

A Comparative Study of Nursing Home-Acquired Pneumonia with Community-Acquired Pneumonia

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Background: Little data is available regarding hospitalized patients with nursing home-acquired pneumonia (NHAP). This is unfortunate because there is an increasing number of elderly persons who are living in nursing homes in Korea. The aim of this study was to compare clinical characteristics and treatment responses of NHAP with community-acquired pneumonia (CAP).

Methods: Patients with pneumonia who were admitted from eight nursing homes or from their own homes were enrolled between May 2007 and April 2009. Their clinical characteristics and treatment responses were reviewed retrospectively, and differences between the two groups were analyzed.

Results: Of 110 Patients with pneumonia, 66 (60%) were from nursing homes and their median age was 84. In the NHAP group, functional performance status was significantly poorer, classical symptoms of pneumonia were less severe, and multi-lobe involvement (on chest radiographs) was more frequent than in the CAP group. Patients with NHAP more frequently showed lymphocytopenia, anemia, hypoalbuminemia, hypoxemia, and elevated blood urea nitrogen on admission. The mean CURB-65 score was 2.2 in the NHAP group, higher than 1.7 in the CAP group ($p=0.004$), and multi-drug resistant pathogens were also highly identified in NHAP group (39% vs. 10%, $p=0.036$). The mean duration of antibiotic therapy was greater for the NHAP (12.6 days) than for the CAP group (6.6 days) ($p<0.001$). The mortality rate was 23% in NHAP group, which was significantly higher than 5% in the CAP group ($p=0.014$).

Conclusion: NHAP should be more intensively investigated because of the higher frequency of multi-drug resistant pathogens and mortality than the CAP.

Key Words: Nursing Homes; Pneumonia, Community-Acquired

Introduction

The classification of pneumonia, traditionally categorized as community-acquired pneumonia (CAP) or hospital-acquired pneumonia (HAP) has been changed because the environmental situations out of hospital are becoming more complex to keep pace with "the aging society"^{1,2}. In Korea, the average annual increasing rate

of long-term care facilities, represented by nursing home, was remarkable during recent 4 years. Unquestionably, this was caused by the elderly population explosion and the introduction of the National Long-Term Care Insurance. There were more than 2,000 nursing homes in Korea, in which about 1.2% of the elderly were lived currently. For the same time, the mortality rate of pneumonia in Korea hold the 9th ranks, increased 70% during the present decade, especially in the elderly people³.

Nursing home-acquired pneumonia (NHAP) is probably the largest subgroup of healthcare-associated pneumonia (HCAP), and the number of cases has increased rapidly in recent years⁴. In addition, the elderly patients who were admitted in hospital due to NHAP would be

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held markedly with exceeding medical problems such as unreliable communication, poor social-economical status, absence of familial representatives, etc^{5,6}. However, there were extremely little evidences about NHAP, mainly being come from both a new category of respiratory infections and the variety of definitions.

Another big problem of NHAP is the choice treatment for patients with risks of multi-drug resistant (MDR) pathogens⁴. In view of the worldwide threat of increasing resistance to antimicrobial drugs, the acceptance of treating NHAP as the guideline of HAP without relevant evidences would increase the overuse or misuse of antimicrobial drugs, before long produce troublesome pressure in selecting antibiotics for drug-resistant organisms. Therefore, more established data are needed to put the clinical problems of NHAP into perspective⁷.

Herein, we tried to compare the clinical characteristics and treatment responses of patients with pneumonia who were admitted from nursing homes (NHAP group) with those from their own homes (CAP group). To our knowledge, this is the first clinical data about NHAP in Korea.

