

# Chronic obstructive pulmonary disease severity is associated with severe pneumonia

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#### Abstract:

**CONTEXT:** Chronic obstructive pulmonary disease (COPD) is a heterogeneous disorder, and various aspects of COPD may be associated with the severity of pneumonia in such patients.

**AIMS:** We examined the risk factors associated with severe pneumonia in a COPD population.

**METHODS:** We performed a retrospective observational study using a prospectively collected database of pneumonia patients who were admitted to our hospital through emergency department between 2008 and 2012. Patients with hospital-acquired pneumonia and those with an immunocompromised status were excluded.

**RESULTS:** Of 148 pneumonia patients with COPD for whom chest computed tomography (CT) scans were available, 106 (71.6%) and 42 (28.4%) were classified as non-severe and severe pneumonia, respectively. Multivariate logistic regression analysis revealed that the severity of airflow limitation [odds ratio (OR), 2.751; 95% confidence interval (CI), 1.074-7.050;  $P=0.035$ ] and the presence of emphysema on a chest CT scan (OR, 3.366; 95% CI, 1.104-10.265;  $P=0.033$ ) were independently associated with severe pneumonia in patients with COPD.

**CONCLUSIONS:** The severity of COPD including the airflow limitation grade and the presence of pulmonary emphysema were independently associated with the development of severe pneumonia.

#### Key words:

Chronic obstructive pulmonary disease, emphysema, pneumonia, pulmonary function test, severity of illness

Chronic obstructive pulmonary disease (COPD) is a progressive lung condition characterized by an accelerated decline in lung function with disease exacerbations.<sup>[1]</sup> COPD is a major global health problem that consumes considerable healthcare costs and has a notable mortality, as shown in a 2010 study.<sup>[2]</sup> Patients with COPD, particularly those with severe disease, who are of older age, and/or who have specific comorbidities, are at a greater risk of developing pneumonia,<sup>[3,4]</sup> and COPD patients with pneumonia have poorer clinical presentations than does the general population with pneumonia.<sup>[5]</sup>

As COPD is a heterogeneous disorder,<sup>[6]</sup> various aspects thereof, including radiological findings, the severity of airflow limitation, the presence of comorbid conditions, and the presence of organisms potentially causing pneumonia, may be associated with the severity of pneumonia in such patients. However, few data are available on the impact of the various possible factors on the development of severe pneumonia in COPD populations. Therefore, we sought to identify risk factors associated with severe pneumonia in a COPD population. We evaluated demographic characteristics, COPD-related variables, and chest computed tomography (CT) findings in

COPD patients hospitalized with community-acquired pneumonia.

## Methods

### Data source

This retrospective observational study used a prospectively collected database on community-acquired pneumonia and was conducted at the Samsung Medical Center (a 1,961-bed, university-affiliated, tertiary referral hospital in Seoul, South Korea) between January 2008 and December 2012. Some clinical data on the patients enrolled between 2008 and 2010 have been included in three articles published in 2010, 2013, and 2014.<sup>[7-9]</sup> The Institutional Review Board of the Samsung Medical Center approved the review and publication of information obtained from the database. The need for informed consent was waived because of the retrospective nature of the study.

### Study population

All consecutive patients with pneumonia admitted to our hospital through our emergency department were registered prospectively during the study period. A total of 2,670 cases of pneumonia were recorded, but we excluded 1,172 of these for the following reasons: 1) 779

cases had hospital-acquired pneumonia that developed after hospitalization for >72 hours or within 10 days of leaving the hospital, or who were transferred from another hospital after prior hospitalization for at least 48 hours;<sup>[10]</sup> and 2) 393 cases were immunocompromised patients.

Thus, 1,498 cases of pneumonia were included in the present study initially, among whom 216 had both pneumonia and COPD (confirmed by spirometry performed either prior to admission or after recovery from pneumonia). If a patient was admitted more than once for pneumonia during the study period, data from only the first admission were analyzed. Penultimately, we included data from 159 COPD patients with pneumonia. Eleven further patients were excluded, because chest CT scans had not been performed within 1 year before or after pneumonia. Thus, a final total of 148 patients were included in the present study [Figure 1].

