

# Disease burden of pneumonia in Korean adults aged over 50 years stratified by age and underlying diseases

Jung Yeon Lee<sup>1</sup>, Chul Gyu Yoo<sup>2</sup>, Hyo-Jin Kim<sup>3</sup>, Ki Suck Jung<sup>4</sup>, and Kwang Ha Yoo<sup>5</sup>

<sup>1</sup>Department of Internal Medicine, Konkuk University Chungju Hospital, Chungju; <sup>2</sup>Department of Internal Medicine, Seoul National University Hospital, Seoul; <sup>3</sup>Outcomes Research/Evidence Based Medicine Team, Market Access Department, Pfizer Pharmaceuticals Korea Ltd., Seoul; <sup>4</sup>Division of Pulmonary Medicine, Department of Internal Medicine, Hallym University Sacred Heart Hospital, Anyang; <sup>5</sup>Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Konkuk University Medical Center, Seoul, Korea

Received: February 28, 2014  
Revised: May 17, 2014  
Accepted: May 27, 2014

Correspondence to  
Kwang Ha Yoo, M.D.

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Konkuk University Medical Center, 120 Neungdong-ro, Gwangjin-gu, Seoul 143-729, Korea  
Tel: +82-2-2030-7173  
Fax: +82-2-2030-5009  
E-mail: khyou@kuh.ac.kr

**Background/Aims:** This study was conducted to assess the disease burden of pneumonia according to age and presence of underlying diseases in patients admitted with community-acquired pneumonia (CAP).

**Methods:** We performed a retrospective, observational study and collected data targeting patients with CAP ( $\geq 50$  years) from 11 hospitals. Disease burden was defined as total per-capita medical fee, severity (CURB-65), hospital length of stay (LOS), and mortality.

**Results:** Of the 693 enrolled subjects, elderly subjects (age,  $\geq 65$  years) had a higher mean CURB-65 score (1.56 vs. 0.25;  $p < 0.01$ ) and higher mortality than nonelderly subjects (4.4% [ $n = 21$ ] vs. 0.5% [ $n = 1$ ];  $p = 0.00$ ). In addition, the total cost of pneumonia treatment was higher in elderly patients compared to in nonelderly patients (KRW 2,088,190 vs. US \$1,701,386;  $p < 0.01$ ). Those with an underlying disease had a higher CURB-65 score (1.26 vs. 0.68;  $p < 0.01$ ), were much older (mean age, 71.24 years vs. 64.24 years;  $p < 0.01$ ), and had a higher mortality rate than those without an underlying disease (3.5% [ $n = 20$ ] vs. 1.7% [ $n = 2$ ];  $p = 0.56$ ). Total per-capita medical fees were higher (KRW 2,074,520 vs. US \$1,440,471;  $p < 0.01$ ) and hospital LOS was longer (mean, 8.38 days vs. 6.42 days;  $p < 0.01$ ) in patients with underlying diseases compared to those without.

**Conclusions:** Due to the relatively high disease burden in Korea, particularly in the elderly and in those with an underlying disease, closer and more careful observation is needed to improve the outcomes of patients with CAP.

**Keywords:** Pneumonia; Costs and cost analysis; Comorbidity; Age factors

## INTRODUCTION

Community-acquired pneumonia (CAP) is a common and potentially serious illness. It is associated with considerable morbidity and mortality, particularly in elderly patients and those with significant underlying diseases

[1,2]. Some studies have indicated that the incidence of CAP increases substantially with age, and patients  $> 60$  years account for 81.2% of all cases [3-5]. Furthermore, the hospitalization rate due to CAP increases with every decade of life until the eighth decade [3-5]. The overall annual incidence of CAP in adults also increases with

age (14 per 1,000 person-year in adults age  $\geq 65$  years) [6]. Additionally, age is an independent risk factor for pneumonia, after controlling for confounding variables, such as underlying disease conditions, immobility, and use of tranquilizers [7,8]. Moreover, the elderly are more susceptible to pneumonia due to the anatomical and physiological changes that occur in the lungs with age [7,8].

A study conducted in Denmark demonstrated that the incidence of pneumonia requiring hospitalization increased by 50% from 1994 to 2004, and reported a persistently high mortality rate [9]. A Korean study of the pneumonia burden in 764 inpatients with CAP (age,  $\geq 50$  years) revealed that 3.2% patients died during treatment [10]. Mortality occurs primarily in the elderly and is frequently associated with underlying diseases. Moreover, CAP is not only an increasing mortality factor in these patients but is associated with a significant economic burden in the Asia-Pacific region [10,11].

