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Original Article

Risk Factors Associated with Frequent Hospital Readmissions for Exacerbation of COPD

Mi Hyun Kim, M.D., Kwangha Lee, M.D., Ki Uk Kim, M.D., Hye-Kyung Park, M.D., Doo Soo Jeon, M.D., Yun Seong Kim, M.D., Min Ki Lee, M.D., Soon Kew Park, M.D.

Department of Internal Medicine, Pusan National University School of Medicine, Busan, Korea

Background: Chronic obstructive pulmonary disease (COPD) is one of the leading causes of disability and mortality worldwide. The aim of this study was to evaluate the risk factors associated with recurrent hospital admissions for exacerbation of COPD in Korea.

Methods: A retrospective study of 77 consecutive patients hospitalized for exacerbation of COPD at Pusan National University Hospital during the time period January 2005 to May 2008 was performed. The information was collected from the hospitalization period: clinical information, spirometric measures, and laboratory variables. In addition, socioeconomic characteristics, co-morbidity, anxiety, and depression were reviewed. Frequent readmission was defined as 2 or more hospitalizations in the year following discharge.

Results: During the 1-year period after discharge, 42 patients (54.6%) reported one hospital admission and 35 patients (45.4%) reported 2 or more hospital readmissions. Among the 35 frequent readmission patients, 4 had more than 10 readmissions. Univariate analysis showed that a body mass index (BMI) <18.5 kg/m^2, duration >36 months, forced expiratory volume in 1 second (FEV_1) $<50\%$ predicted, arterial CO_2 partial pressure ($PaCO_2$) >40 mm Hg, and arterial oxygen saturation (SaO_2) $<95\%$ at discharge were associated significantly with frequent readmissions. The multivariate analysis revealed that BMI <18.5 kg/m^2, $PaCO_2$ >40 mm Hg at discharge were independently associated with frequent readmissions for exacerbation of COPD.

Conclusion: Frequent readmissions for exacerbation of COPD were associated with low BMI and hypercapnia at discharge.

Key Words: Pulmonary Disease, Chronic Obstructive; Exacerbation; Patient Readmission; Body Mass Index; Hypercapnia

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of disability and mortality worldwide[1]. It is the fourth leading cause of chronic morbidity and mortality in the Unites States, and is projected to rank fifth in 2020 in disease burden worldwide, according to a study published by the World Bank/World Health Organization[2,3]. All other major causes of death are declining, whereas COPD is the only leading disease that is increasing in prevalence and mortality; it is probably the major cause of disability, worldwide[4,5].

The outcomes of medical treatment and care remain poor with particularly high rates of hospital readmissions for COPD. Over one half of the patients with COPD that are hospitalized are readmitted at least once in the six months following discharge[6-8]. Hospitalization for COPD accounts for a large part of the high healthcare expenditure needed for the care of patients with COPD, estimated to be 40% of the total direct cost of medical care for COPD in the USA[7].

Though COPD and frequent readmission is a common problem, little has been documented about this

Address for correspondence: **Min Ki Lee, M.D.**
Department of Internal Medicine, Pusan National University School of Medicine, 1-10 Ami-dong, Seo-gu, Busan 602-739, Korea
Phone: 82-51-240-7216, Fax: 82-51-254-3127
E-mail: leemk@pusan.ac.kr
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problem in Korea. The aim of this study was to ascertain the rates of hospital readmissions, the frequency of modifiable and non-modifiable risk factors and to evaluate the risk factors associated with recurrent hospital admissions of patients with COPD in a cross sectional sample survey at Pusan National University Hospital.

Materials and Methods

1. Patients

Between January 2005 and May 2008, a retrospective study of all consecutive patients admitted with exacerbation of COPD to any medical ward in the respiratory medicine departments of Pusan National University Hospital, was carried out. During a 1-year period, the hospital admission database was used to identify eligible COPD patients with a primary discharge diagnosis of COPD. The Global Initiative for Chronic Obstructive Lung Diseases (GOLD) criteria[2] were used to define 1) COPD: forced expiratory volume in 1 second (FEV_1)/ forced vital capacity (FVC) (post bronchodilatation) $<70\%$, with or without chronic cough and sputum production, 2) severity: mild (stage I) $FEV_1 \geq 80\%$ predicted, moderate (stage II) $50\% \leq FEV_1 < 80\%$ predicted, severe (stage III) $30\% \leq FEV_1 < 50\%$ predicted and very severe (stage IV) $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure and 3) exacerbation of COPD: an event during the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough and/or sputum that was beyond the normal day-to-day variation, was considered an acute onset that may warrant a change in routine medications in a patient with underlying COPD. The inclusion criteria were: 1) patients with a principal diagnosis of exacerbation of COPD; 2) age over 40 years; 3) surviving patients with stable COPD status on discharge. The exclusion criteria were patients with active pulmonary tuberculosis, pulmonary fibrosis, lung cancer, acute heart failure, acute myocardial infarction, and severe renal failure.