#### Diagnosis, definition, and risk stratification for pneumonia

A diagnosis of pneumonia required chest radiographic evidence of new infiltrates and fulfilment of one of the following criteria:

1. Fever (body temperature  $\geq 38^{\circ}\text{C}$ ) or hypothermia (body temperature  $\leq 35^{\circ}\text{C}$ ),
2. New-onset cough with or without sputum production, pleuritic chest pain, or dyspnea, and
3. Altered breath sounds on auscultation.<sup>[11]</sup>

Severe pneumonia was defined as the presence of one of two major criteria (presence of septic shock and a requirement for mechanical ventilation including bi-level positive airway pressure) or two of three minor criteria:

1. Systolic blood pressure  $< 90$  mmHg,
2. Multilobar involvement evident on chest radiography, and
3. An arterial oxygen tension to inspired oxygen fraction ratio of  $< 250$ .<sup>[12]</sup> Pneumonia severity index (PSI) and confusion, urea nitrogen, respiratory rate, blood pressure, age  $\geq 65$  years (CURB-65) scores were calculated to allow risk stratification.<sup>[13,14]</sup>

#### Microbiological data and antibiotics

Etiological diagnoses were complemented by immunological assays (the pneumococcal urinary antigen test, the *Legionella*

*pneumophila* urinary antigen test, and the *Mycoplasma pneumoniae* IgM antibody test) and cultures of sputum, bronchial washings, blood, or pleural fluid.<sup>[8]</sup> Methicillin-resistant *Staphylococcus aureus*, *Stenotrophomonas maltophilia*, and extended-spectrum  $\beta$ -lactamase-producing *Enterobacteriaceae* were considered to be potentially drug resistant pathogens.<sup>[15]</sup>

#### Diagnosis, grading, and COPD medication

We diagnosed COPD via post-bronchodilator spirometry as recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD).<sup>[11]</sup> COPD severity was based on the GOLD criteria: GOLD grade I was defined as a forced expiratory volume in 1 second (FEV1)  $> 80\%$  predicted; GOLD grade II as an FEV1 of 50-80% predicted; GOLD grade III as an FEV1 of 30-50% predicted; and GOLD grade IV as an FEV1  $< 30\%$  predicted.<sup>[11]</sup> Inhaled corticosteroids, long-acting beta-agonists, anticholinergics, and theophylline used for at least 30 days prior to the diagnosis of pneumonia were considered to be previous COPD medications.

#### Analysis of chest CT scans

Chest CT scans were reviewed blindly by two pulmonary physicians (Eom JS and Song WJ), and discrepancies were resolved by consensus discussion with a third pulmonary physician (Park HY). All scans were performed within 1 year before or after the diagnosis of pneumonia, as the emphysema progression is minimal over 1 year. CT findings were classified as the presence/absence of pulmonary emphysema and/or bronchiectasis. These conditions were evaluated via a visual assessment method modified from that of previous studies.<sup>[16,17]</sup>

#### Statistical analysis

All data are presented as medians (with interquartile ranges [IQRs]) for continuous variables or as numbers (with percentages) for categorical variables. The Mann-Whitney U-test was used to compare continuous variables, and Pearson's chi-squared or Fisher's exact test was used to compare categorical variables. Multivariate logistic regression analysis was performed after adjustment for age, gender, smoking status, and factors associated with  $P$  value  $< 0.25$  upon univariate analysis, including variables found to be of interest in previous studies (particularly a previous use of inhaled corticosteroids [ICS]<sup>[18-20]</sup>). PSI and CURB-65 scores were excluded from the multivariate logistic regression model, because some variables used to calculate these scores had been entered already. Model goodness-of-fit was evaluated using the test of Hosmer and Lemeshow. A  $P$  value  $< 0.05$  was considered significant. All statistical analyses were performed using statistical package of social sciences (SPSS) version 20.0 (SPSS Inc., Chicago, IL, USA).