Materials and Methods

1. Study setting and subjects

This study was conducted at about 200-bed sized, community-based, secondary hospital in Chuncheon, Kangwon-do. Residents of eight nursing homes located at the same city or own homes were enrolled from May 2007 to April 2009, who admitted with pneumonia through emergency department or outpatient clinic. Targeted nursing homes were managed by registered nurses and care workers, and financially supported by municipal or religious organizations. Patients with autoimmune disorder requiring immunosuppressant, current malignancy underwent with chemotherapy or who suffered acquired immune deficiency syndrome were not included. In addition, patients who received antibiotics within 72 hours or transferred from other hospital before enrollment were also excluded. Their demographics; clinical characteristics such as co-morbidities, rou-

tine laboratory results, functional status, clinical symptoms and signs, and radiographic features; treatment responses such as duration of antibiotic use or hospital admission, empirical antibiotics regimens, the need of intensive care unit (ICU) management including appliance of mechanical ventilation and successful weaning, in-hospital mortality, and post-discharge follow-up of them were reviewed retrospectively and the differences between NHAP and CAP group were analyzed. In NHAP group, more detailed differences were also compared according to the presence of MDR pathogens. Initially, we included 113 patients with pneumonia aged 20 years and over, however, three patients in CAP group who were under fifty years, which was not matched with NHAP group also were excluded for comparable analysis.

2. Definitions

The diagnostic criteria of pneumonia were satisfied with newly detected infiltrates on chest x-ray (CXR) or chest computed tomography (CT) and two or more than clinical findings as follows; 1) fever (temperature $\geq 38.0^{\circ}\text{C}$) or hypothermia (temperature $\leq 35.0^{\circ}\text{C}$), 2) leukocytosis or leukopenia, 3) newly developed cough with or without purulent sputum, pleuritic chest pain, or dyspnea, and 4) altered breath sounds on auscultation or hypoxemia in blood gas analysis^{8,9}. A radiologist working in the study hospital interpreted all of the radiological findings of CXR or CT and one investigator reviewed all of the radiographic results.

Microbiologically, Gram's stain and culture of sputum with a set of blood culture prior to antibiotics administration were done, when available. An etiology diagnosis was based by results of sputum culture only in cases of the acceptable grade 4 or 5 of Gram's stain, epithelial cells $<10/\text{low power field (LPF)}$ or $10\sim 25/\text{LPF}$ with white blood cell (WBC) $>25/\text{LPF}$.

For the scales of evaluating patient's functional status, the Eastern Cooperative Oncology Group (ECOG) Performance Status criteria were borrowed as same as Lim's study¹⁰. Originally, these scales were supposed to assess the progression of cancer patient's disease, that is how

the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis. By the ECOG scale, grade 0 means that the patient is fully active, able to carry on all performance without restriction; grade 1 restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; grade 2 ambulatory but unable to carry out any work activities up and about more than 50% of waking hours, grade 3 capable of only limited self-care, confined to bed or chair more than 50% of waking hours, grade 4 completely disabled and totally confined to bed or chair, grade 5 dead, respectively¹¹.

The confusion, urea nitrogen, respiratory rate, blood pressure (CURB)-65 is a clinical prediction rule that has been validated for predicting mortality in community-acquired pneumonia and the score is an acronym for each of the risk factors measured¹². Each risk factor scores one point, for a maximum score of 5: Confusion of new onset, blood urea nitrogen >19 mg/dL, respiratory rate of 30 breaths per minute or greater, blood pressure less than 90 mm Hg systolic or diastolic blood pressure 60 mm Hg or less, and age 65 or older.

Appropriate antibiotic therapy was defined as the compatible use of empirical or consequent antibiotics directed to the specific microorganism according to susceptibility test criteria for respiratory pathogens with successful clinical response. We also defined the multi-drug resistant pathogens as Methicillin-resistant *Staphylococcus Aureus* (MRSA) or the gram negative pathogen resistant to more than 2 of the following drug classes: 3rd or 4th generation cephalosporins, beta-lactam/beta-lactamase inhibitor combinations, carbapenems, fluoroquinolones, and aminoglycosides.

3. Statistical analysis

Statistical comparisons between the two groups were performed using commercial software (SPSS for Windows version 17.0; SPSS Inc., Chicago, IL, USA). Results are expressed as mean values±standard deviation (SD) or case numbers/total patients (%). To detect significant differences between groups, we used the χ^2 or Fisher exact test for categorical variables, and the Student's

t-test or Mann-Whitney test for continuous variables, whether the variables appropriate parametric or non-parametric method. Statistical significance was assumed at $p < 0.05$, all reported p-values are 2-tailed.