Although many Korean studies have reported the incidence of CAP and its associated risk factors, there is a lack of information regarding the elderly, the group that most frequently experiences severe illness and underlying disease [10-12]. Furthermore, no comparative information is available on disease burden in those patients. To better understand the influence of age and underlying disease, we focused on the disease burden of inpatients with CAP according to aging factors and the presence of underlying diseases. Furthermore, we analyzed the variables associated with disease severity, cost, and outcome.

## METHODS

The study setting and population were described previously by Yoo et al. [10]. This was a retrospective observational study conducted from January 1, 2008 to December 31, 2010. Subjects aged  $\geq 50$  years were recruited from 11 university hospitals and were enrolled in reverse temporal order from the end of treatment. Of the 764 cases of confirmed pneumonia, 56 subjects with malignant cancer and 15 cases with only a fungal pathogen were excluded from analyses.

### Data collection

We reported the methodological details of data collec-

tion previously [10]. Briefly, general and clinical characteristics included sex, age, underlying disease, comorbid conditions (solid organ transplant, neutropenia, use of immunosuppressant within 3 months, use of corticosteroid) and identified pathogen severity using the CURB-65 (confusion, urea  $> 7$  mM/L [19 mg/dL], respiratory rate  $\geq 30$ /min, systolic blood pressure  $< 90$  mmHg or diastolic blood pressure  $\leq 60$  mmHg, and age  $\geq 65$  years) score, hospital length of stay (LOS), and survival status were collected.

### Resource utilization

All resource utilization and economic data were derived from the patient's detailed direct medical costs (insured and uninsured charges). Insured or uninsured charges for medical resource items were calculated to reflect the actual status at each relevant institution. The 2010 health insurance fees were consistently applied as insured charges. Each cost was separated by the following pertinent charge departments: hospitalization, medication, diagnostic testing, laboratory testing, imaging testing, and procedures or surgery. If patient admission days were 2 or more, the transfer and discharge day were excluded from the cost analysis, and only medical resource utilization was applied. Site and frequency of admission were evaluated for hospitalization. Antibiotics and other pneumonia-related drugs were included as medications. Procedures for identifying bacteria (bronchoscopy, thoracentesis, histology, etc.) and sputum, blood, urine, and pleural fluid examinations were included as diagnostic tests. Hematology or urinalysis; names and frequency of imaging tests (simple chest radiography, chest computed tomography, magnetic resonance imaging, ultrasound, and echocardiography); and for procedures or surgery, any procedure to resolve pneumonia-associated complications were performed as laboratory tests. More detailed resource utilization and calculation methods for the cost analysis were described in our previous report [10]. The costs only for evaluating and managing CAP were included.

### Statistical analysis

The SPSS version 20.0 (IBM Co., Armonk, NY, USA) was used for the analysis. Descriptive statistics are presented as results for the general and clinical characteristics of the elderly and nonelderly patients as well as those

with or without an underlying disease. Categorical variables are described with counts and percentages. Means  $\pm$  SD for continuous variables are presented. The *t* test or Mann-Whitney test and chi-square test were used to determine the significance of differences. A multivariate analysis of risk factors that affected hospital LOS and costs of patients with pneumonia was conducted, and log-transformation was applied. A two-tailed  $p < 0.05$  was considered to indicate significance. The average per-capita direct medical cost and average per-capita

daily direct medical cost for all patients with pneumonia and the subgroups of patients (elderly or 50 to 64 years and those with or without underlying diseases) were calculated using the direct medical cost results, which were estimated from medical resources.

**Ethics statement**

The Institutional Review Boards at each site approved this study, and written informed consent was obtained from all patients. The approval number for Hallym Uni-

**Table 1. Baseline characteristics according to age group**

Characteristic	Age $\geq$ 65 yr (n = 480)	Age < 65 yr (n = 213)	<i>p</i> value
<b>Sex</b>			
Male	298 (62.1)	99 (45.5)	< 0.01
Female	182 (37.9)	114 (53.5)	
<b>Underlying disease</b>			
None	50 (10.4)	65 (30.5)	< 0.01
Yes	430 (89.6)	148 (69.5)	
Chronic cardiovascular disorder	282 (58.8)	81 (38.0)	< 0.01
Chronic lung disease	206 (42.9)	53 (24.9)	< 0.01
Chronic metabolic disorders	123 (25.6)	46 (21.6)	0.25
Central nervous system disorders	30 (6.3)	2 (0.9)	0.00
Malignancy	27 (5.6)	3 (1.4)	0.01
Chronic kidney disorders	14 (2.9)	11(5.2)	0.14
Chronic liver diseases	10 (2.1)	9 (4.2)	0.11
Others	105 (21.9)	33 (15.5)	0.05
<b>Comorbid conditions<sup>a</sup></b>			
None	369 (76.9)	161 (75.6)	0.71
Yes	111 (23.1)	52 (24.4)	0.02
<b>Pathogens</b>			
Gram positive	51 (10.6)	16 (7.5)	0.20
<i>Streptococcus pneumoniae</i>	26 (5.4)	12 (5.6)	0.91
Other gram positive	25 (5.4)	4 (1.9)	0.04
Gram negative	55 (11.5)	15 (7.0)	0.08
Atypical pathogens <sup>b</sup>	29 (6.0)	20 (9.4)	0.11
Viruses	0 (0.0)	2 (0.9)	0.09
Mixed <sup>c</sup>	29(6.0)	8 (3.8)	0.56
Others	3 (0.6)	0 (0.0)	0.22
Unknown	313 (65.2)	152 (71.4)	0.11