## Results

#### Patient characteristics

The baseline characteristics of the 148 patients with both COPD and pneumonia are shown in Table 1. The median patient age was 71 years (IQR, 65-76 years), and 86.5% were males. The most common comorbidity was malignant disease (23.0%), followed by diabetes (20.9%) and cerebrovascular disease (14.2%). Fourteen patients (9.5%) had septic shock and 42 (28.4%) severe pneumonia at presentation. The median PSI and CURB-65 scores were 97 (IQR, 76-121) and 1 (IQR, 1-2),

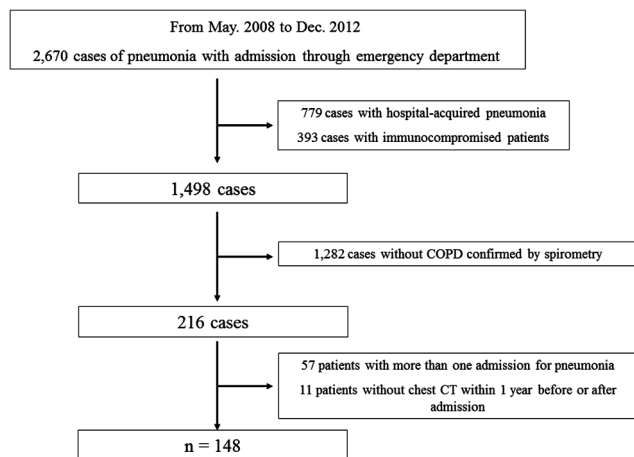


Figure 1: Study flow diagram

respectively. The PSI and CURB-65 scores are shown in Online Supplements 1 and 2.

Eighteen patients (12.2%) were admitted to the intensive care unit, and 11 (7.4%) required mechanical ventilation. The median durations of antibiotic therapy and length of hospital stay were 14 (IQR, 10-16 days) and 8 days (IQR, 6-14 days), respectively. The in-hospital mortality rate of the 148 patients with COPD and pneumonia was 7.4% ( $n = 11$ ).

### Non-severe and severe pneumonia

Of the 148 patients, 106 (71.6%) and 42 (28.4%) were diagnosed with non-severe and severe pneumonia, respectively. Of the patients with both COPD and severe pneumonia, 14 (33.3%) presented with septic shock and 11 (26.2%) required mechanical ventilation. As shown in Table 2, the median PSI and CURB-65 scores were significantly higher in patients with severe pneumonia than in those with non-severe pneumonia (134 [IQR, 104-156] vs. 90 [IQR, 74-107],  $P < 0.001$  for PSI; and 2 [IQR, 1-3] vs. 1 [IQR, 1-1],  $P < 0.001$  for CURB-65). There was a significant difference in previous history of cerebrovascular disease between COPD patients with non-severe and severe pneumonia ( $P = 0.035$ ); however, other comorbidities were not different. In addition, distinct differences were evident in both the rates of admission to the intensive care unit and mortalities between those with non-severe and severe pneumonia (1.9% vs. 38.1%,  $P < 0.001$  for admission to the intensive care unit; and 2.8% vs. 19.0%,  $P = 0.002$  for mortality). However, upon univariate analysis, no significant difference between patients with non-severe and severe pneumonia was evident with respect

to age, gender, GOLD grade, the presence of emphysema or bronchiectasis, systemic corticosteroid use or ICS prior to pneumonia, and identified pathogens [Tables 2 and 3].

