Antimicrobial Resistance and Clinical Outcomes in Nursing Home-Acquired Pneumonia, Compared to Community-Acquired Pneumonia

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Purpose: Patients with nursing home-acquired pneumonia (NHAP) should be treated as hospital-acquired pneumonia (HAP) according to guidelines published in 2005. However, controversy still exists on whether the high mortality of NHAP results from multidrug resistant pathogens or underlying disease. We aimed to outline differences and factors contributing to mortality between NHAP and community-acquired pneumonia (CAP) patients.

Materials and Methods: We retrospectively evaluated patients aged 65 years or older with either CAP or NHAP from 2008 to 2014. Patients with healthcare-associated pneumonia other than NHAP or HAP were excluded.

Results: Among 317 patients, 212 patients had CAP and 105 had NHAP. Patients with NHAP had higher mortality, more frequently used a ventilator, and had disease of higher severity than CAP. The incidences of aspiration, tube feeding, and poor functional status were higher in NHAP. Twenty three out of 54 NHAP patients and three out of 62 CAP patients had multidrug resistant pathogens ($p<0.001$). Eleven patients with NHAP died at discharge, compared to 7 patients with CAP ($p=0.009$). However, there was no association between mortality rate and presence of multidrug-resistant pathogens. The number of involved lobes on chest X-ray [odds ratio (OR)=1.708; 95% confidence interval (CI), 1.120 to 2.605] and use of mechanical ventilation (OR=9.537; 95% CI, 1.635 to 55.632) were significantly associated with in-hospital mortality.

Conclusion: Patients with NHAP had higher mortality than patients with CAP. The excess mortality among patients with NHAP and CAP was related to disease severity but not to the presence of multidrug resistant pathogens.

Key Words: Pneumonia, nursing home, antimicrobial resistance, mortality

INTRODUCTION

The growth of older adult populations has led to increases in the number of nursing home residents globally. In 30 years, about 40% of the adults worldwide will be staying in a nursing home or long-term care facility.[1] In Korea, 12.7% of the population was older than 65 years in 2014 and this will reach about 14% in 2017.[2] In 2009, there were 201226 patients using nursing hospitals and 80025 in nursing homes, and these numbers increased to 296728 and 132235 people, respectively, in 2012.[3] Among the residents in long-term care facilities, the most common cause of hospitalization, morbidity, and mortality was pneumonia.[4] Of potentially preventable diseases, pneumonia is the most common.[5] Nursing home-acquired pneumonia (NHAP) is one form of healthcare-associated pneumonia (HCAP).[6] In 2005, the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) suggested that HCAP patients, including those with NHAP, should be tr-

eated with the same broad-spectrum antibiotics as hospital-acquired pneumonia to cover multidrug resistant (MDR) pathogens.[6] However, treating NHAP and HCAP has been controversial, although the mortality rate of NHAP is higher than that of community-acquired pneumonia (CAP). The microbial distributions of NHAP vary among nations, regions, study designs, and disease severity.[7] The British Thoracic Society guidelines for CAP in 2009 mentioned nursing home residents as a specific population group of CAP and did not recommend specific management for NHAP, in contrast to the 2005 ATS/IDSA guidelines.[8] The nursing home setting has attributes that differ from those of other health care settings in terms of patient age, comorbidities, disease severity, functional status, realistic treatment goals, and aggressive disease monitoring.[9] In addition, it is not clear whether the increased frequency of MDR pathogens leads to inappropriate antibiotic therapy and higher mortality.[10] Therefore, we conducted this study to analyze factors contributing to the mortality rates of NHAP, in comparison to those for CAP, among elderly patients.