Values are presented as number (%).

<sup>a</sup>Comorbid conditions: solid organ transplant, neutropenia, use of immunosuppressant within 3 months, use of corticosteroid.

<sup>b</sup>Atypical pathogens: *Mycoplasma*, *Legionella*, and *Chlamydia* spp.

<sup>c</sup>Mixed: two or more pathogens.

versity Sacred Heart Hospital was 2011-S016.

## RESULTS

### Baseline characteristics

After excluding 71 (56 patients with active malignancy and 15 with a single fungal pathogen) of 764 patients, the results for 693 patients were analyzed. We separated all patients with pneumonia into groups according to age (elderly [age  $\geq$  65 years] or nonelderly [age, 50 to 64 years]), and presence of underlying disease (with or without underlying disease), and compared the baseline characteristics. Males comprised the majority of elderly patients (62.1% [298 patients] vs. 37.9% [182 patients],  $p < 0.01$ ) (Table 1). We also separated all patients with pneumonia into those with or without an underlying disease

(Table 2). Of all patients with pneumonia, 83.4% (578) had an underlying disease. Mean ages of patients with and without an underlying disease were  $71.24 \pm 9.97$  and  $64.24 \pm 11.16$  years ( $p < 0.01$ ), respectively, and that for males was 60% ( $n = 347$ ) versus 40% ( $n = 231$ ), respectively ( $p < 0.01$ ). A greater proportion of males had an underlying disease, and the mean age of males was greater than that of females.

A pathogen was identified in 32.9% of cases (228 patients). *Streptococcus pneumoniae* was detected in 26 (5.4%) of the nonelderly patients and 12 cases (5.6%) of the elderly had a pathogen (Table 1). *S. pneumoniae* was isolated from 32 cases (5.5%) with an underlying disease and six (5.2%) without (Table 2). Mixed infection with *S. pneumoniae* was noted in nine elderly patients (1.9%;  $p = 0.10$ , data not shown) and 12 patients (2.1%) with an underlying disease ( $p = 0.71$ , data not shown). The distribution

**Table 2. Baseline characteristics according to the presence of underlying disease**

Characteristic	With underlying disease (n = 578)	Without underlying disease (n = 115)	p value
<b>Sex</b>			
Male	347 (60.0)	50 (43.5)	0.01
Female	231 (40.0)	65 (56.5)	
<b>Age, yr</b>			
50–64	148 (25.6)	65 (56.5)	< 0.01
65–74	201 (34.8)	28 (24.3)	< 0.01
$\geq 75$	229 (39.6)	22 (19.1)	< 0.01
<b>Comorbid conditions<sup>a</sup></b>			
None	432 (74.7)	98 (85.2)	0.02
Yes	146 (25.3)	17 (14.8)	0.43
<b>Pathogens</b>			
Gram positive	58 (10.0)	9 (7.8)	0.46
<i>Streptococcus pneumoniae</i>	32 (5.5)	6 (5.2)	0.89
Other gram positive	26 (4.5)	3 (2.6)	0.45
Gram-negative	62 (10.7)	8 (7.0)	0.22
Atypical pathogens <sup>b</sup>	41 (7.1)	8 (7.0)	0.96
Viruses	2 (0.3)	0 (0.0)	1.00
Mixed <sup>c</sup>	34 (5.9)	3 (2.6)	0.15
Others	2 (0.3)	1 (0.9)	0.42
Unknown	379 (65.6)	86 (74.8)	0.06

Values are presented as number (%) or mean  $\pm$  SD.

<sup>a</sup>Comorbid conditions: solid organ transplant, neutropenia, use of immunosuppressant within 3 months, use of corticosteroid.

<sup>b</sup>Atypical pathogens: *Mycoplasma*, *Legionella*, and *Chlamydia* spp.