### Online Supplement 1: Severity analysis by PSI scoring system

Variables associated with PSI scoring system	Median (IQR) or No. (%)
Component of PSI	
Age*, years	70 (64-75)
Nursing home resident	4 (2.7)
Co-existing illnesses	
Neoplastic disease	34 (23.0)
Liver disease	7 (4.7)
Congestive heart failure	16 (10.8)
Cerebrovascular disease	21 (14.2)
Renal disease	11 (7.4)
Physical examination findings	
Altered mental status	9 (6.1)
Respiratory rate $\geq 30$ /min	24 (16.2)
Systolic blood pressure $< 90$ mmHg	12 (8.1)
Temperature $< 35^\circ\text{C}$ or $\geq 40^\circ\text{C}$	3 (2.0)
Pulse $\geq 125$ /min	29 (19.6)
Laboratory and radiographic findings	
Arterial pH $< 7.35$	11 (8.6)
Blood urea nitrogen $\geq 30$ mg/dl	15 (10.1)
Sodium $< 130$ mmol/l	15 (10.1)
Glucose $\geq 250$ mg/dl	14 (9.9)
Hematocrit $< 30\%$	15 (10.1)
Partial pressure of arterial oxygen $< 60$ mmHg	71 (48.0)
Pleural effusion	27 (18.2)
Risk class	
Class I	2 (1.4)
Class II	23 (15.5)
Class III	37 (25.0)
Class IV	58 (39.2)
Class V	28 (18.9)

PSI = Pneumonia severity index, IQR = Interquartile range, \*Ten was subtracted from women's age according to PSI

### Online Supplement 2: Severity analysis by CURB-65 scoring system

Variables associated with CURB-65 scoring system	No. (%)
Component of CURB-65	
Patient with confusion at admission	9 (6.1)
Urea $> 19$ mg/dl	44 (29.7)
Respiratory rate $> 30$ /min	23 (15.5)
Systolic BP $< 90$ mmHg or diastolic BP $\leq 60$ mmHg	12 (8.1)
Age $\geq 65$	114 (77.0)
Total score	
0	24 (16.2)
1	71 (48.0)
2	33 (22.3)
3	15 (10.1)
4	5 (3.4)
5	0 (0)

CURB-65 = Confusion, urea, respiratory rate, blood pressure, age  $\geq 65$ , BP = Blood pressure

**Table 1: Baseline characteristics of the patients**

Characteristic	Median (IQR) or No. (%)
Age, years	71 (65-76)
Male gender	128 (86.5)
Body mass index, kg/m <sup>2</sup>	21 (19-24)
Comorbidities (overlapping)	
Malignant disease	34 (23.0)
Diabetes	31 (20.9)
Cerebrovascular disease	21 (14.2)
Chronic heart disease	19 (12.8)
Chronic kidney disease	11 (7.4)
Chronic liver disease	7 (4.7)
Smoking status	
Never-smoker	48 (32.4)
Current or ex-smoker	100 (67.6)
Laboratory findings	
White blood cell count/ $\mu\text{l}$	11,430 (8,393-16,638)
Neutrophil count/ $\mu\text{l}$	9,119 (6,043-13,983)
C-reactive protein, mg/l	11.6 (5.7-19.8)
Systemic corticosteroid use prior to pneumonia*	22 (14.9)
Extent of pneumonia	
Multilobar	56 (37.8)
Bilateral	39 (26.4)
Septic shock at presentation	14 (9.5)
Severe pneumonia at presentation	42 (28.4)

IQR = interquartile range, CURB-65 = confusion, urea, respiratory rate, blood pressure, age  $\geq 65$  years, \*Systemic corticosteroid use prior to the development of pneumonia was defined as recent use of an oral or intravenous steroid for more than 7 days before the diagnosis of pneumonia