MATERIALS AND METHODS

Study design and patients
We retrospectively analyzed patients older than 65 years old admitted to a single teaching hospital (600 beds) in South Korea with either CAP or NHAP from January 2008 to December 2014. Categories of HCAP other than NHAP were excluded: hospitalization for 2 days or more in the preceding 90 days, long-term dialysis within 30 days of entering the study, immunocompromised status including AIDS, active malignancy receiving chemotherapy, history of solid-organ transplantation on immunosuppressive agents, or immunosuppressive therapy including 10 mg prednisone/day for at least 30 days or equivalent. The patients who had do-not-resuscitate (DNR) status were excluded. We analyzed medical records for baseline characteristics, orientation disturbance, functional status, the degree of aspiration, comorbidities, severity, pathogen, antibiotics, and clinical outcomes. This study was approved by the local Ethics Committees of the Institutional Review Board of the Dongguk University Hospital.

Definitions
The diagnosis of pneumonia was based on the following criteria: 1) new or persistent pulmonary infiltrate and 2) two or more symptoms and signs, including body temperature greater than 38.5°C or less than 35.5°C, leukocyte count greater than 12000/mm³ or less than 4000/mm³, and purulent sputum. NHAP and CAP were divided according to ATS/IDSA guidelines.[6] Pneumonia severity was evaluated using CURB-65 score, which consists of five variables: confusion of new onset, blood urea nitrogen greater than 7 mmoL/L (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 of 65 years or older.[11] Patients with poor functional status were defined as being bedridden or those who used a wheelchair. Probable aspiration was defined as any witnessed aspiration before hospital admission or aspiration confirmed by video associated swallowing test.[12] Patients with tube feeding were defined as the administration of liquefied foods through a nasogastric tube or percutaneous endoscopic gastrostomy tube. Initial treatment failure was defined as death during initial antibiotics treatment or change of antibiotics from first agents to others after 48 hours due to clinical instability.[12]

Microbiological evaluation
Respiratory samples such as sputum, endotracheal suction and bronchoalveolar washing, blood cultures, urinary antigen test for *Streptococcus pneumonia* and *Legionella* species, were obtained and investigated. Standard serologic methods were used to determine antibodies against atypical agents, such as *Mycoplasma pneumoniae*. MDR pathogens included methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*, carbapenem resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia*.[6,13] *Pseudomonas* species were included as MDR pathogens regardless of the drug susceptibility test.

Clinical outcomes
The primary outcome was in-hospital mortality. Secondary outcomes were length of stay and intensive care unit (ICU) stay.

Statistical analysis
All statistical analysis was performed using Statistical Package for the Social Science ver. 12.0 (SPSS Inc., Chicago, IL, USA). Shapiro-Wilk's W test was performed for normality of the data. For inter-group comparisons, continuous variables were analyzed using Student's t-test, and when data were not normally distributed, the non-parametric Mann-Whitney U test was used. Descriptive variables were analyzed using chi-squared test or Fisher's exact test if more than 20% of the expected cell frequencies <5. Logistic regression analysis was used to assess the risk factors of mortality. Further, variables that were associated with in-hospital mortality at p values less than 0.1 in univariate analysis (age and sex) were included in multivariable logistic regression analysis. Assessment of the applicability of multicollinearity indicated no multicollinearity issues (tolerance >0.1 and variance inflation factor values <10) between the chosen independent variables in this study. p values less than 0.05 were considered statistically significant. The contribution of each potential risk factor was denoted by the odds ratio (OR) and associated 95% confidence interval (CI).

RESULTS

Patient characteristics

A total of 317 patients with pneumonia aged 65 years or more were analyzed. One hundred five patients had NHAP, and 212 patients had CAP. The baseline characteristics of the patients with NHAP and CAP are presented in Table 1. The median age of the patients with NHAP was 80 years, and that of patients with CAP was 75 years. NHAP patients had a lower body mass index (BMI), compared to CAP patients ($p<0.001$), and fewer current smokers ($p=0.005$). NHAP patients had a higher frequency of poor functional status (66.7% vs. 9.4%; $p<0.001$), confusion rate (68.6% vs. 10.4%; $p<0.001$), use of tube feeding (23.8% vs. 0.5%; $p<0.001$), and probable aspiration (48.6% vs. 13.2%; $p<0.001$) than CAP patients. The incidence of chronic respiratory disease, heart disease, diabetes mellitus, and chronic renal diseases were not different between the two groups. Patients with cerebrovascular disease (50.5% vs. 16.5%; $p<0.001$) and other neurologic disease (54.3% vs. 6.6%; $p<0.001$) were more frequent in NHAP patients than in CAP patients.