2. Measurements

Demographic factors, body mass index (BMI) (kg/m^2), duration of COPD, number of admissions for COPD in the past year, history of smoking, comorbidities, previous use of steroids, use of psychotropic agents, pulmonary function testing (spirometry and bronchodilator tests), and laboratory factors (e.g., arterial blood gases, serum white blood cell [WBC], C-reactive protein [CRP], blood urea nitrogen [BUN], and creatinine [Cr]) were recorded. Anxiety or depression was diagnosed in patients taking psychotropic drugs or that already had a diagnosis of a mental health problem. Variables were selected based on previous studies on readmission for COPD or other chronic diseases. Frequent readmission was defined as two or more hospitalizations during the following year after discharge.

3. Statistical analysis

The prevalence of 'frequent' and 'non-frequent' readmissions and associated risk factors were expressed as numbers. Univariate analysis of the risk factors associated with frequent readmissions was performed in this case-control study using the chi-square statistic and estimates of odds ratios (ORs) with their 95% confidence intervals (CIs). Multivariate analysis was performed to evaluate the independent risk factors associated with frequent readmissions in cases with exacerbation of COPD using logistic regression analysis for dichotomous dependent variables. Both forward stepwise selection and full saturated models were constructed and used to evaluate estimates of ORs. And a p-value <0.05 was considered as statistically significant.

All statistical analyses were performed using the SPSS version 12.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 77 patients were included. During a 1-year period, 42 patients (54.6%) reported one hospital admission and 35 patients (45.4%) reported two or more hospital admissions. Among the 35 patients with frequent

readmission, four had more than 10 readmissions.

The baseline characteristics and lung function of the patients with COPD related frequent and non-frequent readmissions are summarized in Tables 1 and 2. The mean age was 69.2±9.4 years (range, 40～85); 64 patients (83%) were males and 13 were females; 18% (14) were non smokers and the other subjects were current smokers or ex-smokers with a history of smoking the

Table 1. Baseline characteristics of COPD patients with frequent and non-frequent readmissions

Variables	All (n=77)	Frequent (n=35)	Non-frequent (n=42)	p-value
Sex				
Male	64 (83.1)	30 (85.7)	34 (81)	0.546
Female	13 (16.9)	5 (14.3)	8 (29.0)	
Age, years±SD	69.2±9.4	68.2±9.9	70.1±9.1	
≥65	55 (71.4)	24 (68.6)	31 (73.8)	0.466
<65	22 (28.6)	11 (31.4)	11 (26.2)	
Smoking (Pack-year)	44.8±25.6	42.1±26.5	47.2±24.9	
Non-smoker	14 (18.2)	7 (20.0)	7 (16.6)	0.619
Ex&current smoker	63 (81.2)	28 (80.0)	35 (83.4)	
BMI, kg/m^2				
≥18.5	25 (32.5)	6 (17.2)	22 (52.4)	<0.001
<18.5	52 (67.5)	29 (82.8)	20 (47.6)	
Anxiety or depression				
Yes	9 (11.9)	7 (20.0)	2 (4.8)	0.072
No	68 (88.3)	28 (80.0)	40 (95.2)	
Previous steroid therapy				
Yes	25 (32.5)	18 (54.3)	7 (16.7)	0.053
No	46 (59.7)	16 (45.7)	30 (71.4)	
Unknown	6 (7.8)	1 (0.0)	5 (11.9)	

Data are presented as number (%).
COPD: chronic obstructive pulmonary disease; BMI: body mass index.

