Risk factors for early readmission after acute exacerbation of chronic obstructive pulmonary disease

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Abstract

Background and aims: Patients discharged after treatment for acute exacerbation of chronic obstructive pulmonary disease (COPD) are at high risk for readmission. We aimed to identify the prevalence and risk factors for readmission.

Methods: We included 16,105 patients who had claimed their medical expenses from 1 May 2014 to 1 May 2016 after discharge from any medical facility in Korea, following treatment for acute exacerbation of COPD. We analysed the potential risk factors for readmission within 30 days of discharge.

Results: Readmission rate was 26.4% (3989 patients among 15,101 patients) and over 50% of readmissions occurred within 10 days of discharge. Approximately 57% of readmissions occurred due to respiratory causes. Major causes of readmission were COPD (27%), pneumonia (14.2%), and lung cancer (7.1%), in that order. Patients who were readmitted were male, had more comorbidities and were less frequently admitted to tertiary hospitals than those who were not readmitted. Risk factors for readmission within 30 days of discharge were male sex, medical aid coverage, longer hospital stay, longer duration of systemic steroid use during hospital stay, high comorbid condition index, and discharge to skilled nursing facility.

Conclusion: Readmission occurred in approximately one-quarter of patients, and was associated with patient-related and clinical factors. Using these results, we can identify high-risk patients for readmission and precautions are needed to be taken before deciding on a discharge plan. Further research is needed to develop accurate tools for predicting the risk of readmission before discharge, and development and evaluation of an effective care programme for COPD patients are necessary.

The reviews of this paper are available via the supplemental material section.

Keywords: chronic obstructive pulmonary disease, exacerbation, nationwide database

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Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most common leading causes of mortality worldwide.[1] Prevalence of COPD was reported to be 13.1–14.6% in Korea, which is higher than the worldwide prevalence.[2] Acute exacerbation of COPD can be defined as the acute deterioration of the status of COPD patients, and it is characterized by aggravation of respiratory symptoms such as cough, sputum, and dyspnoea. It leads to patients visiting clinics earlier than scheduled and can even result in hospitalization. Acute exacerbation of COPD (AECOPD) can occur during the natural course of COPD and is related to disease progression. Furthermore, exacerbation of COPD not only affects an individual's physical health with regard to decrease in lung function,[3] increased risk of future events of exacerbation,[4] and mortality,[5] but also their socioeconomic status due to increased medical expenses and strain on resources.[6] Severe exacerbation of COPD requires hospitalization, which is responsible for 70% of COPD-related healthcare expenditure.[7] Patients who have been admitted to the hospital for severe

exacerbation are at high risk of being readmitted, further worsening the situation.

Readmission within 30 days of discharge from previous hospitalization for AECOPD is reported to occur in 20% of patients.[8,9] Regardless of the cause of readmission, patients who are readmitted within 30 days of discharge from index hospitalization have unfavourable clinical outcomes and even have increased mortality for the next three years. Interestingly, these adverse effects were not exclusively dependent on impaired lung function.[10]

South Korea implemented a single, compulsory government-established health insurance system called the National Health Insurance (NHI) in 1998 that covers 97% of the population in South Korea, and the remaining 3% is covered by the Medical Aid Programme.[11] The Health Insurance Review and Assessment Service (HIRA), an agency responsible for evaluating all medical claim data from all hospitals in Korea, evaluates the eligibility of claimed medical expenses and approves insurance reimbursements from the NHI service. It also collects all medical records of patients provided by physicians for insurance claims.

Identifying prevalence and risk factors associated with early readmission within 30 days of previous hospitalization could be helpful in developing practical interventions for reducing readmission. There have been recent studies related to this, but few data from Asia countries. In the present study, we aimed to estimate the prevalence and clinical characteristics of patients who early readmitted after AECOPD. We also identified factors that would allow clinicians to distinguish patients who are at high risk for early readmission in actual practice.

Material and methods

Data source and subjects

We analysed all medical information as recorded in the HIRA database from 1 May 2014 to 1 May 2016, keeping in mind the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) for diagnoses. To define index hospitalization due to AECOPD we used the following criteria: (1) ICD-10 code for COPD (J44) as the primary or secondary (first or second) diagnosis; (2) and use of systemic steroids for at least 3 consecutive days during hospital stay. Early readmission was defined as readmission within 30 days of discharge from index hospitalization with the presence of ICD-10 code for COPD (J44) as the primary or secondary diagnosis. Patients who had no insurance claim history after discharge from index hospitalization for the following year were considered deceased.

Patients with insurance claims for reimbursements from oriental hospitals, dental clinics, and maternity clinics were excluded. We also excluded claim data from hospitals which were unable to admit patients (e.g. primary health clinics and public health centres). Patients with no history of hospital visits within 3 months after index hospitalization were also excluded.