Initial clinical features and severity at presentation

The initial clinical characteristics and severity in the NHAP and CAP groups are shown in Table 2. The time from symptom to admission was shorter in NHAP patients, compared with CAP patients. CURB-65 was higher in NHAP patients than in CAP

Table 1. Baseline Characteristics and Comorbidity

	NHAP, n=105	CAP, n=212	*p* value
Median age, yrs (IQR)	80 (74–84)	75 (71–81)	<0.001
Male, n (%)	61 (58.1)	113 (53.3)	0.420
BMI, kg/m²	19.06±3.52	21.88±4.04	<0.001
Current smoker, n (%)	4 (3.8)	25 (11.8)	0.005
Smoking amount (pack yrs)	12.9±24.0	18.3±23.4	0.059
Probable aspiration*, n (%)	51 (48.6)	28 (13.2)	<0.001
Tube feeding, n (%)	25 (23.8)	1 (0.5)	<0.001
Poor functional status†, n (%)	70 (66.7)	20 (9.4)	<0.001
Confusion, n (%)	72 (68.6)	22 (10.4)	<0.001
Comorbidities, n (%)			
Diabetes mellitus	24 (22.9)	67 (31.6)	0.105
Hypertension	58 (55.2)	107 (50.5)	0.424
Hepatitis	4 (3.8)	4 (1.9)	0.447
Chronic respiratory disease	14 (13.3)	45 (21.2)	0.089
Heart disease	17 (16.2)	26 (12.3)	0.337
CVD	53 (50.5)	35 (16.5)	<0.001
Other neurologic disease	57 (54.3)	14 (6.6)	<0.001
CVD and other neurologic disease	93 (88.6)	47 (22.2)	<0.001
Chronic renal disease	5 (4.8)	3 (1.4)	0.083

IQR, interquartile range; NHAP, nursing home-acquired pneumonia; CAP, community-acquired pneumonia; BMI, body mass index; CVD, cerebrovascular disease.
Data are presented as mean±standard deviation or n (%), unless otherwise stated.
*Probable aspiration was defined as any witnessed aspiration before hospital admission, †Patients with poor functional status were defined as being bedridden or those who used a wheelchair.

Table 2. Initial Clinical Features and Severity

	NHAP, n=105	CAP, n=212	*p* value
Time from symptom until admission, days	1 (0–3) 2.3±4.1	3 (1–7) 5.3±7.1	<0.001
Median initial WBC (IQR), count/µL	10320 (7820–14230)	9950 (7560–13782)	0.817
Initial CRP, mg/dL	11.7±8.2	11.9±10.1	0.524
CURB-65	2.7±1.2	1.8±1.0	<0.001
Chest X-ray, bilateral, n (%)	58 (55.2)	75 (35.4)	0.001
Mechanical ventilation, n (%)	22 (21.0)	19 (9.0)	0.003
ICU admission, n (%)	50 (47.6)	39 (18.4)	<0.001

NHAP, nursing home-acquired pneumonia; CAP, community-acquired pneumonia; IQR, interquartile range; WBC, white blood cell; CRP, C-reactive protein; ICU, intensive care unit.
Data are presented as mean±standard deviation and/or median (IQR) or n (%), unless otherwise stated.

patients. NHAP patients had higher rates of mechanical ventilation (MV) use (21% vs. 9%; *p*=0.003) and ICU admission (47.6% vs. 18.4%; *p*<0.001) than CAP patients. Laboratory findings, such as C-reactive protein level or leukocytosis, revealed no differences between two groups, although NHAP patients had more severe pneumonia on chest X-ray, as defined by bilateral involvement of pneumonia, compared with the CAP patients.