Results

1. Baseline characteristics

Of 110 patients, 66 (60%) patients were admitted from nursing home due to pneumonia. Their median age was 84 years, which was significantly older than that of CAP group. Sex distribution was similar between both groups. Common co-morbidities of the NHAP group were hypertension, dementia, cerebrovascular accident (CVA), and ileus; 46 (69.7%), 33 (50.0%), 31 (47.0%), and 16 (24.2%), in order. These co-morbidities were significantly more frequent than CAP group, however, chronic airway disease and sequelae of tuberculosis were vice versa (Table 1). In NHAP group, the average score of functional status based by ECOG scale was 3.4 ± 1.3 compared with 1.4 ± 0.7 in CAP group ($p < 0.001$). Of laboratory parameters, lymphocytopenia, anemia, hypoalbuminemia, hypoxemia, and elevated blood urea nitrogen (BUN) were significant findings in NHAP group. There were no significant difference in prior treatment of antibiotics within 3 months between both groups (12/66 [18.2%] in NHAP vs. 5/44 [11.4%] in CAP; $p=0.424$).

2. Clinical manifestations and radiographic outcomes

Patients with NHAP complained less frequently classical respiratory symptoms of pneumonia such as cough (26 [39.4%] vs. 34 [77.3%]; $p < 0.001$) and purulent sputum (34 [51.5%] vs. 32 [72.7%]; $p=0.030$) with statistically significance, whereas the differences of other symptoms were non-specific except macro-aspiration, that means an aspiration identified with the naked eye of patient's caregivers (9 [13.6%] vs. 1 [2.3%]; $p=0.048$). The most common clinical symptoms in NHAP group was fever (47/66, 71.2%), however the frequency of fever between both groups was not significantly different. Abnormal lung sound in physical examination per-

Table 1. Baseline characteristics of the study subjects

	Nursing home group (n=66)	Community group (n=44)	p-value
Demographics			
Mean age, median range	84 (53~100)	77.5 (52~95)	0.014*
Age group, yr			
<65	2/66 (3.0)	6/44 (13.6)	
65~79	19/66 (28.8)	17/44 (38.6)	0.035*
>80	45/66 (68.2)	21/44 (47.7)	
Female	43/66 (65.2)	22/44 (50.0)	0.120
Co-morbidities			
Cerebrovascular accident	31/66 (47.0)	7/44 (15.9)	0.001*
Dementia	33/66 (50.0)	2/44 (4.5)	<0.001*
Parkinson's disease	2/66 (3.0)	0/44 (0.0)	0.516
Hypertension	46/66 (69.7)	21/44 (47.7)	0.028*
Congestive heart failure	11/66 (16.7)	5/44 (10.6)	0.583
Atrial fibrillation	6/66 (9.1)	2/44 (4.5)	0.472
Diabetes	16/66 (24.2)	6/44 (13.6)	0.226
Chronic airway disease	12/66 (18.2)	23/44 (52.3)	<0.001*
Sequelae of tuberculosis	4/66 (6.1)	11/44 (25.0)	0.009*
Chronic liver disease	2/66 (3.0)	2/44 (4.3)	1.000
Chronic kidney disease	5/66 (7.6)	1/44 (2.3)	0.399
Cancer	1/66 (1.5)	2/44 (4.6)	0.297
Use of immunosuppressant	3/66 (4.5)	0/44 (0.0)	0.273
Pressure ulcer	8/66 (12.1)	1/44 (2.3)	0.083
Ileus	16/66 (24.2)	4/44 (9.1)	0.048*
Prior antibiotics, <3 mo	12/66 (18.2)	5/44 (11.4)	0.424
Laboratory findings			
White blood cell, /mm ³	11,469.7±6,058.2	11,325.0±6,650.4	0.906
Neutrophil	9,492.7±5,747.6	8,742.9±5,350.5	0.492
Lymphocyte	993.8±562.1	1,500.9±1,449.9	0.012*
Hemoglobin, g/dL	10.5±1.8	11.6±1.5	0.001*
Albumin, g/dL	3.2±0.6	3.5±0.4	0.004*
ALT, IU/L	22.5±27.1	25.8±42.6	0.623
BUN, mg/dL	24.6±13.1	18.7±9.1	0.007*
Creatinine, mg/dL	1.0±0.6	1.0±0.4	0.932
C-Reactive Protein, mg/dL	113.0±76.1 [†]	95.5±65.1	0.215
Na, mmol/L	136.6±7.8	137.7±5.8	0.421
K, mmol/L	3.9±0.7	4.0±0.6	0.227
Arterial blood gas [†]			
pH	7.5±0.1	7.5±0.6	0.465
PaCO ₂ , mm Hg	32.8±6.3	33.5±7.6	0.611
PaO ₂ , mm Hg	64.0±17.6	72.6±20.0	0.031*
SaO ₂ , %	91.1±5.0	93.7±3.4	0.003*
Functional status			
ECOG scale	3.4±1.3	1.4±0.7	<0.001*
Not limited active	0/66 (0.0)	0/44 (0.0)	
Limited activity	2/66 (3.0)	32/44 (72.7)	
Ambulatory >50%	10/66 (15.2)	7/44 (15.9)	
Ambulatory <50%	24/66 (36.4)	5/44 (11.4)	
Bedridden	30/66 (45.5)	0/44 (0.0)	
Levin tube or gastrostomy	5/66 (7.6)	0/44 (0.0)	0.082
Foley catheter	4/66 (6.1)	0/44 (0.0)	0.148
Swallowing difficulty	9/66 (13.6)	1/44 (2.3)	0.048*