The institutional review board at the Kangdong Sacred Heart Hospital approved this study and waived the requirement for consent as we used publicly accessible and anonymized data (IRB No. KANGDONG 2019-04-006).

Items for evaluation

We evaluated demographic data (e.g. age and sex), type of insurance (e.g. health insurance and medical aid), type of hospital (secondary or tertiary centre), comorbid conditions with ICD-10 codes, and medication data in the HIRA service database. Intensive management measures during hospitalization such as transfer to intensive care unit (ICU), use of mechanical ventilator (MV) or non-invasive ventilation (NIV) were also identified in the HIRA database. The details of administration of systemic steroids (duration and cumulative dosage during hospitalization and prescription at discharge) and location of discharge (e.g. skilled nursing facility) were also included in the analysis.

Statistical analysis

The baseline characteristics of the patients and their hospital courses were compared using the *t*-test and Chi square test for continuous and categorical variables, respectively.

Logistic regression analysis was used to identify risk factors for readmission. Univariate and stepwise multivariate logistic analyses with variables

selected by a significance level of entry of 0.1 were conducted to identify significant risk factors for early readmission. Data of Cox proportional hazards model analyses were presented as hazard ratios (HRs) and 95% confidence intervals.

All analyses were two-sided and conducted at a significance level of 0.05, unless otherwise stated. All analyses were conducted using the SAS software, version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Cohort selection

Among the 16,612 patients who were hospitalized for AECOPD, 16,142 were discharged but after excluding patients lost to follow-up and transferred to other hospitals, 15,101 patients were included in the analysis. The study flow is outlined in Figure 1.

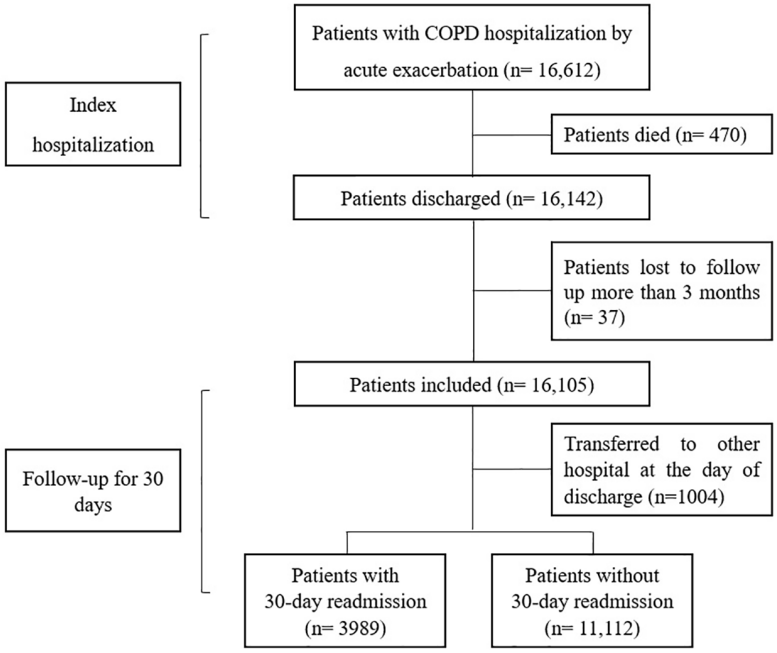

Figure 1. Flowchart of data extracted from Health Insurance Review and Assessment Service, dated 1 May 2014 to 1 May 2016.
COPD, chronic obstructive pulmonary disease

Readmission occurred in 26.4% of patients (3989 among 15,101 patients) after index hospitalization due to AECOPD. Among all causes of readmission, 38.6% and 66.4% occurred within 7 and 15 days after discharge, respectively (Figure 2).

Characteristics of subjects

Patients were divided into two groups: with readmission ($n=3989$) and without readmission ($n=11{,}112$). A greater proportion of patients with readmission were male and covered by medical aid than those without readmission (Table 1). Patients who were admitted to tertiary facilities were less likely to be readmitted. Almost all comorbid conditions were more common in patients with readmission, except peripheral vascular disease, and the Charlson Comorbidity Index was significantly higher in the readmission group (8.3 ± 2.5 with readmission *vs.* 7.3 ± 2.5 without readmission; $p < 0.001$). Comparing the