<sup>c</sup>Mixed: two or more pathogens.

of pneumonia pathogens did not differ between the elderly and nonelderly groups and those with or without underlying diseases. Furthermore, gram-positive and -negative bacteria were isolated at a similar rate in elderly and nonelderly groups, same as the with underlying disease and without underlying diseases (Tables 1 and 2).

**Disease severity, treatment duration, and treatment outcomes**

The mean CURB-65 score in all patients with pneumonia was 1.16 points, and was higher in the elderly ( $1.56 \pm 0.78$  vs.  $0.25 \pm 0.52$ ,  $p < 0.01$ ) and those with an underlying disease than the nonelderly group without underlying disease ( $1.26 \pm 0.85$  vs.  $0.68 \pm 0.85$ ,  $p < 0.01$ ). Patients who scored  $\geq 3$  points comprised 10.2% of the elderly, which was significantly higher than that in the 50- to 64-year age group (10.2% [n = 49] vs. 0.5% [n = 1],  $p < 0.01$ ). Moreover, subjects with an underlying disease scored  $\geq 3$  points significantly more frequently than those without (7.6% [n = 44] vs. 5.2% [n = 6],  $p < 0.01$ ) (Table 3).

LOS was longer in elderly patients (8.45 days vs. 7.16 days,  $p = 0.00$ ), and in those with than without an underlying disease (8.38 days vs. 6.42 days,  $p < 0.01$ ) (Table 3). A total of 3.2% of the 693 patients with pneumonia died. The mortality rate was 4.4% (21 patients) in the elderly and 0.5% (one patient) in the nonelderly group ( $p = 0.00$ ). Similarly, the mortality rate was 3.5% (20 patients) in those with an underlying disease and 1.7% (two patients) in those without ( $p = 0.56$ ) (Table 3).

**Cost analysis**

Total per-capita medical fees for all patients with pneumonia were KRW 1,969,303 (US \$1,969; US \$1 = 1,000 KRW); they were 2,088,190 KRW in the elderly group and 1,701,386 KRW in the nonelderly group ( $p < 0.01$ ). Furthermore, the medical fees summed to 2,074,520 KRW in patients with an underlying disease and 1,440,471 KRW in those without ( $p < 0.01$ ) (Table 4). The costs for hospitalization, medication, diagnostic testing, laboratory testing, imaging, and a procedure or surgery in those with an underlying disease were higher than in those without an underlying disease ( $p < 0.01$ ) (Table 4). Elderly patients had a higher cost for each item compared to nonelderly patients, with the exception of diagnostic tests (Table 4). The percentage breakdown of costs for each item in the elderly was 28.2% for hospitalization, 22.3% for medication, 14.5% for diagnostic testing, 14.8% for laboratory testing, 10.4% for imaging, and 9.8% for a procedure or surgery. The underlying disease group had higher cost percentages for hospitalization (27.9%), medication (22.1%), diagnostic testing (15.2%), laboratory testing (14.7%), imaging (10.8%), and a procedure or surgery (9.3%). Subjects aged 50 to 64 years and those without an underlying disease showed similar proportions.

**Associations among disease severity, hospital LOS, and cost**

A univariate analysis presumed that the following factors were important for predicting patient outcome: age > 65 years, chronic cardiovascular disorder, chronic

**Table 3. Severity, hospital length of stay, and mortality according to age (elderly vs. 50 to 65 years) and presence of underlying disease**

Variable	Age $\geq$ 65 yr (n = 480)	Age < 65 yr (n = 213)	p value	With underlying disease (n = 578)	Without underlying disease (n = 115)	p value
CURB-65 <sup>a</sup>	$1.56 \pm 0.78$	$0.25 \pm 0.52$	$< 0.01$	$1.26 \pm 0.85$	$0.68 \pm 0.85$	$< 0.01$
Low	275 (57.3)	207 (97.2)	$< 0.01$	381 (65.9)	101 (87.8)	$< 0.01$
Moderate	156 (32.5)	5 (2.3)	$< 0.01$	153 (26.5)	8 (7.0)	$< 0.01$
High	49 (10.2)	1 (0.5)	$< 0.01$	44 (7.6)	6 (5.2)	$< 0.01$
Hospital LOS	$8.45 \pm 5.68$	$7.16 \pm 4.77$	0.00	$8.38 \pm 5.63$	$6.42 \pm 3.99$	$< 0.01$
Mortality	21 (4.4)	1 (0.5)	0.00	20 (3.5)	2 (1.7)	0.56

Values are presented as mean  $\pm$  SD or number (%).

LOS, length of stay.