Data are presented as numbers/total patients (%) or mean±standard deviation unless otherwise indicated.

*p<0.05, [†]One patient missing, [‡]63 patients in Nursing home group and 34 in Community group.

ECOG: Eastern Cooperative Oncology Group; ALT: alanine aminotransferase; BUN: blood urea nitrogen.

Table 2. Clinical manifestations and Radiographic outcomes of pneumonia

	Nursing home group (n=66)	Community group (n=44)	p-value
Clinical symptoms			
Respiratory			
Cough	26/66 (39.4)	34/44 (77.3)	<0.001*
Sputum	34/66 (51.5)	32/44 (72.7)	0.030*
Dyspnea	22/66 (33.3)	20/44 (45.5)	0.232
Pleuritic pain	1/66 (1.5)	4/44 (9.1)	0.155
Hemoptysis	0/66 (0.0)	1/44 (2.3)	0.400
Non-respiratory			
Fever	47/66 (71.2)	23/44 (52.3)	0.068
Chill/Myalgia	4/66 (6.1)	8/44 (18.2)	0.062
Altered mentality	4/66 (6.1)	1/44 (2.3)	0.646
Macro-aspiration [†]	9/66 (13.6)	1/44 (2.3)	0.048*
Uncommon	16/66 (24.2)	8/44 (18.2)	0.490
Abnormal lung sounds	38/66 (57.6)	32/44 (72.7)	0.525
Radiographic features			
Involvement of location			
RU+RM	20/66 (30.3)	16/44 (36.4)	0.539
RL	52/66 (78.8)	27/44 (61.4)	0.054
LU	7/66 (10.6)	2/44 (4.5)	0.311
LL	42/66 (63.6)	13/44 (29.5)	0.001*
Multi-lobes involvement	46/66 (69.7)	13/44 (29.5)	<0.001*
One	20 (30.3)	31 (70.5)	
Two	37 (56.1)	12 (27.3)	
Three	9 (13.6)	1 (2.3)	
Pleural effusions	22/66 (33.3)	6/44 (13.6)	0.095
CURB-65 [‡]	2.2±0.9	1.7±1.0	0.004*

Data are presented as numbers/total patients (%) or means±standard deviation.

*p<0.05, [†]Aspiration identified with the naked eye of patient's caregivers, [‡]Confusion of new onset; Blood Urea Nitrogen, >19 mg/dL; Respiratory rate of 30 breaths per minute or greater; Blood pressure less than 90 mm Hg systolic or diastolic blood pressure 60 mm Hg or less, and age 65 years or older.