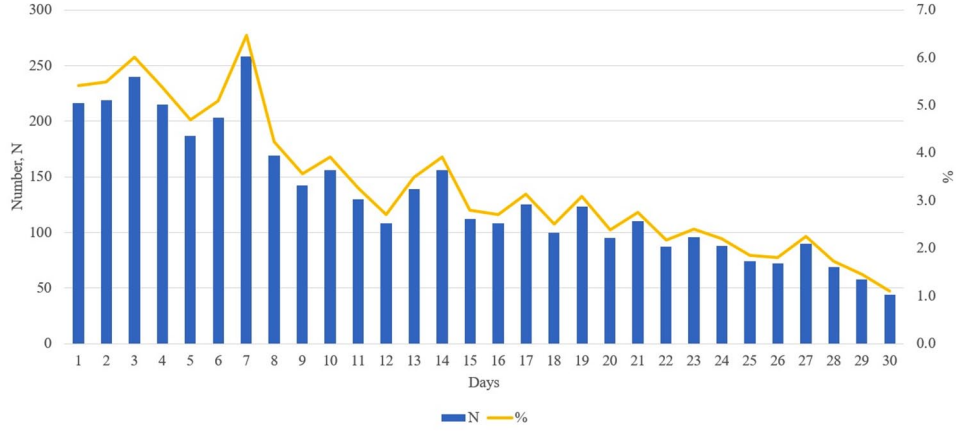

Figure 2. Frequency and percentage of readmission after discharge from index hospitalization for acute exacerbation of chronic obstructive pulmonary disease.

Table 1. Differences in patient characteristics depending on readmission status at 30 days after discharge.

Characteristics	With readmission *n* = 3989	Without readmission *n* = 11,112	*p* value
Patient-related			
Age, years	73.5 ± 9.69	73.4 ± 9.75	0.484
Sex, male (%)	3067 (76.9)	8201 (73.8)	<0.001
Insurance type			
Health insurance	2966 (74.4)	9022 (81.2)	<0.001
Medical Aid	1023 (25.6)	2090 (18.8)	
Hospital-related			
Size of hospital, tertiary facility	3195 (80.1)	9184 (82.7)	<0.001
Comorbidity			
Myocardial infarction	638 (16.0)	1305 (11.7)	<0.001
Congestive heart failure	970 (24.3)	2141 (19.3)	<0.001
Atrial fibrillation	482 (12.1)	1089 (9.8)	<0.001
Hypertension	2747 (68.9)	7122 (64.1)	<0.001
Peripheral vascular disease	583 (14.6)	1582 (14.2)	0.559
Cerebrovascular disease	558 (14.0)	1178 (10.6)	<0.001
Chronic liver disease	1854 (46.5)	4085 (36.8)	<0.001
Diabetes mellitus	2063 (51.7)	4756 (42.8)	<0.001
Chronic kidney disease	202 (5.1)	419 (3.8)	<0.001
Solid tumour other than lung cancer	251 (6.3)	477 (4.3)	<0.001
Lung cancer	628 (15.7)	630 (5.7)	<0.001
Charlson Comorbidity Index	8.2 ± 2.5	7.3 ± 2.5	<0.001
Medication			
LABA	509 (12.8)	1273 (11.5)	0.029
LAMA	2514 (63.0)	7079 (63.7)	0.442
LABA/LAMA	2 (0.05)	4 (0.04)	0.701
ICS/LABA	2625 (65.8)	7621 (68.6)	0.001
Triple: ICS/LABA/LAMA	1679 (42.1)	4856 (43.7)	0.078
Oral beta agonist	1918 (48.1)	5336 (48.0)	0.946
Roflomilast	377 (9.5)	943 (8.5)	0.064
SABA	3633 (91.1)	10004 (90.0)	0.055

Data are presented as number (%) or mean ± standard deviation.
ICS, inhaled corticosteroid; LABA, long acting beta$_2$ receptor agonist; LAMA, long acting muscarinic receptor agonist; SABA, short acting beta$_2$ receptor agonist.

Table 2. Features of treatment measures, hospital course, and discharge of the index hospitalization.

Variables	Total	With readmission	Without readmission	*p* value
ICU admission	1429 (9.5)	337 (8.5)	1092 (9.8)	0.011
ICU stay, days	18.2 ± 11.65	191 ± 12.6	17.9 ± 11.3	0.118
MV care	654 (4.3)	141 (3.5)	513 (4.6)	0.004
NIV use	126 (0.8)	25 (0.6)	101 (0.9)	0.093
Systemic steroids during index hospitalization				
Equivalent dose per day	44.2 ± 51.4	41.5 ± 47.7	45.2 ± 52.6	<0.001
Period of use, days	10.3 ± 7.1	10.3 ± 7.5	10.2 ± 6.9	0.479
Total hospital length of stay, days	16.3 ± 35.7	15.3 ± 21.1	16.7 ± 39.7	0.006
Discharge with steroid	11974 (79.3)	3085 (77.3)	8889 (80.0)	<0.001
Prescription period, days	8.2 ± 6.6	8.4 ± 7.0	8.2 ± 6.5	0.149
Discharged to skilled nursing facility	200 (1.3)	200 (5.0)	0	N/A