<sup>a</sup>CURB-65 was analyzed using the nonparametric Mann-Whitney test. CURB-65, confusion, urea > 7 mM/L (19 mg/dL), respiratory rate  $\geq$  30/min, systolic blood pressure < 90 mmHg, or diastolic blood pressure  $\leq$  60 mmHg, and age  $\geq$  65 years.

**Table 4. Cost analysis according to age (elderly vs. 50 to 64 years) and presence of underlying disease**

Variable	Age ≥ 65 yr (n = 480)	Age < 65 yr (n = 213)	p value	With underlying disease (n = 578)	Without underlying disease (n = 115)	p value
Total cost	2,088,190 ± 1,759,161	1,701,386 ± 1,372,268	< 0.01	2,074,520 ± 1,750,060	1,440,471 ± 926,638	< 0.01
Hospitalization	588,041 ± 483,029 (28.2)	472,385 ± 345,977 (27.8)	< 0.01	578,442 ± 473,649 (27.9)	422,071 ± 253,344 (29.3)	< 0.01
Medication	465,115 ± 536,776 (22.3)	358,632 ± 421,408 (21.1)	0.01	459,020 ± 533,263 (22.1)	298,524 ± 307,541 (20.7)	< 0.01
Diagnostic test	302,821 ± 240,059 (14.5)	308,221 ± 225,393 (18.1)	0.47	314,957 ± 244,139 (15.2)	251,828 ± 177,818 (17.5)	0.02
Laboratory test	309,090 ± 257,181 (14.8)	248,447 ± 162,196 (14.6)	0.00	304,030 ± 245,354 (14.7)	222,200 ± 145,845 (15.4)	< 0.01
Imaging test	217,599 ± 207,200 (10.4)	211,253 ± 289,254 (12.4)	0.07	224,440 ± 245,080 (10.8)	171,461 ± 172,230 (11.9)	0.01
Procedure/surgery	205,525 ± 512,960 (9.8)	102,447 ± 343,173 (6.0)	< 0.01	193,631 ± 505,254 (9.3)	74,387 ± 185,227 (5.2)	< 0.01

Values are presented as mean ± SD (% of total). Unit, KRW (US \$1 = 1,000 KRW).

lung disease, CNS disorder, and chronic renal disorder (data not shown). Using these variables, we analyzed the factors associated with hospital LOS, cost, and severity (CURB-65 score). Hospital LOS was increased in the elderly ( $p < 0.033$ ) and those with chronic lung disease ( $p = 0.035$ ). Cost was increased in the elderly ( $p = 0.005$ ), and those with a chronic cardiovascular disorder ( $p = 0.028$ ) or chronic lung disease ( $p = 0.006$ ) (Table 5). The propensity to score low on the CURB-65 was increased in the elderly ( $p < 0.001$ ), in those with chronic renal disease ( $p < 0.001$ ), and in those with a CNS disorder ( $p = 0.024$ ). Moreover, a high CURB-65 score was more likely in patients with chronic lung disease ( $p = 0.014$ ).

## DISCUSSION

This study involved a subgroup analysis, which was first conducted by Yoo et al. [10]. In the current study, we focused on disease burden measured by total per-capita medical fees, severity (CURB-65), hospital LOS, and mortality, according to age and underlying diseases. Our findings demonstrated that disease burden was higher in the elderly ( $\geq 65$  years) and in patients with an underlying disease compared to those aged 50 to 64 years or without an underlying disease.

A cost analysis for pneumonia across studies is challenging due to differences in coding and data sources for the definition of pneumonia as well as the analytical methods used to calculate costs [1,5,13-16]. According to a US pneumonia burden study, the mean LOS per hospital admission was 7.6 days, with a mean cost of US \$6,949 per person (1997 value) [5]. This is consistent with the results of the retrospective analysis by Niederman et al. [16], who reported that mean hospital LOS and cost were 7.8 days and US \$7,166 per person (1995 value) in patients > 65 years of age [16]. The overall annual hospital cost for CAP in elderly patients in the US is \$4.4 billion to \$4.8 billion [5,16]. A US pneumonia cost analysis of hospital-treated pneumonia as a primary diagnosis in the elderly population in 2010, reported a conservative estimate of > US \$7 billion, or US \$9,749 per person (2005 to 2007 value); this imposes a tremendous burden on the US healthcare system [14]. However, those studies relied on Medicare administrative claims for the cost analysis, and the subjects selected may not have provided the ac-

**Table 5. Multivariate analysis of the associations among hospital length of stay, cost, and CURB-65**

Variable	Hospital LOS		Cost		CURB-65 <sup>a</sup>	
	B	p value	B	p value	B	p value
Age ≥ 65 yr	0.099	0.033	0.146	0.005	-3.063	< 0.001
<b>Underlying diseases</b>						
Chronic cardiovascular disorder	0.065	0.126	0.105	0.028	-0.146	0.323
Chronic lung disease	0.091	0.035	0.133	0.006	0.367	0.014
CNS disorders	0.061	0.536	0.033	0.769	-0.561	0.024
Chronic renal disorders	0.180	0.104	0.161	0.196	-1.299	< 0.001

CURB-65, confusion, urea > 7 mM/L (19 mg/dL), respiratory rate ≥ 30/min, systolic blood pressure < 90 mmHg or diastolic blood pressure ≤ 60 mmHg, and age ≥ 65 years; LOS, length of stay; CNS, central nervous system.