Microbiology and initial antibiotics

The microbes identified in the NHAP and CAP groups are listed in Table 3. The numbers of both the total population and cases with any pathogen are shown in Table 3. The patients identified with causative pathogens accounted for 51.4% of NHAP and 29.2% of CAP cases. *Streptococcus pneumoniae* was the most frequent pathogen in both groups. MDR pathogens were isolated more frequently in NHAP patients than in CAP patients (21.9% vs. 1.4%; *p*<0.001). MDR pathogens were isolated in 42.6% of NHAP patients with any identified pathogens. In particular, MRSA was a common MDR pathogen in NHAP patients. Pseudomonas species was not frequently identified. Mixed bacteria were detected in 5 patients among NHAPs and 3 patients among CAPs. The antibiotics used initially and fail-

Table 3. Microbes Identified in NHAP and CAP Patients

	Total population			Case with identified pathogen		
	NHAP, n=105	CAP, n=212	*p* value	NHAP, n=54	CAP, n=62	*p* value
Pathogen identified, n (%)	54 (51.4)	62 (29.2)	<0.001			
MDR* pathogens identified, n (%)	23 (21.9)	3 (1.4)	<0.001	23 (42.6)	3 (4.8)	<0.001
Gram positive, n (%)						
Streptococcus pneumoniae	19 (18.1)	43 (20.3)	0.644	19 (35.2)	43 (69.4)	<0.001
MSSA	2 (1.9)	7 (3.3)	0.723	2 (3.7)	7 (11.3)	0.172
MRSA	11 (10.5)	1 (0.5)	<0.001	11 (20.4)	1 (1.6)	0.001
Gram negative, n (%)						
Pseudomonas species	7 (6.7)	2 (0.9)	0.007	7 (13.0)	2 (3.2)	0.080
Klebsiella species	8 (7.6)	3 (1.4)	0.007	8 (14.8)	3 (4.8)	0.067
ESBL *Klebsiella*	4 (3.8)	0 (0.0)	0.012	4 (7.4)	0 (0.0)	0.044
Escherichia coli	5 (4.8)	0 (0.0)	0.001	5 (9.3)	0 (0.0)	0.117
ESBL *Escherichia coli*	1 (1.0)	0 (0.0)	0.331	1 (1.9)	0 (0.0)	0.466
Haemophilus influenzae	0 (0.0)	7 (3.3)	0.100	0 (0.0)	7 (11.3)	0.014
Moraxella catarrhalis	2 (1.9)	2 (0.9)	0.602	2 (3.7)	2 (3.2)	>0.999
CRAB	2 (1.9)	0 (0.0)	0.109	2 (3.7)	0 (0.0)	0.215
Others	1 (1.0)	0 (0.0)	0.331	1 (1.9)	0 (0.0)	0.466
Polymicrobial, n (%)	5 (4.8)	3 (1.4)	0.121	5 (9.3)	3 (4.8)	0.470

NHAP, nursing home-acquired pneumonia; CAP, community-acquired pneumonia; MDR, multi-drug resistance; MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; ESBL, extended-spectrum beta-lactamase; CRAB, carbapenem resistant *Acinetobacter baumannii*.
Data are presented as n (%).
*MRSA, *Pseudomonas* species, CRAB, *Stenotrophomonas maltophilia*, and ESBL-producing *Enterobacteriaceae* were considered as MDR pathogens.

Table 4. Initial Antibiotics Among Patients with NHAP and CAP

	NHAP, n=105	CAP, n=212	*p* value
Initial antibiotics treatment, n (%)			
Monotherapy	33	30	<0.001
Quinolone	1 (1.0)	3 (1.4)	
Antipseudomonal penicillin	30 (28.6)	27 (12.7)	
Carbapenem	2 (1.9)	0 (0.0)	
Combination therapy	72	182	<0.001
3rd cephalosporin and macrolide	9 (8.6)	116 (54.7)	
3rd cephalosporin and quinolone	1 (1.0)	5 (2.4)	
Antipseudomonal penicillin and macrolide	9 (8.6)	20 (9.4)	
Antipseudomonal penicillin and quinolone	50 (47.6)	40 (18.9)	
Others	5 (4.8)	1 (0.5)	
Failure of initial antibiotics, n (%)	7 (6.7)	3 (1.4)	0.017

NHAP: nursing home acquired pneumonia; CAP: community acquired pneumonia.
Data are presented as n (%).

ures of initial antibiotics are presented in Table 4. Patients with CAP received more combinations of antipneumococcal β-lactamase and macrolide. However, patients with NHAP received more antipseudomonal penicillin. Failure of initial antibiotics (6.7% vs. 1.4%; *p*=0.017) were more frequent in NHAP patients than in CAP.