Data are presented as number (%) or mean ± standard deviation.
ICU, intensive care unit; MV, mechanical ventilation; N/A, not-applicable; NIV, non-invasive ventilation.

medications for COPD management, long acting beta$_2$ receptor agonist (LABA) was more frequently prescribed, whereas inhaled corticosteroid/long acting muscarinic receptor agonist was less frequently prescribed in the readmission group. The treatment measures, hospital course, and discharge characteristics at the time of index hospitalization are shown in Table 2. Patients with readmission were less likely to be admitted to the ICU (8.5% with readmission *vs.* 9.8% without readmission; $p = 0.011$) and less administered MV care (3.5% *vs.* 4.6%; $p = 0.004$). There was no significant difference in NIV use between the two groups. The dose of systemic steroids used for AECOPD was low in the readmission group (41.5 ± 47.7 with readmission *vs.* 45.2 ± 52.6, without readmission; $p < 0.001$), but there was no difference in duration of use. Total duration of hospital stay was shorter in the readmission group (15.3 ± 21.1 with readmission *vs.* 16.7 ± 39.7 without readmission; $p = 0.006$) than in the other group. Patients with readmission were less frequently prescribed systemic steroids at the time of discharge (77.3% *vs.* 80%; $p < 0.001$) than in the other group. None of the patients in the without readmission group were admitted to skilled nursing facilities during 30 days of discharge, while in the readmission group 5% were admitted.

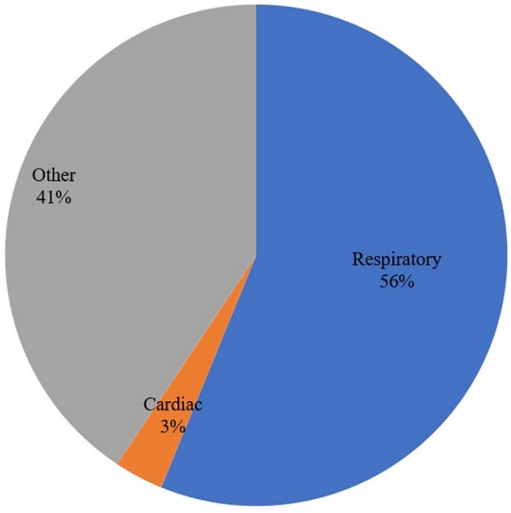

Figure 3. Causes of 30-day readmission.

Cause of readmission

Respiratory causes accounted for 57% of readmissions and cardiac causes were found in only 3% of patients (Figure 3). Among patients with early readmission, the main cause of readmission based on the ICD-10 code for their primary diagnosis was extracted and these are given in

Table 3. Cause of 30-day readmission.

Rank	Total		40–64 years		⩾65 years		Male		Female	
	Main cause of readmission	%	Main cause of readmission	%	Main cause of readmission	%	Main cause of readmission	%	Main cause of readmission	%
1	COPD	27.0	COPD	30.3	COPD	28.8	COPD	30.0	COPD	27.4
2	Pneumonia	14.2	Pneumonia	12.5	Pneumonia	14.5	Pneumonia	14.7	Pneumonia	13.0
3	Lung cancer	7.1	Lung cancer	11.8	Lung cancer	6.4	Lung cancer	8.7	Dementia	7.4
4	Dementia	3.6	Asthma	4.2	Dementia	4.1	Cerebral infarct	2.3	Asthma	5.9
5	Asthma	2.4	Mental disorder	3.4	Femur fracture	2.7	Dementia	2.2	Femur fracture	4.1
6	Femur fracture	2.4	Emphysema	2.5	Cerebral infarct	2.2	Fracture of lower limbs	1.8	Lung cancer	2.6
7	Cerebral infarct	2.0	Mycobacterial infection	1.7	Asthma	2.2	Asthma	1.6	Delirium	2.6
8	Respiratory failure	1.6	Hemiplegia	1.7	Respiratory failure	1.6	Respiratory failure	1.6	Parkinson's disease	2.2
9	Delirium	1.3	Respiratory failure	1.7	Delirium	1.5	Aspiration	1.5	CHF	1.9
10	ILD	1.3	Respiratory tuberculosis	0.8	Parkinson's disease	1.4	Emphysema	1.4	ILD	1.5

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease.

Table 3. The major cause of readmission after acute exacerbation was COPD (27%), followed by pneumonia (14.2%) and lung cancer (7.1%), irrespective of age 65. In males, the causes of readmission were identified as COPD (30.0%), pneumonia (14.7%), and lung cancer (8.7%), in that order. In females, the most frequent causes of readmission were COPD (27.4%), pneumonia (13.0%), and dementia (7.4%).