<sup>a</sup>Confusion, urea > 7 mM/L (19 mg/dL), respiratory rate ≥ 30/min, systolic blood pressure < 90 mmHg or diastolic blood pressure ≤ 60 mmHg, and age ≥ 65 years.

tual costs of care. Additionally, limited clinical details of each individual were provided. This suggests the costs may have been overestimated as a result of inclusion of treatments unrelated to pneumonia or unobserved morbidities. In contrast, the costs in our study included both insured and uninsured charges for each medical resource item. Furthermore, we consistently applied the actual cost case by case when a difference existed between hospitals, particularly for uninsured charges. In contrast to these previous studies, which used only the International Classification of Diseases code to select subjects, the definition of pneumonia in our study was clear due to the diagnosis being confirmed by pulmonary specialists in tertiary teaching hospitals. In support of these results, another US study reported that the mortality rate can change according to the pneumonia disease coding used [17]. Few studies in Asia have determined whether the CAP economic burden can be compared with that of other regions. In Taiwan, the cost of one hospital admission and the total cost for CAP in the elderly were approximately US \$3,221 and US \$1,897,137, respectively [18]. Among all age groups in rural Thailand, the cost of hospitalization for an episode of pneumonia ranges from US \$490.80 to US \$628.60 [19]. However, the Thai study used national health insurance claims data only; therefore, selection bias may have existed. Furthermore, the case definition for the inclusion criteria and the cost analysis method were unclear.

In addition to the cost analysis method and disease coding, the population examined is an important factor for a cost analysis study. A multicenter, hospital-based

study of the clinical and economic burden of invasive pneumococcal disease (IPD) reported mean direct medical costs of US \$7,452 (mean, US \$5,404 or US \$8,756/case), and no difference between age and risk groups [20]. Similarly, Weycker et al. [13] reported that the direct medical cost per case did not differ significantly between risk and age groups (US \$15,402 to US \$31,849/case) [13]. The former calculated direct medical costs by adding only IPD-related costs for each subject, whereas the latter involved data from the 2004 Healthcare Cost and Utilization Project Nationwide Inpatient Sample using mean age- and risk-specific charges [13,20]. Those results are in agreement with our findings. Total costs for CAP in our elderly and underlying disease groups were significantly higher than in the nonelderly and without underlying disease groups, suggesting that the initial disease severity is an important factor for the cost analysis, as are the cost analysis and disease coding methods. As only subjects with severe disease were included, selection bias could have existed in those studies. Moreover, those studies may have reported considerably higher costs because they did not include actual costs, such as uninsured charges, as in our study. Therefore, our data are more accurate and can be generalized to an inpatient CAP population.

CAP is one of the most common causes of death in the infectious diseases category in Korea, and mortality rates reach 12% to 14%, even with antibiotic use [21]. A prospective surveillance study conducted in 14 tertiary hospitals in Asian countries (South Korea, China, Taiwan, Hong Kong, India, Singapore, Vietnam, and Phil-

ippines; Asian Network for Surveillance of Resistant Pathogens), showed that old age was a risk factor for mortality [11]. In fact, when patients were stratified by age, the mean CURB-65 severity score increased gradually with age (50 to 54 years, 0.16; 55 to 59 years, 0.30; 60 to 64 years, 0.29; 65 to 70 years, 1.40; data not shown) as in our study. Furthermore, the percentage of patients with a high CURB-65 score also increased markedly starting at age 65 yr (50 to 54 years,  $n = 0$  [0%]; 55 to 59 years,  $n = 0$  [0%]; 60 to 64 years,  $n = 1$  [1.3%]; 65 to 70 years,  $n = 7$  [6.9%]; data not shown). This is possibly because the CURB-65 score includes age  $\geq 65$  years as a factor in the severity scoring. We divided the patients into elderly ( $\geq 65$  years) or nonelderly (50 to 64 years) groups. The elderly group developed a higher disease burden. However, age is itself an important risk or prognostic factor for pneumonia. Age was not a predictive factor for mortality in a Korean study conducted to determine predictors of in-hospital mortality in patients with severe CAP who required mechanical ventilation [22]. Therefore, severity is more important than age in terms of mortality.