Clinical outcomes

The clinical outcomes of patients with NHAP and CAP are shown in Table 5. The proportion of in-hospital mortalities was over two-fold higher in the NHAP group than the CAP group (10.5% vs. 3.3%; *p*=0.009). NHAP patients had a longer duration of hospital day, ICU stay, and antibiotics use than CAP patients.

Contributing factors to in-hospital mortality

Table 6 lists the risk factors for in-hospital mortality by logistic regression analysis models. According to univariate analysis, mortality was significantly associated with NHAP, CURB-65, confusion, involved lobes in chest X-ray, initial ICU care, MV use, and presence of MDR pathogen. After adjustment for age, sex, and other confounding factors, the number of involved lobes in chest X-ray (OR=1.708; 95% CI, 1.120 to 2.605; *p*=0.013) and MV use (OR=9.537; 95% CI, 1.635 to 55.632; *p*=0.012) were

significantly associated with increased in-hospital mortality.

DISCUSSION

This study revealed significant differences in mortality and contributing factors between NHAP and CAP, especially in hospitalized elderly patients. The significant findings of this study were that overall in-hospital mortality of NHAP is about twice as high as that of CAP (10.5% vs. 3.3%) and patients with NHAP had more frequent cerebrovascular disease, neurologic disease, poor functional status, aspiration tendency, and tube feeding than those with CAP. In addition, the patients with NHAP had more severe pneumonia in terms of the clinical and radiological findings, MV use, and ICU admission. NHAP patients had more frequent MDR pathogens, especially MRSA, and higher incidences of initial treatment failure. We treated most patients with NHAP (85%) with antipseudomonal penicillin, with/without fluoroquinolones as recommended in the ATS/IDSA 2005 guidelines, to cover potential MDR pathogens, such as *Pseudomonas* or MRSA.[6] Excess mortality was related to disease severity, such as the MV use and the number of the involved lobes in chest X-ray, but not to the presence of MDR pathogens. To

Table 5. Treatment Outcomes of Patients with NHAP and CAP

	NHAP, n=105	CAP, n=212	*p* value
In-hospital mortality, n (%)	11 (10.5)	7 (3.3)	0.009
Hospital stay, days	12.3±13.0	9.7±7.8	0.035
ICU stay, days	6.93±11.0	1.8±6.2	<0.001
Duration of antibiotics, days	18.5±10.5	15.7±7.1	0.010

NHAP: nursing home acquired pneumonia; CAP: community acquired pneumonia; ICU: intensive care unit.
Data are presented as mean±standard deviation or n (%), unless otherwise stated.

Table 6. Factors Contributing to in-Hospital Mortality

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.017 (0.951–1.088)	0.613	1.005 (0.915–16.230)	0.914
Male	2.229 (0.775–6.408)	0.137	3.854 (0.915–16.230)	0.066
BMI	0.961 (0.851–1.085)	0.519		
Poor functional status	2.117 (0.808–5.550)	0.127		
Confusion	2.518 (0.966–6.559)	0.059	1.667 (0.390–7.124)	0.490
Neurologic disease	2.672 (0.977–7.310)	0.056	2.425 (0.467–12.586)	0.292
CURB–65	2.879 (0.921–4.314)	<0.001	1.326 (0.730–2.408)	0.355
Time from symptom until admission	0.970 (0.879–1.072)	0.552		
Mechanical ventilation	35.259 (10.84–114.68)	<0.001	9.537 (1.635–55.632)	0.012
ICU admission	24.767 (5.563–110.276)	<0.001	1.698 (0.197–14.655)	0.680
Involved lobes in chest X–ray	2.566 (1.805–3.649)	<0.001	1.708 (1.120–2.605)	0.013
MDR pathogen	3.597 (1.091–11.860)	0.035	1.232 (0.275–5.516)	0.716
Pathogen identified	1.794 (0.691–4.657)	0.230		
NHAP	3.427 (1.288–9.118)	0.014	1.412 (0.317–6.297)	0.651