The distribution of readmissions due to respiratory and cardiac reasons within 30 days of discharge is presented in Supplemental Material Figures 1 and 2 online.

Risk factors for readmission

Using multiple logistic regression analysis, we found that factors related to increased risk of readmission within 30 days of discharge were being male (HR, 1.20), getting medical aid care (HR, 1.15), hospital stay more than 7 days (HR, 26.87), higher comorbidity index (HR, 1.20), discharge to skilled nursing facilities (HR, 1.82), and longer duration of systemic steroid use in hospital stay (HR, 1.23) (Table 4). Type of inhaler treatment did not significantly affect the risk of readmission. Factors associated with respiratory causes of readmission were similar to those for any other cause of readmission (Supplemental Table 1).

Discussion

This report details the prevalence of COPD and its clinical features using a nationwide database of COPD patients. We found that a considerable number of COPD patients who were hospitalized for acute exacerbation eventually went through repeated hospitalizations. We also demonstrated that a number of patient-related and clinical factors were associated with readmission, including sex, higher comorbidity burden, medical aid coverage, duration of systemic steroid use during index hospitalization.

Each year, COPD is responsible for as many as 800,000 hospitalizations, and approximately 20% of patients experience rehospitalization within 30 days of discharge.[8,12] It is estimated that nearly 50 billion US dollars are spent on COPD-related healthcare expenditure annually, and rehospitalization-related healthcare costs alone account for over 15 billion US dollars in the United States.[6,13]

Table 4. Risk factors associated with all causes of readmission.

Characteristics	Univariate		Multivariate	
	30-day readmission		30-day readmission	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Patient factors				
Age ⩾65 years	1.05 (0.97–1.14)	0.267		
Gender, male	1.15 (1.07–1.24)	<0.001	1.20 (1.12–1.30)	<0.001
Medical Aid patients	1.42 (1.32–1.52)	<0.001	1.15 (1.07–1.23)	<0.001
Hospital and clinical factors				
Length of stay, ⩾ 7days	28.64 (26.61–30.83)	<0.001	26.87 (24.92–28.96)	<0.001
ICU admission	0.88 (0.79–0.98)	0.023	0.98 (0.85–1.12)	0.725
MV care	0.80 (0.68–0.95)	0.009	1.02 (0.83–1.26)	0.851
NIV use	0.72 (0.49–1.07)	0.105		
Charlson Comorbidity Index ⩾8	1.76 (1.65–1.87)	<0.001	1.20 (1.12–1.28)	<0.001
Size of hospital, tertiary facility	0.85 (0.79–0.92)	<0.001	0.95 (0.88–1.03)	0.199
Discharged to skilled nursing facility	10.30 (8.92–11.89)	<0.001	1.82 (1.57–2.10)	<0.001
Medication				
LAMA and/or LABA	0.97 (0.91–1.04)	0.394		
ICS containing inhaler (ICS/LABA, ICS/LABA/LAMA, ICS/LAMA)	0.90 (0.84–0.96)	0.001	0.97 (0.91–1.04)	0.407
Roflomilast	1.10 (0.99–1.23)	0.073	1.02 (0.92–1.14)	0.690
Duration of systemic steroids during index hospitalization, ⩾5 days	1.26 (1.17–1.36)	<0.001	1.23 (1.13–1.35)	<0.001
Discharge with systemic steroid	0.86 (0.80–0.93)	<0.001	0.98 (0.90–1.06)	0.579

CI, confidence interval; HR, hazard ratio; ICS, inhaled corticosteroid; ICU, intensive care unit; LABA, long acting beta$_2$ receptor agonist; LAMA, long acting muscarinic receptor agonist; MV, mechanical ventilation; NIV, non-invasive ventilation.

Considering the social and financial impact of rehospitalization in COPD patients, there have been several clinical trials[14–16] for developing a COPD-specific risk stratification tool to predict patients who are at high risk of readmission or interventions to reduce rehospitalization. However, no such tool has been found to be effective. Boourbeau *et al.*[16] and Casas *et al.*[15] reported interventions that focused on disease-specific programmes (e.g. COPD education and teaching inhaler use) and post-discharge programmes (e.g. home visits, telephone call, and patient hotline) to reduce rehospitalization. Notably, they only focused on reducing rehospitalizations at 12 months and not on decreasing early rehospitalization as the endpoint. On the other hand, Fan *et al.*[14] reported termination of a clinical trial due to unanticipated excess mortality in an intervention group that received a COPD care programme including education. In addition to the heterogeneity of study designs, many trials have dealt with the effectiveness of post-discharge interventions that may not have consistent results.