**Table 2: Factors associated with the severity of pneumonia in COPD patients**

Variable	Non-severe pneumonia (n = 106)	Severe pneumonia (n = 42)	P value
Age, years	70 (65-75)	72 (67-79)	0.201
Male gender	93 (87.7)	35 (83.3)	0.480
Current or ex-smoker	72 (67.9)	28 (66.7)	0.883
Body mass index, kg/m <sup>2</sup>	22 (19-25)	21 (19-24)	0.315
Comorbidities (overlapped)			
Malignant disease	22 (20.8)	12 (28.6)	0.308
Diabetes	23 (21.7)	8 (19.0)	0.721
Cerebrovascular disease	11 (10.4)	10 (23.8)	0.035
Chronic heart disease	12 (11.3)	7 (16.7)	0.381
Chronic kidney disease	6 (5.7)	5 (11.9)	0.294
Chronic liver disease	6 (5.7)	1 (2.4)	0.673
Number of comorbidities	0 (0-1)	1 (0-2)	0.052
Severity of pneumonia			
PSI	90 (74-107)	134 (104-156)	<0.001
PSI ≥ class 4	49 (46.2)	37 (88.1)	<0.001
CURB-65	1 (1-1)	2 (1-3)	<0.001
CURB-65 ≥ 2	26 (24.5)	27 (64.3)	<0.001
Pulmonary function test			
FEV <sub>1</sub> , % predicted	62 (45-80)	54 (39-78)	0.364
FVC, % predicted	81 (65-94)	77 (64-91)	0.372
FEV <sub>1</sub> /FVC	54 (44-62)	52 (39-60)	0.312
GOLD grade III or IV	30 (28.3)	17 (40.5)	0.151
CT findings			
Emphysema	58 (54.7)	30 (71.4)	0.062
Bronchiectasis	24 (22.6)	10 (23.8)	0.879
Previous ICS use	48 (45.3)	15 (35.7)	0.289
Use of oral corticosteroid medication prior to pneumonia*	18 (17.0)	4 (9.5)	0.250
Potentially drug-resistant pathogen <sup>†</sup>	6/28 (21.4)	5/16 (31.3)	0.492
Prior antibiotics treatment <sup>‡</sup>	41 (38.7)	16 (38.1)	0.948

COPD = Chronic obstructive pulmonary disease, PSI = Pneumonia severity index, CURB-65 = Confusion, urea nitrogen, respiratory rate, blood pressure, age ≥ 65 years, FEV<sub>1</sub> = Forced expiratory volume in 1 s, FVC = Forced vital capacity, GOLD = Global Initiative for Chronic Obstructive Lung Disease, ICS = Inhaled corticosteroid, \*Systemic corticosteroid use prior to development of pneumonia was defined as recent use of an oral or intravenous steroid for more than 7 days before the diagnosis of pneumonia, <sup>†</sup>Potentially drug-resistant pathogens included *Pseudomonas* species, methicillin-resistant *Staphylococcus aureus*, *Acinetobacter* species, extended-spectrum β-lactamase-producing *Enterobacteriaceae*, and *Stenotrophomonas maltophilia*, <sup>‡</sup>Prior antibiotics treatment was defined as the presence of history of antibiotics medication within 90 days from the date of pneumonia diagnosis

**Table 3: Microbiological data and antibiotic-resistance status**

Variables	All patients (n = 148)	Non-severe pneumonia (n = 106)	Severe pneumonia (n = 42)	P value*
Pathogen identified	44 (29.7)	28 (26.4)	16 (38.1)	0.137
<i>Streptococcus pneumoniae</i>	15/44 (34.1)	11/28 (39.3)	4/16 (25.0)	0.336
Streptococcus other than <i>S. pneumoniae</i>	1/44 (2.3)	0/28 (0.0)	1/16 (6.3)	0.364
<i>Staphylococcus aureus</i>	4/44 (9.1)	3/28 (10.7)	1/16 (6.3)	1.000
MRSA	1/44 (2.3)	1/28 (3.6)	0/16 (0.0)	1.000
<i>Pseudomonas aeruginosa</i>	9/44 (20.5)	4/28 (14.3)	5/16 (31.3)	0.250
<i>Hemophilus influenzae</i>	7/44 (15.9)	6/28 (21.4)	1/16 (6.3)	0.393
<i>Klebsiella pneumoniae</i>	1/44 (2.3)	0/28 (0.0)	1/16 (6.3)	0.364
Others	7/44 (15.9)	4/28 (14.3)	3/16 (18.8)	0.692