BMI: body mass index; ICU: intensive care unit; MDR: multi-drug resistance; NHAP: nursing home acquired pneumonia.
For each variable, the odds ratio (OR) and 95% confidence interval (95% CI) were given. *p* values <0.05 were considered statistically significant. Risk factors that were determined as significant by univariate analysis (*p*<0.1) were then subjected to multivariate analysis.

avoid the effect of age, we restricted the analysis to patients aged 65 years or more. Klapdor, et al.[14] showed that NHAP in older adult patients was different from younger patients. CAP in older adults also has different clinical characteristics and outcomes, compared with CAP, in younger patients.[15] Our study is in line with another study of NHAP in terms of mortality. In other studies, the reported 30-day mortality of NHAP ranged from 16.8% to 26.6%, as in our study (19.5%).[10,14,16-19] The higher mortality in NHAP, compared with CAP, is well known, while greater detection of MDR pathogens is controversial. In our study, the prevalence of MDR pathogens was 21.9% (MRSA: 10.5%, *Pseudomonas* 6.7%, ESBL 4.8%) for the total NHAP population and 1.4% for CAP; the most common pathogen was *Streptococcus pneumonia* in both groups. However, the identification of MDR pathogens differs across countries and studies. In the United States, Dhawan, et al.[9] reported that the most frequent pathogens of NHAP were gram-negative bacteria (GNB) (up to 55%), *Streptococcus pneumoniae* (up to 48%), *Staphylococcus aureus* (up to 33%), and *Pseudomonas aeruginosa* (up to 7%). In severe pneumonia, *Staphylococcus aureus* and GNB were detected more frequently.[20] A prospective German cohort study of 518 NHAP patients aged 65 years and older found that MDR pathogens were very rare (5%), and MRSA was relatively more frequent in the NHAP patients (2.3% of all NHAP).[10] A Spanish study detected potential MDR pathogen in 7%, MRSA in 2%, *Pseudomonas* in 1%, and GNB in 3%.[17] In a prospective cohort study of 116 NHAP patients aged 65 years and older in Hong Kong, Ma, et al.[21] found that the patients with NHAP had more viral infections (55.9%), whereas those with CAP had more bacterial infections (69.9%). MDR pathogens were found only in six patients in the entire study population. In a Japanese study of 138 NHAP aged 65 years or older, MRSA (8.7% vs. 2.3%), *Klebsiella pneumoniae* (11.6% vs. 3.9%), and *Proteus mirabilis* (2.9% vs. 0%) were identified more frequently in NHAP than in CAP patients.[22] Our study had similar results for MDR pathogens as Japanese, while the rate was higher in the United States and lower in Europe. There are a few reported Korean studies on NHAP, while there are several studies on HCAP. In a Korean study of 58 NHAP patients, potential drug-resistant pathogens were detected more frequently in the NHAP group (22.4% vs. 9.9%; *p*=0.018), compared to CAP, and *Pseudomonas aeruginosa* and MRSA were detected in 8.6% and 10.3%, respectively.[19] In another Korean study of 66 NHAP patients, MDR pathogens were also highly detected in NHAP (39% vs. 10%), compared to CAP. However, the isolation rate of *Pseudomonas aeruginosa* and MRSA were 3.0% and 4.5%, respectively.[23] These studies showed a similar rate of MDR pathogens in NHAP groups with our study. However, the rate of MDR pathogens in CAP patients was relatively higher than our study. Our study had a greater number of enrolled patients in both groups and included more patients living in the metropolitan area than previous Korean studies. As shown in this and other studies, the mortality in NHAP was

