004	0.014
Immunosuppression	4.541	1.133–18.195	0.033			
BUN (mg/dL)	1.019	1.000–1.039	0.048			
Creatinine (mg/dL)	4.400	1.627–11.898	0.004	5.107	1.800-14.491	0.002
All patients						
ADL score ≥ 4	6.001	1.620–22.231	0.007	8.180	1.988-33.494	0.003
Congestive heart failure	3.216	1.049–9.866	0.041			
Chronic renal dysfunction	4.283	1.310–14.001	0.016			
Malignancy	6.411	1.964–20.932	0.002	13.370	3.291-54.313	<0.001
Systolic BP ≤ 90 mmHg	4.161	1.139–15.197	0.031			
SpO_2 ≤ 90%	4.774	1.034–22.040	0.045	7.464	1.422-39.185	0.018
BUN (mg/dL)	1.026	1.008–1.043	0.004			
Creatinine (mg/dL)	2.522	1.250–5.086	0.010			
K (mEq/L)	2.170	1.304–3.610	0.003			
Initial treatment failure	3.537	1.144–10.943	0.028			

HR: hazard ratio, CI: confidence interval, CAP: community-acquired pneumonia, HCAP: healthcare-associated pneumonia, ADL: activity of daily living, BP: blood pressure, BUN: blood urea nitrogen, SpO_2: pulse oximetric oxygen saturation

rate tended to be higher in patients with diminished ADL. A multivariate analysis indicated that ADL decline was an independent predictor of 30-day mortality in CAP patients and all patients. A previous report identified ADL dependency as an independent risk factor for both in-hospital and post-discharge mortality (18). Our results support those of a previous study in which functional status was the main determinant of outcome in elderly patients with pneumonia (7). Additionally, previous reports have indicated that performance status (PS) evaluation is useful for predicting the outcome of patients with pneumonia (19, 20). Therefore, PS is one of the criteria of nursing and healthcare-associated pneumonia (NHCAP), which was newly categorized in the 2011 Japanese Respiratory Society guidelines (6, 21). Although PS could not be documented from the medical records in the present study, our results, which focus on ADL dependency, correspond with the concept of NHCAP which includes patients with diminished PS in addition to HCAP patients.

We did not detect a significant difference between the 30-day mortalities of HCAP-A (6.9%) and HCAP-B (17.9%) patients, and ADL decline was not identified as an inde-

pendent risk factor for 30-day mortality in HCAP patients. Therefore, we should consider other factors when predicting prognosis in HCAP patients, a group that mainly includes patients with diminished ADL.

We found that malignancy was an important predictor of 30-day mortality in HCAP and all patients. A recent study reported that it was an independent risk factor for in-hospital mortality in HCAP patients (22). The number of outpatients undergoing cancer therapy is increasing as a result of dramatic advances in cancer treatment and care (23). Therefore, we should recognize malignancy as a risk factor for mortality in patients with pneumonia, excluding those with HAP.

Previous studies reported that serum albumin was an independent prognostic factor in CAP, NHAP, and HAP patients (19, 20). In the present study, the low serum albumin levels observed in the diminished ADL group could be indicative of malnutrition, which is probably related to the high frequency of tube feeding in these patients. However, we could not adequately assess it as a prognostic factor because serum albumin was not measured in 17.8% of the patients. Aspiration pneumonia, defined by the presence of risk factors for aspiration and chest computed tomography (CT) findings, is also an independent risk factor for 30-day mortality among CAP and HCAP patients (24). However, we could not apply a strict definition for aspiration pneumonia in this study because CT was not performed in all patients.

In the All-B group, the mortality rate within 30 days (19.2%) tended to be higher than the proportion of patients in whom primary treatment failed (17.3%). Primary antibiotic therapy was successful in seven of 10 patients who subsequently died, with the ultimate poor outcome in these patients attributed to the development of secondary complications or exacerbation of comorbidities. Therefore, the systemic management of these complications and preventing the onset of pneumonia, such as by prophylaxis against aspiration or vaccination, are as essential as treatment with appropriate antibiotics in patients with diminished ADL.

The identities of the causative pathogens are also important when considering pathophysiology in patients with pneumonia. Lopez et al. previously described that MDR pathogens are implicated in a variable percentage of HCAP patients and do not seem to be the unique or direct cause of their increased mortality (25). In the present study, the rate of MRSA isolation was significantly higher in All-B patients. However, MRSA was not identified from the sputum of any of the All-B patients who died within 30 days of admission (except from fecal culture in one of the patients who died). This indicates that the high 30-day mortality of the All-B patients was not directly associated with the increased frequency of MRSA isolation from sputum.

Because our study was retrospective, there are some limitations associated with it that should be considered. First, microbiological evaluations were not uniformly and sufficiently performed, particularly with respect to anaerobic pathogens that are an important cause of aspiration pneumonia. However, because about 60% of patients in the All-B group were suspected to have developed aspiration pneumonia, treatment to cover anaerobic pathogens should be prescribed for patients with decreased ADL. Second, previous studies indicated that the sensitivity of IgM antibodies against *Mycoplasma pneumoniae* was 33.3% (26). Therefore, our diagnosis using IgM against *Mycoplasma pneumoniae* might be insufficient. Third, two of 12 patients with MRSA isolation in this study ultimately required treatment with anti-MRSA drugs, but we were not able to assess whether empirical broad-spectrum antibiotic therapy with anti-MRSA drugs could improve the outcome of patients with ADL decline. Additionally, the frequency of HCAP (31.1%) was lower than that of CAP (68.9%) in the present study. Because the proportion of HCAP or NHCAP compared to CAP is very diverse and varies according to the geographic region and medical environment, some of our results might not apply to other institutions (12, 21, 22).

In conclusion, our findings revealed that ADL dependency correlates with high mortality and that subgrouping based on ADL score is useful for predicting the outcome in CAP and all CAP and HCAP patients. Furthermore, patients with decreased ADL have several disadvantages, including multiple comorbidities and malnutrition (hypoalbuminemia). Because they are predisposed to a poor outcome, appropriate antibiotic usage and systemic management, including prophylaxis, are required for adult patients with diminished ADL.

Functional assessment using the modified version of the Katz index is simple, useful, and important for predicting outcome and managing CAP and HCAP patients.

The authors state that they have no Conflict of Interest (COI).

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