Because we defined the costs for disease burden, severity (CURB-65), hospital LOS, and mortality, we identified the variables associated with these factors. Cost and hospital LOS were significantly higher in the elderly and in patients with an underlying disease; however, no significant association with any variable was found in the multivariate analysis (data not shown). This might have been caused by a lower or slightly higher mortality rate in those with an underlying disease or the elderly. Although we cannot explain the low mortality, several factors are likely involved, such as the modest effect of higher pneumococcal vaccination rates on pneumonia risk; reduced smoking; and better treatment for chronic underlying disease; these are risk factors for pneumonia. Pooled data from observational studies have demonstrated the overall burden of CAP in patients with other medical conditions, such as chronic respiratory diseases, cardiovascular diseases, cerebrovascular diseases, dementia, and diabetes mellitus, which were the most frequent underlying diseases [3,23]. Up to two-thirds of patients had a chronic respiratory disease and almost half had a chronic cardiovascular disease [3,6,23]. Our results also indicate that ~90% of those with an underlying disease had chronic cardiovascular disease (52.4%,  $n = 363$ ) or chronic lung disease (37.4%,  $n = 259$ ).

Disease severity and frequency of an underlying condition affected the outcomes. Mortensen et al. reported that about half of deaths in patients with CAP were attributable to worsening of a pre-existing condition [24]. Although we cannot explain these factors separately, we understand that age and underlying disease are important factors for predicting disease burden. An analysis of each individual patient with an underlying disease and a longitudinal assessment of outcomes are needed to better understand the associations between age and underlying disease, cost, disease severity, and hospital LOS. Some limitations of this investigation should be mentioned. As our study was performed in a tertiary referral center and did not include an outpatient population, in which CAP is treated more commonly, it is difficult to generalize our results. Another limitation of our study is that only subjects age  $\geq 50$  years were included; thus, our results may not be representative of the entire population of pneumonia patients in Korea.

The strengths of this study are the accuracy of the cost analysis for inpatient CAP. Due to the lack of information about the most frequent independent risk factors (elderly, patients with underlying disease) in Korea, we analyzed these patients using accurate medical resources, including uninsured items, which had not been applied in previous studies. Insured items were adjusted for annual inflation by consistently applying the 2010 insurance fees for each insurance medical resources. Furthermore, the nursing (or intensive care unit nursing) personnel category was applied by identifying the actual status in each institution. An accurate economic burden for uninsured items was calculated by focusing on publicly available uninsured data, as disclosed on the website of each institution. Although this was a retrospective study, patients with pneumonia at each hospital were identified in reverse temporal order from the treatment completion date (December 31, 2010) and were extracted relatively randomly; hence, little bias existed according to disease severity, age, sex, or the presence of underlying disease. Third, the study was conducted mostly in the pulmonary divisions of university hospitals; thus, the diagnosis of pneumonia and assessment of underlying diseases were accurate. We identified pathogens more aggressively using every possible diagnostic tools such as bronchoscopy, thoracentesis, histology, etc., and assessed treatment outcomes in > 90% of



all cases.

In summary, we report herein the characteristics and medical costs of Korean pneumonia patients aged  $\geq 50$  years who received inpatient care. Patients were divided into elderly and non-elderly and those with and without an underlying disease. Total costs, hospital LOS, and disease severity were higher in the elderly and in those with an underlying disease than in the non-elderly and those without an underlying disease. Therefore, this disease imposes a considerable on both the individual, particularly the elderly and those with an underlying disease, and society in general. Furthermore, an actual cost analysis regarding all medical resources, including noninsurance charges, is essential; this should be based on an accurate disease diagnosis as well as on the presence of underlying disease, as discussed above. Given that being elderly and having chronic lung disease were associated with a higher disease burden, closer and more careful observations in these populations are essential to improve the outcomes of inpatient treatment of CAP.

### KEY MESSAGE

1. Among patients hospitalized for community-acquired pneumonia (CAP), the elderly and those with an underlying disease had higher disease burdens.
2. A cost analysis that considers all medical resources based on accurate diagnoses is essential to assess more accurately the disease burden associated with CAP.

### Conflict of interest

No potential conflict of interest relevant to this article was reported.

### Acknowledgments

This study was supported by Pfizer Pharmaceuticals Korea Ltd. Hyo-Jin Kim is a Pfizer employee.