Table 2. Respiratory function of COPD patients with frequent and non-frequent readmissions

Variables	All (n=77)	Frequent (n=35)	Non-frequent (n=42)	p-value
Duration of COPD, months±SD	62.38±92.07	83.97±112.44	43.56±65.60	
≥36	40 (51.9)	23 (65.7)	17 (40.5)	0.010
<36	37 (48.1)	12 (34.3)	25 (59.5)	
COPD severity				
Mild & moderate	34 (44.1)	11 (31.4)	23 (54.8)	0.051
Severe & very severe	43 (55.9)	24 (68.6)	19 (45.2)	
FEV_1% predicted				
≥50	23 (29.9)	6 (17.1)	17 (40.5)	<0.001
<50	54 (80.1)	29 (82.9)	25 (59.5)	
SaO_2 at discharge				
≥95%	29 (37.7)	13 (37.1)	16 (38.1)	0.022
<95%	48 (62.3)	22 (62.9)	26 (61.9)	
$PaCO_2$ at discharge				
≥40 mm Hg	33 (42.9)	24 (68.6)	9 (21.4)	<0.001
<40 mm Hg	44 (57.1)	11 (31.4)	33 (78.6)	

Data are presented as number (%).
COPD: chronic obstructive pulmonary disease; FEV_1: forced expiratory volume in 1 second; SaO_2: arterial oxygen saturation; $PaCO_2$: arterial CO_2 partial pressure.

Table 3. Associated factors of frequent readmission in COPD (univariate analysis)

Variables	OR	95% CI	p-value
Duration of COPD (≥36 months)	3.409	1.318~8.817	0.010
BMI (kg/m^2) <18.5	4.912	1.648~14.638	<0.001
FEV_1 <50% predicted	4.765	1.745~13.007	<0.001
SaO_2 at discharge <95%	2.933	1.152~7.471	0.022
$PaCO_2$ at discharge >40 mm Hg	7.758	2.776~21.679	<0.001

COPD: chronic obstructive pulmonary disease; OR: odds ratio; CI: confidence interval; BMI: body mass index; FEV_1: forced expiratory volume in 1 second; SaO_2: arterial O_2 saturation; $PaCO_2$: arterial CO_2 partial pressure.

equivalent of 44.6 pack-years (range, 5~120); 32% (25) of the patients were underweight (BMI <18.5 kg/m^2); 84% (65) had at least one comorbid disease, and 12% (9) had anxiety or depression; 40% (31) were treated previously with steroid therapy. Infection was the most common (70%) aggravating factor. There were no statistically significant differences in the laboratory tests (ABGA, WBC, CRP, BUN, Cr), clinical course (hospital stay, ICU admission, intubation), and aggravating factors between the two groups.

The results of the univariate analysis showed that gender, age, COPD severity at admission, smoking, comorbidities, anxiety or depression, use of psychotropic medications and previous steroid use were not significantly associated with frequent hospital readmissions. On the other hand, a long duration of symptoms (≥36 months) (OR, 3.409; 95% CI, 1.318~8.817; p=0.010), underweight patients (BMI <18.5 kg/m^2) (OR, 4.912; 95% CI, 1.648~14.638; p<0.001), FEV_1 <50% predicted (OR, 4.765; 95% CI, 1.745~13.007; p<0.001), SaO_2 <95% at discharge (OR, 2.933; 95% CI, 1.152~7.471; p=0.022) and $PaCO_2$ >40 mm Hg at discharge (OR, 7.758; 95% CI, 2.776~21.679, p<0.001) were significantly associated with frequent readmissions (Table 3).

The results of the multivariate logistic regression analysis of factors associated with frequent hospitalization are shown in Table 4. There were five predictive variables included as categorical or dichotomous variables in the forward stepwise multiple selection logistic regression analysis: duration of COPD, BMI, FEV_1%, SaO_2, and $PaCO_2$ at discharge. Only two variables were significantly associated with frequent hospital readmissions: underweight patients (BMI <18.5 kg/m^2) (OR, 5.306; 95% CI, 1.254~22.454; p=0.023) and hypercapnia at discharge (OR, 4.213; 95% CI, 1.193~14.880; p=0.025).

Table 4. Multiple logistic regression analysis of the association with frequent readmission in COPD

Significant independent predictors	OR	95% CI	p-value
BMI (kg/m^2) <18.5	5.306	1.254~22.454	0.023
$PaCO_2$ at discharge >40 mm Hg	4.213	1.193~14.880	0.025

COPD: chronic obstructive pulmonary disease; OR: odds ratio; CI: confidence interval; BMI: body mass index; $PaCO_2$: arterial CO_2 partial pressure.

Discussion

Many studies have reported on the variables associated with hospital readmission in COPD patients, but reliable epidemiological data regarding the burden of COPD on readmission are lacking in Korea. In this study, frequent readmission was compared to non-frequent readmission of COPD patients along with the associated factors. The main findings were that underweight patients and those with hypercapnia at discharge were independent predictors of frequent readmission to the hospital.