MRSA = Methicillin-resistant *Staphylococcus aureus*, \*When patients with non-severe and severe pneumonia were compared

### Factors contributing to severe pneumonia

Multivariate logistic regression analysis was performed to identify the risk factors associated with severe pneumonia in the 148 patients with COPD [Table 4]. The severity of airflow limitation (OR, 2.751; 95% CI, 1.074-7.050;  $P = 0.035$ ) and the presence of emphysema on a chest CT scan (OR, 3.366; 95% CI, 1.104-10.265;  $P = 0.033$ ) were

independently associated with severe pneumonia in COPD patients.

### In-hospital mortality

As shown in Table 5, chronic heart disease, number of comorbidities, PSI, severe pneumonia at presentation, and intensive care unit (ICU) admission were related with mortality. However, the

severity of airflow limitation and the presence of emphysema on a chest CT scan were not related with in-hospital mortality.

## Discussion

The current study included 148 patients with radiographically confirmed pneumonia and COPD diagnosed via spirometry.

**Table 4: Multivariate logistic regression analysis identifying factors associated with the severity of pneumonia in COPD patients (n = 148)**

Variables	P value	Odds ratio	95% confidence interval
Age	0.283	1.025	0.980-1.072
Male gender	0.140	2.866	0.707-11.612
Smoking status	0.564	0.726	0.245-2.153
Cerebrovascular disease	0.271	1.935	0.598-6.267
Number of comorbidities	0.255	1.339	0.810-2.216
GOLD grade III or IV	0.035	2.751	1.074-7.050
Emphysema on CT scan	0.033	3.366	1.104-10.265
Inhaled corticosteroid	0.131	0.511	0.214-1.221

COPD = Chronic obstructive pulmonary disease, GOLD = Global initiative for chronic obstructive lung disease, Hosmer and Lemeshow test;  $\chi^2 = 10.593$ ,  $df = 8$ ,  $P = 0.226$

We performed a wide-ranging evaluation of COPD- and pneumonia-related factors. A previous study showed that COPD patients presented with more severe pneumonia than did those without COPD.<sup>[5]</sup> We extended this finding by showing that the severity of COPD including the airflow limitation grade and the presence of pulmonary emphysema, affected the severity of pneumonia in patients with COPD significantly. However, COPD severity did not associated with in-hospital mortality.

Both emphysema and the severity of airflow limitation have significant impacts on COPD prognosis. Compared with COPD patients with minimal or no emphysema evident on chest CT scan, patients with emphysema were at an increased risk of a significant annual decline in FEV1, indicating rapid disease progression.<sup>[21,22]</sup> In addition, pulmonary emphysema evident on a chest CT scan has been shown as a strong independent predictor of mortality in COPD populations.<sup>[23-25]</sup> Emphysema on chest CT was also associated with poor prognoses of patients with both COPD and early-stage lung cancer.<sup>[26]</sup> To the best of our knowledge, this is the first work to suggest a further impact of emphysema on the severity of pneumonia. Despite of lack of association with in-hospital mortality, COPD patients with emphysema were more