higher than in CAP, although the incidence of MDR pathogens varied across the studies. However, there was little evidence that more MDR pathogens caused excess mortality in NHAP. Even for HCAP, including NHAP, the association between high MDR pathogens and high mortality remains controversial. In a meta-analysis, Chalmers, et al.[24] showed that HCAP had increased risk of MRSA, *Enterobacteriaceae*, and *Pseudomonas aeruginosa*, although HCAP itself was not associated with a significant increase in mortality after adjusting for age and comorbid illnesses. In a British study of 437 NHAP patients, atypical pathogen, MRSA, *Enterobacteriaceae*, and poor functional status were risk factors for mortality.[18] In a Spanish study of 150 NHAP patients, neurological disease, septic shock, pleural effusion, GNB, and MRSA accounted for the high mortality in NHAP.[17] In our study, neither MDR pathogens in their entirety nor individual MDR pathogens were associated with mortality, even in the univariate analyses, unlike in some studies. Contrary to other studies that showed HCAP itself was an important risk factor for mortality,[25,26] significant risk factors for mortality in our study were the extent of pneumonia on chest X-ray and MV use after adjusting for age, sex, and other confounding factors. MDR pathogens, initial ICU admission, CURB-65, and NHAP were not significant after adjusting for other factors. Disease severity in terms of clinical and radiological severity, rather than MDR pathogen and NHAP, resulted in excess mortality in our study. This result was similar to another Korean study in which a higher pneumonia severity index score was significantly associated with mortality.[27] Although we excluded patients who had DNR order, treatment restriction, such as a DNR order, may be more frequent in NHAP patients because NHAP patients are older, disabled, and have a poor functional status, and more neurological and cerebrovascular disease. Thus, NHAP may result in higher morality in real world situation. Unfortunately, in the present study, almost 85% of NHAP patients were treated with antipseudomonal penicillin without regard to the severity of illness, as recommended by the 2005 ATS/IDSA guidelines. *Pseudomonas* species were cultured in only 6.7%, leading them to recommend targeting these pathogens in all of their NHAP patients. Such overtreatment might lead to the development of resistant pathogens and increase costs.

This study has several limitations. First, the data were collected retrospectively from a single institution. Therefore, our results should be interpreted with caution. Second, most of the pathogens were defined based on a positive culture of sputum or endotracheal aspirate, instead of semiquantitative or quantitative cultures. Viral pathogens were not identified. Third, the proportion of patients with the causative pathogens identified was relatively low, especially in CAP (29.2%). Therefore, we could not determine whether the appropriateness of antibiotics was a significant risk factor for mortality or not. Although, more than half of the patients had normal flora in their sputum, we included only patients with positive sputum culture result. Most patients were tested with other microbiologic stud-

ies, such as blood culture and urinary antigen. Despite these limitations, our results include meaningful information about clinical and microbiological features and predictors of mortality in NHAP, compared with CAP, especially for Korean populations.

In conclusion, patients with NHAP had higher mortality rates than patients with CAP. However, the excess mortality was related to disease severity and not to the presence of multidrug-resistant pathogens or NHAP itself. Therefore, not all patients with NHAP may need broad-spectrum antibiotics, and other clinical predictive factors for specific MDR pathogens should be assessed in both CAP and NHAP.