Under these circumstances, the Hospital Readmission Reduction Programme (HRRP) included AECOPD as a targeted medical condition.[17] In response to the HRRP, Ohar JA *et al.*[18] performed a retrospective observational cohort study and reported that a comprehensive care plan for AECOPD admission reduced all-cause readmission and mortality at 30 days from discharge. This implies that an effective intervention could improve outcomes for COPD patients. However, before the implementation of an intervention, it is necessary to find and validate the causes of readmission and predictors in a large cohort and to develop an individual-focused readmission risk stratification tool. Relatively consistent predictors of readmission include a history of previous admission, comorbid conditions, prolonged length of stay, and Medicaid support[19] but there are no uniformly accepted prediction tools that can reliably assess the risk for early readmission. Moreover, there have been few data in Asia, so trials to reduce readmission are difficult to launch.

Recently, David *et al.*[20] analysed a nationwide readmission database in the United States for AECOPD in accordance with the HRRP, and found early readmission within 30 days after index AECOPD admission was associated with both patient-related factors (Medicaid payer status, low household income, and more comorbid condition) and clinical factors (longer hospital stay and discharge to a skilled nursing facility). Similarly, these factors were reconfirmed in our study using another nationwide database. In addition, our study found that sex and systemic steroid use significantly influenced rehospitalization. The effect of sex on susceptibility to readmission after AECOPD is controversial. Male sex was one of the risk factors for death and rehospitalization after a severe event of AECOPD.[4,21,22] However, some have suggested that males have a lower risk of adverse outcomes from COPD than females.[23] Although the characteristics and prognosis of COPD patients by sex have not been fully elucidated, susceptibility to toxic inhalation, airway structures, and female sex hormone have been identified as relevant factors.[24,25] Recommendations for the management of COPD include systemic steroid treatment for 5 to 7 days[26] and a daily dose of 40 mg prednisone.[27] Although the mechanisms for clinical improvement of lung function, oxygenation, and outcomes (i.e. early relapse, treatment failure, and length of hospitalization) among patients who are administered corticosteroids during exacerbation events have not been fully elucidated, reduction in airway inflammation or decrease in airway oedema may be contributing factors.[28] We reported interesting results for association between corticosteroids and early readmission in AECOPD patients by showing that corticosteroid use for more than 5 days was associated with an increased risk of rehospitalization. Our results correspond to recent meta-analysis results and recommendations that long-term corticosteroid use during hospitalization has no benefit compared with short-term use.[29]

This is the first study to report on the status and related predictors of AECOPD rehospitalization using a nationwide healthcare database in Korea. Although the prevalence of readmission was relatively high, predictors of rehospitalization in this study were similar to those according to a US study by David *et al.*[20] However, we further discovered that the use of systemic steroids was a significant factor associated with readmission.

Respiratory reasons account for 57% of readmissions and were the most common causes of readmission for COPD-related events regardless of both age and sex. Cardiac causes of readmission included heart failure, ischaemic heart disease, and arrhythmias, which cumulatively accounted for 3% of readmissions. The remaining 40% of readmissions were due to conditions other than respiratory and cardiac causes. We evaluated the natural course (up to 30 days) of patients who were discharged after acute exacerbation of COPD and found that there were some differences in the pattern of occurrence depending on the cause of readmission. In particular, respiratory causes of readmission showed a pattern similar to that of all causes of readmission, accounting for more than half of the events (51.7%) that occurred within 10 days of discharge. The occurrence of events gradually decreased after this period. On the other hand, the majority of cardiac cause-related readmissions (48.5%) also occurred within 10 days of discharge, but even after 3 weeks of discharge more than 10% of events occurred and there was no pattern of gradual decrease. Congestive heart failure (CHF) has been reported to be the most common readmission diagnosis after respiratory-based disease according to studies conducted in the United States,[8,9] and also one-fifth of COPD patients have been known to have unrecognized coexisting heart failure.[30]

Unlike previous studies,[8,9,20,31] we reported that the cardiac reasons for readmission after AECOPD in Korea accounted for as little as 3% of patients. Nationwide data have shown that Korean COPD patients have a lower body mass index, lower comorbid hypertension and dyslipidaemia, which are known as risk factors for cardiac disease, and a lower prevalence of myocardial infarct than other races or ethnic groups.[32] Similarly, low rates of cardiac cause-related readmissions may be due to racial differences. Additionally, it is not easy to distinguish symptoms and signs between heart failure and AECOPD in actual clinical practice. Thus, the clinical manifestations of heart failure commonly mimic those of AECOPD. Since there is no acceptable biomarker for COPD, unlike cardiac troponin in ischaemic heart disease[33] and B-type natriuretic peptide in CHF,[34] this overlap of symptoms and signs makes diagnosis difficult and complicates coding of the diagnosis at the time of hospitalization. Even readmission in patients with COPD is a very complex phenomenon considering various well-known comorbidities. A single disease-specific approach for prediction is probably not sufficient, especially since readmission itself in COPD patients is related to high healthcare costs and adverse outcomes.[6]