RU: right upper; RM: right middle; RL: right lower; LU: left upper; LL: left lower; CURB: confusion, urea nitrogen, respiratory rate, blood pressure.

formed by the investigator also was not significantly different between both groups (38 [57.6%] vs. 32 [72.7%]; p=0.525). On chest radiographs, the most commonly involved lobe of the lung in NHAP group was right lower field (52/66, 78.8%), however, the statistically significant difference between both groups was found in left lower field of the lung (42 [63.6%] vs. 13 [29.5%]; p<0.001). In addition, multi-lobe (two or more than) involvement of the lung due to pneumonia was also more frequent in NHAP group (46 [69.7%] vs. 13 [29.5%]; p<0.001). The CURB-65 score was significantly higher in NHAP group (2.2±0.9 vs. 1.7±1.0; p=0.004). Other details were described in Table 2.

3. Microbiological results

Table 3 showed the microbiological results of both groups. Not all of the pneumonia was confirmed microbiologically because of poor expectoration or inappropriate group-categorized Gram's stain of sputum. Of all, 44 (40%) patients were diagnosed with microbiologically confirmed pneumonia, 23 in NHAP group and 21 in CAP group. The most common pathogen was *Streptococcus species* (9/23 [39.1%] in NHAP vs. 12/21 [66.6%] in CAP) and overall distribution of microorganisms between both groups was not significantly different (p=0.263). However, MDR pathogens were significantly more frequent in patients with NHAP (9

Table 3. Microbiological results of pneumonia

	Nursing home group (n=66)	Community group (n=44)	p-value
Acceptable sputum	23/66 (34.8)	21/44 (47.8)	0.380
Microbiological features			0.263
<i>Streptococcus species</i>	9/23 (39.1)	14/21 (66.6)	
<i>Acinetobacter baumannii</i>	2/23 (8.7)	1/21 (4.8)	
<i>Pseudomonas aeruginosa</i>	3/23 (13.0)	0/21 (0.0)	
MRSA	3/23 (13.0)	0/21 (0.0)	
<i>Klebsiella pneumoniae</i>	2/23 (8.7)	1/21 (4.8)	
<i>Escherichia coli</i>	2/23 (8.7)	1/21 (4.8)	
<i>Enterobacter/Enterococcus</i>	1/23 (4.3)	2/21 (9.5)	
Others	1/23 (4.3)	2/21 (9.5)	
Multi-drug resistance	9/23 (39.1)	2/21 (9.5)	0.036*
MRSA	3	-	
<i>Acinetobacter baumannii</i>	1	-	
<i>Pseudomonas aeruginosa</i>	2	-	
<i>Klebsiella pneumoniae</i>	1	1	
<i>Enterobacter cloacae</i>	1	-	
Others [†]	1	1	

Data are presented as numbers/total patients (%).

*p<0.05, [†] *Stenotrophomonas maltophilia*, *Burkholderia cepacia*.

MRSA: Methicillin-resistant *Staphylococcus aureus*.

Table 4. Subgroup analysis according to Multi-drug resistance (MDR) pathogen

In NHAP group	MDR (n=9)	Non-MDR (n=14)	p-value
Age	81.4±10.3	84.1±5.9	0.507
Sex	6/9 (66.7)	11/14 (78.6)	0.643
CVA	4/9 (44.4)	5/14 (35.7)	1.000
Prior antibiotics, <3 mo	3/9 (33.3)	0/14 (0.0)	0.047*
Lymphocyte	1,157.5±314.5	1,071.7±719.8	0.284
BUN	25.6±19.6	22.5±11.1	0.850
Albumin	3.0±0.7	3.4±0.7	0.219
PaO ₂	66.3±19.8	64.1±22.6	0.728
ECOG scale	3.7±0.7	3.1±0.9	0.121
Swallowing difficulty	3/9 (33.3)	0/14 (0.0)	0.047*
Multi-lobes involvement	8/9 (88.9)	11/14 (78.6)	0.771
Appropriate antibiotic therapy	5/9 (55.6)	8/14 (57.1)	1.000
Total duration of antibiotics	16.6±8.5	18.4±12.1	0.824
Mechanical ventilated	2/9 (22.2)	1/14 (7.1)	0.538
In hospital mortality	5/9 (55.6)	4/14 (28.6)	0.383
CURB-65	2.0±0.9	2.1±0.9	0.810

Data are presented as number/total patients (%) or mean±standard deviation.