**Table 5: Factors associated with overall in-hospital mortality of pneumonia in COPD patients**

Variable	Survivor (n = 137)	Dead (n = 11)	P value
Age, years	71 (65-76)	69 (62-85)	0.821
Male gender	119 (86.9)	9 (81.8)	0.645
Current or ex-smoker	92 (67.2)	8 (72.7)	1.000
Body mass index, kg/m <sup>2</sup>	21 (19-24)	21 (18-25)	0.766
Comorbidities (overlapped)			
Malignant disease	29 (21.2)	5 (45.5)	0.127
Diabetes	29 (21.2)	2 (18.2)	1.000
Cerebrovascular disease	18 (13.1)	3 (27.3)	0.191
Chronic heart disease	15 (10.9)	4 (36.4)	0.036
Chronic kidney disease	10 (7.3)	1 (9.1)	0.586
Chronic liver disease	6 (4.4)	1 (9.1)	0.424
Number of comorbidities	1 (0-1)	1 (1-2)	0.007
Severity of pneumonia			
PSI	95 (76-119)	135 (112-174)	< 0.001
PSI ≥ class 4	75 (54.7)	11 (100)	0.003
CURB-65	1 (1-2)	1 (1-3)	0.342
CURB-65 ≤ 4	48 (35.0)	5 (45.5)	0.524
Severe pneumonia at presentation	34 (24.8)	8 (72.7)	0.002
Pulmonary function test			
FEV <sub>1</sub> , % predicted	60 (44-78)	53 (35-81)	0.627
FVC, % predicted	80 (65-93)	69 (68-94)	0.465
FEV <sub>1</sub> /FVC	53 (41-61)	54 (41-63)	0.887
GOLD grade III or IV	42 (30.7)	5 (45.5)	0.327
Intensive care unit admission	13 (9.5)	5 (45.5)	0.004
CT findings			
Emphysema	80 (58.4)	8 (72.7)	0.526
Bronchiectasis	33 (24.1)	1 (9.1)	0.458
Previous inhaled corticosteroid use	61 (44.5)	2 (18.2)	0.117
Use of oral corticosteroid medication prior to pneumonia	21 (15.3)	1 (9.1)	1.000
Potentially drug-resistant pathogen	11/42 (26.2)	0/2 (0)	1.000

PSI = Pneumonia severity index, CURB-65 = Confusion, urea nitrogen, respiratory rate, blood pressure, age ≥ 65 years, FEV<sub>1</sub> = Forced expiratory volume in 1 second, FVC = Forced vital capacity, GOLD = Global initiative for chronic obstructive lung disease

critically ill at the time of hospital admission for pneumonia than those without emphysema.

In contrast to what has been observed in pulmonary emphysema patients, bronchiectasis was not associated with severe pneumonia in COPD patients. We diagnosed bronchiectasis in 35 patients (23%), and 4-57.6% of COPD patients have been reported to have coexisting bronchiectasis.<sup>[27-31]</sup> It has been recognized recently that the presence of bronchiectasis is a predictor of poor prognosis in COPD population, which were thought to be attributed to colonization with or infection by a potentially pathogenic organism.<sup>[27,31]</sup> However, we found that bronchiectasis did not influence the severity of pneumonia, in agreement with the suggestion that a microbiological etiology, especially invasion by a potentially drug-resistant pathogen, may not have played a role in patients of our COPD population with particularly severe pneumonia.

The current use of ICS has been suggested to be a potential risk factor for development of pneumonia in COPD populations.<sup>[18,32]</sup> However, effect of ICS on the severity of pneumonia still remains controversial. Chen *et al.*, showed that prior use of ICS reduced the risk of short-term mortality and the need for mechanical ventilation after hospitalization for pneumonia.<sup>[19]</sup> Whereas, an epidemiological study using a health insurance database reported that serious pneumonia (defined as hospitalization for or death from pneumonia) was related to the use of ICS, particularly high-dose fluticasone.<sup>[20]</sup> In current study, we found no effect of ICS use on the development of severe pneumonia.

Our study had several potential limitations. First, our analysis was retrospective in nature. Since the original study design did not seek to identify factors associated with severe pneumonia in COPD patients, COPD-associated factors were identified retrospectively from medical records. Thus, some COPD-associated factors including previous hospitalization or exacerbations were not limited to collect for analysis. Second, we evaluated only a relatively small number of patients treated at a single institution. A prospective study with a larger population is required to validate our results.

In conclusion, we found that severe airflow limitation and pulmonary emphysema evident on a CT scan were associated independently with severe pneumonia in a COPD population. This suggests that patients with severe COPD and emphysema who present to emergency rooms with pneumonia require specific attention in clinical practice.

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