This study has a strong advantage since it can be generalized; we could analyse medical claim data for all citizens due to the unique nature of the health insurance system in Korea. However, when interpreting the results of this study, some limitations should be considered. First, our study was based on the HIRA database and was observational and retrospective. Although a nationwide database provides a large sample size and various clinical data related to hospitalization and discharge, we did not include clinically important biomarkers for prediction of readmission risk such as forced expiratory volume in 1 s (FEV_1),[35] body mass index,[36] and severity of dyspnoea.[37] Second, there is no objective index such as FEV_1 to assess disease severity at the time of index hospitalization. However, considering the serious admission indicators, including ICU admission or MV care, it is estimated that the severity of AECOPD at that time was comparable between groups. Third, our 30-day readmission rate was relatively high and length of hospital stay at index hospitalization was longer compared with previous studies, possibly due to the relatively easy access to medical care in Korea and more comorbidities associated with prolonged treatment. Last, biases in estimating health care utilization and cause of readmission may be present because we used the ICD-10 code for defining hospitalization and readmission.

In conclusion, after AECOPD, a considerable number of Korean patients experience rehospitalization, which is one of the major concerns in the healthcare system considering the prevalence and socioeconomic impact of COPD. Considering the incidence of readmission within the first few days after discharge, a full assessment of the prognosis before discharge is necessary. We found that both patient-related and clinical factors contribute to the risk of readmission. These results are meaningful as they provide a better understanding of an individual patient's risk of readmission. Further research is needed to develop accurate tools for predicting any possible subsequent adverse events. Clinicians can use these tools to understand when precautions need to be taken and to guide comprehensive care plans to reduce early readmission.

Author contribution(s)

Yong Suk Jo: Conceptualization; Project administration; Writing-original draft; Writing-review & editing.

Chin Kook Rhee: Conceptualization; Investigation; Project administration; Supervision; Writing-review & editing.

Kyungjoo Kim: Formal analysis; Investigation; Methodology; Writing-review & editing.

Kwang Ha Yoo: Conceptualization; Investigation; Project administration; Supervision; Writing-review & editing.

Yong-Bum Park: Conceptualization; Investigation; Methodology; Project administration; Supervision; Writing-review & editing.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Supplemental material

The reviews of this paper are available via the Supplemental Material section.

References

1. Mannino DM and Braman S. The epidemiology and economics of chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 2007; 4: 502–506.
2. Hwang YI, Park YB and Yoo KH. Recent trends in the prevalence of chronic obstructive pulmonary disease in Korea. *Tuberc Respir Dis (Seoul)* 2017; 80: 226–229.
3. Suissa S, Dell'Aniello S and Ernst P. Long-term natural history of chronic obstructive pulmonary disease: severe exacerbations and mortality. *Thorax* 2012; 67: 957–963.
4. McGhan R, Radcliff T, Fish R, *et al.* Predictors of rehospitalization and death after a severe exacerbation of COPD. *Chest* 2007; 132: 1748–1755.
5. Garcia-Aymerich J, Serra Pons I, Mannino DM, *et al.* Lung function impairment, COPD hospitalisations and subsequent mortality. *Thorax* 2011; 66: 585–590.
6. Press VG, Konetzka RT and White SR. Insights about the economic impact of chronic obstructive pulmonary disease readmissions post implementation of the hospital readmission reduction program. *Curr Opin Pulm Med* 2018; 24: 138–146.
7. Halpern MT, Stanford RH and Borker R. The burden of COPD in the U.S.A.: results from the Confronting COPD survey. *Respir Med* 2003; 97: S81–S89.
8. Jencks SF, Williams MV and Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. *N Engl J Med* 2009; 360: 1418–1428.
9. Shah T, Churpek MM, Coca Perraillon M, *et al.* Understanding why patients with COPD get readmitted: a large national study to delineate the Medicare population for the readmissions penalty expansion. *Chest* 2015; 147: 1219–1226.
10. Guerrero M, Crisafulli E, Liapikou A, *et al.* Readmission for acute exacerbation within 30 days of discharge is associated with a subsequent progressive increase in mortality risk in COPD Patients: a long-term observational study. *PLoS One* 2016; 11: e0150737.
11. Kim DS. Introduction: health of the health care system in Korea. *Soc Work Public Health* 2010; 25: 127–141.
12. Ford ES. Hospital discharges, readmissions, and ED visits for COPD or bronchiectasis among US adults: findings from the nationwide inpatient sample 2001-2012 and Nationwide Emergency Department Sample 2006-2011. *Chest* 2015; 147: 989–998.
13. Toy EL, Gallagher KF, Stanley EL, *et al.* The economic impact of exacerbations of chronic obstructive pulmonary disease and exacerbation definition: a review. *COPD* 2010; 7: 214–228.
14. Fan VS, Gaziano JM, Lew R, *et al.* A comprehensive care management program to prevent chronic obstructive pulmonary disease hospitalizations: a randomized, controlled trial. *Ann Intern Med* 2012; 156: 673–683.
15. Casas A, Troosters T, Garcia-Aymerich J, *et al.* Integrated care prevents hospitalisations for exacerbations in COPD patients. *Eur Respir J* 2006; 28: 123–130.
16. Bourbeau J, Julien M, Maltais F, *et al.* Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. *Arch Intern Med* 2003; 163: 585–591.
17. Centers for Medicare and Medicaid Services. Hospital readmissions reduction program. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program (accessed 20 October 2019).
18. Ohar JA, Loh CH, Lenoir KM, *et al.* A comprehensive care plan that reduces readmissions after acute exacerbations of COPD. *Respir Med* 2018; 141: 20–25.
19. Freedman N. Reducing COPD readmissions: strategies for the pulmonologist to improve outcomes. *Chest* 2019; 156: 802–807.
20. Jacobs DM, Noyes K, Zhao J, *et al.* Early hospital readmissions after an acute exacerbation of chronic obstructive pulmonary disease in the nationwide readmissions database. *Ann Am Thorac Soc* 2018; 15: 837–845.
21. Shah T, Press VG, Huisingh-Scheetz M, *et al.* COPD readmissions: addressing COPD in the era of value-based health care. *Chest* 2016; 150: 916–926.
22. Patil SP, Krishnan JA, Lechtzin N, *et al.* In-hospital mortality following acute exacerbations of chronic obstructive pulmonary disease. *Arch Intern Med* 2003; 163: 1180–1186.
23. Machado MC, Krishnan JA, Buist SA, *et al.* Sex differences in survival of oxygen-dependent patients with chronic obstructive pulmonary