*p<0.05.

NHAP: nursing home-acquired pneumonia; CVA: cerebrovascular accident; BUN: blood urea nitrogen; ECOG: Eastern Cooperative Oncology Group; CURB: confusion, urea nitrogen, respiratory rate, blood pressure.

[39.1%] vs. 2 [9.5%]; p=0.036). The detailed MDR pathogens were showed in Table 3. In sub-group analysis (Table 4), MDR pathogens in NHAP group were found more frequently in cases of prior treatment of antibiotics

within three months or presence of swallowing difficulty (33.3% vs. 0%; p=0.047 in both).

4. Treatment courses and responses (Table 5)

The total duration of treatment with intravenous antibiotics in hospital was 12.6 ± 8.8 days in NHAP group vs. 6.6 ± 3.2 days in CAP group ($p < 0.001$). The most common initial regimen of antibiotics was the combination of 3rd cephalosporin plus fluoroquinolone (30/66, 45.5%) in NHAP group vs. 3rd cephalosporin plus macrolide (20/44, 45.5%) in CAP group and the distribution of antimicrobial choice was not significantly different between both groups. In NHAP group, more patients were treated with additional antibiotics covering anaerobes without significant difference (11 [16.7%] vs. 3 [6.8%]; $p=0.154$), however, less could be treated with appropriate antibiotic therapy with significant difference (39 [59.1%] vs. 40 [90.0%]; $p=0.001$). In addition, 37

(56.1%) patients with NHAP had to need supportive managements in ICU on admission day, and 10 (15.2%) eventually had been ventilated mechanically. As unexpected result, 90% of them were weaned from the mechanical ventilation successfully. Total duration of hospitalization in NHAP group was 14.4 ± 10.6 days, significantly longer than in CAP group (7.3 ± 3.4 days) and in-hospital mortality was also higher in NHAP group (15 [22.7%] vs. 2 [4.3%], $p=0.007$). There were more patients with high CURB-65 score in NHAP group; however, the trend of mortality according to CURB-65 score did not showed significant difference within each group (Table 6).

Table 5. Treatment courses and Responses of antibiotics

	Nursing home group (n=66)	Community group (n=44)	p-value
Mean duration of medication (day)			
Intravenous	12.6 ± 8.8	6.6 ± 3.2	$<0.001^*$
Total	17.4 ± 8.9	12.2 ± 3.5	$<0.001^*$
Regimens			0.261
3rd cephalosporin+Macrolide	14/66 (21.2)	20/44 (45.5)	
Quinolone only	12/66 (18.2)	8/44 (18.2)	
3rd cephalosporin+Quinolone	30/66 (45.5)	12/44 (27.3)	
Piperacillin+Tazobactam	6/66 (9.1)	2/44 (4.5)	
Imipenem/Meropenem	1/66 (1.5)	0/44 (0.0)	
Others	3/66 (4.5)	2/44 (4.5)	
Coverage of anaerobe	11/66 (16.7)	3/44 (6.8)	0.154
Appropriate antibiotic therapy	39/66 (59.1)	40/44 (90.9)	0.001*
Combined systemic steroid	26/66 (39.4)	21/44 (47.7)	0.502
Need of Intensive Care Unit			
Initial	37/66 (56.1)	13/44 (29.5)	0.007*
Transferred	2/66 (3.0)	1/44 (2.3)	1.000
Mechanical ventilated	10/66 (15.2)	0/44 (0.0)	0.006*
Tracheostomy	3/10	-	
Weaning	9/10	-	
Treatment Outcome			
Duration of hospitalization (day)	14.4 ± 10.6	7.3 ± 3.4	$<0.001^*$
In hospital mortality	15/66 (22.7)	2/44 (4.5)	0.014*
Respiratory failure	9	1	
Shock/multiorgan failure	5	1	
Congestive heart failure	1	-	
Post-discharge follow-up			
No readmission within one month	48/51 (94.1)	38/42 (90.5)	0.697
Live after three months	21/44 (47.7)	27/30 (90.0)	0.001*

Data are presented as number/total patients (%) or mean \pm standard deviation.