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REFERENCES

1. Furman CD, Rayner AV, Tobin EP. Pneumonia in older residents of long-term care facilities. Am Fam Physician 2004;70:1495-500.
2. Statics Korea. 2014 Statistics for ageing population in Korea. 2014. [accessed on 2015 July 11]. Available at: http://kostat.go.kr/portal/eng/pressReleases/1/index.board?bmode=read&aSeq=331389.
3. Kim JS, Seon WD, Lee GJ, Choi ID, Lee HY, Kim KA. A study on the reinforcing medical service linkage between nursing home facilities and health care institutes. Seoul: Korea Institute for Health and Social Affairs; 2013.
4. Muder RR, Aghababian RV, Loeb MB, Solot JA, Higbee M. Nursing home-acquired pneumonia: an emergency department treatment algorithm. Curr Med Res Opin 2004;20:1309-20.
5. Gruneir A, Bell CM, Bronskill SE, Schull M, Anderson GM, Rochon PA. Frequency and pattern of emergency department visits by long-term care residents--a population-based study. Frequency and pattern of emergency department visits by long-term care residents--a population-based study. J Am Geriatr Soc 2010;58:510-7.
6. 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;171:388-416.
7. Liapikou A, Polverino E, Cilloniz C, Peyrani P, Ramirez J, Menendez R, et al. A worldwide perspective of nursing home-acquired pneumonia compared with community-acquired pneumonia. Respir Care 2014;59:1078-85.
8. Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax 2009;64 Suppl 3:iii1-55.
9. Dhawan N, Pandya N, Khalili M, Bautista M, Duggal A, Bahl J, et al. Predictors of mortality for nursing home-acquired pneumonia: a systematic review. Biomed Res Int 2015;2015:285983.
10. Ewig S, Klapdor B, Pletz MW, Rohde G, Schütte H, Schaberg T, et al. Nursing-home-acquired pneumonia in Germany: an 8-year pro-

11. spective multicentre study. Thorax 2012;67:132-8.
11. 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.
12. 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;135:633-40.
13. Yamaya M, Yanai M, Ohrui T, Arai H, Sasaki H. Interventions to prevent pneumonia among older adults. J Am Geriatr Soc 2001;49:85-90.
14. Klapdor B, Ewig S, Schaberg T, Rohde G, Pletz MW, Schütte H, et al. Presentation, etiology and outcome of pneumonia in younger nursing home residents. J Infect 2012;65:32-8.
15. Klapdor B, Ewig S, Pletz MW, Rohde G, Schütte H, Schaberg T, et al. Community-acquired pneumonia in younger patients is an entity on its own. Eur Respir J 2012;39:1156-61.
16. El Solh AA, Akinnusi ME, Alfarah Z, Patel A. Effect of antibiotic guidelines on outcomes of hospitalized patients with nursing home-acquired pneumonia. J Am Geriatr Soc 2009;57:1030-5.
17. Polverino E, Dambrava P, Cillóniz C, Balasso V, Marcos MA, Esquinas C, et al. Nursing home-acquired pneumonia: a 10 year single-centre experience. Thorax 2010;65:354-9.
18. Lim WS, Macfarlane JT. A prospective comparison of nursing home acquired pneumonia with community acquired pneumonia. Eur Respir J 2001;18:362-8.
19. Koh SJ, Lee JH. Clinical characteristics of nursing home-acquired pneumonia in elderly patients admitted to a Korean teaching hospital. Korean J Intern Med 2015;30:638-47.
20. El-Solh AA, Sikka P, Ramadan F, Davies J. Etiology of severe pneumonia in the very elderly. Am J Respir Crit Care Med 2001;163(3 Pt 1):645-51.
21. Ma HM, Wah JL, Woo J. Should nursing home-acquired pneumonia be treated as nosocomial pneumonia? J Am Med Dir Assoc 2012;13:727-31
22. 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.
23. Cho YJ, Jung BK, Ahn JS. A Comparative study of nursing home-acquired pneumonia with community-acquired Pneumonia. Tuberc Respir Dis 2011;70:224-34.
24. Chalmers JD, Rother C, Salih W, Ewig S. Healthcare-associated pneumonia does not accurately identify potentially resistant pathogens: a systematic review and meta-analysis. Clin Infect Dis 2014;58:330-9.
25. Micek ST, Kollef KE, Reichley RM, Roubinian N, Kollef MH. Health care-associated pneumonia and community-acquired pneumonia: a single-center experience. Antimicrob Agents Chemother 2007;51:3568-73.
26. Kollef MH, Shorr A, Tabak YP, Gupta V, Liu LZ, Johannes RS. Epidemiology and outcomes of health-care-associated pneumonia: results from a large US database of culture-positive pneumonia. Chest 2005;128:3854-62.
27. Lee JC, Hwang HJ, Park YH, Joe JH, Chung JH, Kim SH. Comparison of severity predictive rules for hospitalised nursing home-acquired pneumonia in Korea: a retrospective observational study. Prim Care Respir J 2013;22:149-54.