disease. *Am J Respir Crit Care Med* 2006; 174: 524–529.

24. Jaques PA and Kim CS. Measurement of total lung deposition of inhaled ultrafine particles in healthy men and women. *Inhal Toxicol* 2000; 12: 715–731.
25. Choi HJ, Chung YS, Kim HJ, *et al.* Signal pathway of 17beta-estradiol-induced MUC5B expression in human airway epithelial cells. *Am J Respir Cell Mol Biol* 2009; 40: 168–178.
26. Global Initiative for Chronic Obstructive Lung Disease. *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2019 update*. http://www.goldcopd.org/ (accessed 20 October 2019).
27. Leuppi JD, Schuetz P, Bingisser R, *et al.* Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. *JAMA* 2013; 309: 2223–2231.
28. Wedzicha JA. Oral corticosteroids for exacerbations of chronic obstructive pulmonary disease. *Thorax* 2000; 55 (Suppl. 1): S23–S27.
29. Walters JA, Tan DJ, White CJ, *et al.* Different durations of corticosteroid therapy for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2018; 3: Cd006897.
30. Padeletti M, Jelic S and LeJemtel TH. Coexistent chronic obstructive pulmonary disease and heart failure in the elderly. *Int J Cardiol* 2008; 125: 209–215.
31. Gershon AS, Thiruchelvam D, Aaron S, *et al.* Socioeconomic status (SES) and 30-day hospital readmissions for chronic obstructive pulmonary (COPD) disease: a population-based cohort study. *PLoS One* 2019; 14: e0216741.
32. Lee H, Shin SH, Gu S, *et al.* Racial differences in comorbidity profile among patients with chronic obstructive pulmonary disease. *BMC Med* 2018; 16: 178.
33. Alpert JS, Thygesen K, Antman E, *et al.* Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000; 36: 959–969.
34. Januzzi JL, van Kimmenade R, Lainchbury J, *et al.* NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients: the International Collaborative of NT-proBNP Study. *Eur Heart J* 2006; 27: 330–337.
35. Miravitlles M, Guerrero T, Mayordomo C, *et al.* Factors associated with increased risk of exacerbation and hospital admission in a cohort of ambulatory COPD patients: a multiple logistic regression analysis. The EOLO Study Group. *Respiration* 2000; 67: 495–501.
36. Oostenbrink JB and Rutten-van Molken MP. Resource use and risk factors in high-cost exacerbations of COPD. *Respir Med* 2004; 98: 883–891.
37. Vestbo J and Rasmussen FV. Respiratory symptoms and FEV1 as predictors of hospitalization and medication in the following 12 years due to respiratory disease. *Eur Respir J* 1989; 2: 710–715.