* $p < 0.05$.

Table 6. In hospital mortality according to CURB-65 score

	CURB-65 score					p-value
	0	1	2	3	4	
NHAP, n=66	-	15 (22.7)	29 (43.9)	18 (27.3)	4 (6.1)	0.496
Mortality	-	5 (33.3)	7 (24.1)	2 (11.1)	1 (25.0)	
CAP, n=44	3 (6.8)	19 (43.2)	14 (31.8)	6 (13.6)	2 (4.5)	0.943
Mortality	0 (0.0)	1 (5.3)	1 (7.1)	0 (0.0)	0 (0.0)	
Total, n=110	3 (2.7)	34 (30.9)	43 (39.1)	24 (21.8)	6 (5.5)	0.747
Mortality	0 (0.0)	6 (17.6)	8 (18.6)	2 (8.3)	1 (16.7)	

Data are presented as number/total patients (%) or mean±standard deviation.

CURB: confusion, urea nitrogen, respiratory rate, blood pressure; NHAP: nursing home-acquired pneumonia; CAP: community-acquired pneumonia.

Discussion

Though regarded to limited data, our study elucidated the first and unique characteristics of NHAP in Korea. In summary, patients with NHAP had more common co-morbidities in hypertension, dementia, CVA, and ileus; showed poor functional status with swallowing difficulty; were identified with lymphocytopenia, anemia, hypoalbuminemia, elevated blood urea nitrogen, and hypoxemia; presented less classical respiratory symptoms and involved with more lobes of the lung; manifested multi-drug resistant pathogens more predominantly; were hospitalized with longer duration and poor prognosis, compared to those with CAP.

Recently, Yoon et al.¹³ reported clinical and microbial characteristics of HCAP compared with HAP in their tertiary hospital experiences. HCAP in their study showed similar characteristics with HAP, but limitation should be considered that their population was comprised of mixed groups such as long term care hospital, traditional medicine hospital, psychiatric hospital, and nursing home. In contrary, our study population was comprised of relatively homogenous groups directly from nursing home or community. Indeed, our results are closely similar to the first prospective comparative study¹⁰ of NHAP with CAP in the United Kingdom and recent 10-year observational study⁵ of NHAP, as the matter of clinical symptoms or signs, functional statuses, microbiological results, and mortalities. Considering that

informational limitation and selection bias of studies dealing with HCAP in tertiary hospital, our clinical presentations and outcomes about NHAP in Korea would be paid attention to beyond expectation despite of the secondary hospital setting.

Most of all, the results of less frequent classical presentations of NHAP in this study are important to detect pneumonia at the early stage in nursing home residents. Not uncommonly, patient with NHAP would remain asymptomatic or only febrile before diagnosis¹⁴, although exactly not as same as our results. Johnson et al.¹⁵ found that nonspecific symptoms were common in the presentation of pneumonia in elderly people, which could apply to patients with NHAP. In addition, patients with NHAP suffered swallowing difficulty at nursing home or macro-aspiration before visiting hospital more frequently as our results. The preservation of swallow function and cough reflex is important defense mechanisms against oropharyngeal aspiration, with abnormalities of both increasing the risk of aspiration pneumonia. While the etiology of aspiration pneumonia is multi-factorial, there is a strong association between dysphagia and the development of aspiration pneumonia in the elderly¹⁶. Additionally, only aging *per se* would not be held responsible to increase the risk of aspiration. The incidence of cognitive or neurologic diseases increase with aging and these disorders are strongly associated with impaired swallow function and decreased cough reflex, which resulted in the increased

risk of aspiration. That's why kinds of protocol assessing and managing dysphagia at nursing home should be needed^{17,18}.