### REFERENCES

1. File TM. Community-acquired pneumonia. *Lancet*

- 2003;362:1991-2001.
2. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2007;44 Suppl 2:S27-S72.
3. Ewig S, Birkner N, Strauss R, et al. New perspectives on community-acquired pneumonia in 388 406 patients. Results from a nationwide mandatory performance measurement programme in healthcare quality. *Thorax* 2009;64:1062-1069.
4. Jackson ML, Neuzil KM, Thompson WW, et al. The burden of community-acquired pneumonia in seniors: results of a population-based study. *Clin Infect Dis* 2004;39:1642-1650.
5. Kaplan V, Angus DC, Griffin MF, Clermont G, Scott Watson R, Linde-Zwirble WT. Hospitalized community-acquired pneumonia in the elderly: age- and sex-related patterns of care and outcome in the United States. *Am J Respir Crit Care Med* 2002;165:766-772.
6. Torres A, Peetermans WE, Viegi G, Blasi F. Risk factors for community-acquired pneumonia in adults in Europe: a literature review. *Thorax* 2013;68:1057-1065.
7. Chong CP, Street PR. Pneumonia in the elderly: a review of the epidemiology, pathogenesis, microbiology, and clinical features. *South Med J* 2008;101:1141-1145.
8. Marik PE, Kaplan D. Aspiration pneumonia and dysphagia in the elderly. *Chest* 2003;124:328-336.
9. Thomsen RW, Riis A, Norgaard M, et al. Rising incidence and persistently high mortality of hospitalized pneumonia: a 10-year population-based study in Denmark. *J Intern Med* 2006;259:410-417.
10. Yoo KH, Yoo CG, Kim SK, et al. Economic burden and epidemiology of pneumonia in Korean adults aged over 50 years. *J Korean Med Sci* 2013;28:888-895.
11. Song JH, Oh WS, Kang CI, et al. Epidemiology and clinical outcomes of community-acquired pneumonia in adult patients in Asian countries: a prospective study by the Asian network for surveillance of resistant pathogens. *Int J Antimicrob Agents* 2008;31:107-114.
12. Kim HI, Kim SW, Chang HH, et al. Mortality of community-acquired pneumonia in Korea: assessed with the pneumonia severity index and the CURB-65 score. *J Korean Med Sci* 2013;28:1276-1282.
13. Weycker D, Strutton D, Edelsberg J, Sato R, Jackson LA. Clinical and economic burden of pneumococcal disease

- in older US adults. *Vaccine* 2010;28:4955-4960.
14. Thomas CP, Ryan M, Chapman JD, et al. Incidence and cost of pneumonia in medicare beneficiaries. *Chest* 2012;142:973-981.
  15. Marston BJ, Plouffe JF, File TM Jr, et al. Incidence of community-acquired pneumonia requiring hospitalization: results of a population-based active surveillance Study in Ohio: the Community-Based Pneumonia Incidence Study Group. *Arch Intern Med* 1997;157:1709-1718.
  16. Niederman MS, McCombs JS, Unger AN, Kumar A, Popovian R. The cost of treating community-acquired pneumonia. *Clin Ther* 1998;20:820-837.
  17. Lindenauer PK, Lagu T, Shieh MS, Pekow PS, Rothberg MB. Association of diagnostic coding with trends in hospitalizations and mortality of patients with pneumonia, 2003-2009. *JAMA* 2012;307:1405-1413.
  18. Chen YH, Yang GY, Loh CH, et al. Cost benefits of targeting the pneumococcal vaccination program to the elderly population in Taiwan. *Am J Infect Control* 2006;34:597-599.
  19. Olsen SJ, Laosiritaworn Y, Siasiriwattana S, Chunsuttiwat S, Dowell SF. The incidence of pneumonia in rural Thailand. *Int J Infect Dis* 2006;10:439-445.
  20. Song JY, Choi JY, Lee JS, et al. Clinical and economic burden of invasive pneumococcal disease in adults: a multi-center hospital-based study. *BMC Infect Dis* 2013;13:202.
  21. Lee MK. Community acquired pneumonia. *Tuberc Respir Dis* 2011;70:1-9.
  22. Lee JH, Ryu YJ, Chun EM, Chang JH. Outcomes and prognostic factors for severe community-acquired pneumonia that requires mechanical ventilation. *Korean J Intern Med* 2007;22:157-163.
  23. Viegi G, Pistelli R, Cazzola M, et al. Epidemiological survey on incidence and treatment of community acquired pneumonia in Italy. *Respir Med* 2006;100:46-55.
  24. Mortensen EM, Coley CM, Singer DE, et al. Causes of death for patients with community-acquired pneumonia: results from the Pneumonia Patient Outcomes Research Team cohort study. *Arch Intern Med* 2002;162:1059-1064.