It should be focused that MDR pathogens was identified more frequently in patients with NHAP. There are many reports supporting that microbiological results of NHAP is similar with HAP^{5,7,8,10,14,17,19}, including recent one Korean study as mentioned¹³. The problem is how to choosing the empirical antibiotic regimens to treat NHAP as CAP or HAP, however, established clinical trials are still unavailable. There are two aspects prior to think considering the treatment of NHAP; one is the place to treatment, in nursing home *in situ* or in hospital which patients are admitted, and the other is how to deal with MDR pathogens²⁰. Although the former is out of our discussion, the latter is still debating problems because of many conflict evidences between several studies or expert's opinions. Until now, the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guideline⁴ currently assumes that nursing home residence by itself is one of the major risk factors for MDR organisms; therefore, the recommendation of empirical treatment focuses on these pathogens. However, there is no confident evidence that the broad-spectrum regimens recommended by the ATS/IDSA guideline could be more efficacious compared with the regimens recommended by other CAP guidelines for treating NHAP requiring hospitalization. This is why as follows: basically, these concerns are originated from that the ATD/IDSA guideline is based exclusively on the findings of intubated patients in the ICU setting; additionally, patients who were admitted from nursing home are at a higher risk of upper airway colonization by Gram-negative bacteria or MRSA because of their impaired functional status, which possibly explains a high rate of Gram-negative bacteria or MRSA identified in sputum samples, occurring an overestimation of Gram-negative bacteria or MRSA as true pathogens in NHAP⁶.

Besides microbiological issues, it should be considered that severe elderly patients with NHAP are more likely to suffer from CVA or dementia, to present with

delirium and malnutrition, to have a lower functional status, or to be bed-ridden when compared with simple elderly patients with CAP. Such co-morbidities have all been associated with a higher mortality. Indeed, in recent studies of older patients with NHAP and CAP, patients with NHAP have more severity scores such as the pneumonia severity index, and accordingly mortality remains higher for NHAP²¹. Frankly, in the real world, we cannot but consider the term "end-of-life pneumonia" that affects the elderly who are left (to die) in nursing homes.

For these several reasons, it is convincing that NHAP should not always be treated the same as HAP²². There were patients who might be treated with too broad spectrum of antibiotics unnecessarily if this approach were used routinely. In reality, whether patients from nursing home treated in the hospital or in the nursing home, many studies have also demonstrated the efficacy of monotherapy regimens, such as fluoroquinolone or cefepime that would not be recommended for patients with HAP at risk for MDR pathogens²³. In our study, MDR pathogens were more frequently in NHAP group in cases of prior treatment of antibiotics within three months or swallowing difficulty. This result was relatively compatible to other study indicating that risk factors of drug resistant bacteria in severe NHAP was prior antibiotic therapy in the past 3 to 6 months and poor functional status²⁴. Based on these evidences, patients with NHAP would need to be divided into each sub-groups by evaluating the risk of MDR pathogens²². After all, more randomized controlled studies for NHAP should be needed.

Several important limitations of this study should be noted. Firstly, we could not get lower respiratory tract specimens from patients by invasive technique such as bronchoscopy and employ non-cultured methods (eg, serologies, urinary antigen tests, or polymerase chain reaction techniques) to establish the etiologic diagnosis of pneumonia. Therefore, we may have missed other microbiological results of pneumonia due to either early antibiotic administration or inadequate specimens submitted for microbiologic evaluation. As same reason,

our findings could not be applicable to patients with atypical pathogens or viruses. Secondly, although we tried to apply the severity-of-illness score by CURB-65, the result of mortality related to CURB-65 score could not show statistically significant trends in both groups. First of all, small number of study population, especially in higher subgroup of CURB-65 score, probably could cause this limitation. In addition, the CURB-65 would not be appropriate to apply for prediction of mortality in NHAP so far as we allow that NHAP has to be distinct from CAP.

In conclusion, NHAP should be more considerably investigated because of high frequency of multi-drug resistant pathogens and fatal mortality compared with CAP.

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