The high rate of hospital readmissions for exacerbations was consistent with previous studies. The frequency of readmission varies from 11.6% (48 hours after discharge from the emergency room)[9] to 63% (1 year after admission to a general hospital)[10-13]. In a study in hospitalized COPD patients older than 65 years carried out in the USA between 1984 and 1991, only 14% did not require rehospitalization, while 48% were admitted

on five or more occasions[14]. In a large unselected population of COPD patients, one half of the patients that were hospitalized were expected to be readmitted at least once in the six months following discharge[6-8]; the majority (86%) of readmissions occurred within the first three months after hospital discharge[6]. Few studies have evaluated risk factors for hospital readmission in COPD patients. These investigations have shown that social and psychological variables, lowest FEV_1, poor performance status or previous admission for COPD are associated with a greater risk of readmission[10,12,15]. The other studies have found that a worse quality of life measured by the St. George's Respiratory Questionnaire[11,16], a lower than usual physical activity[11] or FEV_1 stratified according to the European Respiratory Society and Global Obstructive Lung Disease[17] scales were related to a higher risk of readmission.

Among the clinical variables in this study, a BMI <18.5 kg/m^2 and a $PaCO_2$ >40 mm Hg at discharge were both independently and significantly associated with frequent hospital readmissions.

Previous studies have demonstrated that a low BMI is related to an increased risk for readmission[18,19]. In patients with COPD, malnutrition is associated with significant impairment in respiratory muscle strength and endurance, increased airflow limitation and therefore aggravation in already existing respiratory muscle dysfunction caused by hyperinflation[20]. However, other studies have not demonstrated this association[21,22]. A possible explanation for the absence of a positive association with the BMI is that the anthropomorphic measures of nutritional status in non-Caucasian adults, such as BMI <20 kg/m^2, may not be an adequate indicator of poor nutritional status in a non-Caucasian population. Since studies of the association between BMI and COPD have been conducted primarily in Western populations, it is uncertain whether the findings of these studies can be applied to Korean patients with COPD. We used a different cut-off value (<18.5 kg/m^2) and found that low BMI was associated with frequent readmissions to the hospital.

In addition to low BMI, hypercapnia at hospital discharge was associated with readmissions in this study. This finding is in agreement with the experience of Kessler et al.[18], who showed that in patients with stable disease, only $PaCO_2$ and the mean pulmonary artery pressure were independently related to the risk of hospitalization. Although the presence of hypercapnia during exacerbation has been considered an indicator of a poor prognosis[8], some patients develop hypercapnia only during acute exacerbation and revert to normocapnia during recovery; the prognosis in these patients with reversible hypercapnia has been reported to be similar to normocapnic patients[21,22].

A number of putative predisposing factors were not confirmed in this study to be independently associated with frequent readmission. Neither age nor gender was associated with frequent hospital admissions in this study, consistent with other studies[16,18,23]. More severe disease (lower FEV_1 and longer duration) was significantly associated with more frequent readmissions for exacerbation of COPD in the univariate analysis, but this was not confirmed in the multivariate model.

There was a high prevalence of comorbid diseases in patients, but the presence of any number of comorbidities was not significantly associated with frequent readmissions. The presence of comorbidity has been previously identified as a risk factor for increased hospital admissions in ambulatory patients with mild to moderate COPD in the EOLO Study[24]. The data from the current study are similar to two other studies that evaluated patients with moderate to severe COPD and indicated that comorbidities with COPD had no significant association with increased hospitalization for acute exacerbation of COPD[18,23].

Frequent readmissions were not associated with current smoking. The role of smoking has been studied in previous studies[18,23]. The first found no significant impact of smoking on the risk of hospitalization[18]; the second found paradoxically that current smoking, compared with ex-smoking, was associated with a reduced risk of COPD related hospital admission[23].

Our study has some limitations. First, it was performed in only one center; however, FEV_1 values and

median age of our patients were similar those of previous studies performed in hospitalized patients[10,11,13,16], suggesting that our population is representative of the patients hospitalized for COPD exacerbation. Second, this study was retrospective, and there were several things that are thought to be important in patients with COPD that there was no information on in the current study: For instance, we had no information on physical capability and dyspnea that can be part of such grading systems. This may lead to residual confounding.

In conclusion, the results of this study allowed us to identify additional variables associated with readmission to the hospital in patients with exacerbation of COPD in Korea: low BMI and hypercapnia at discharge. These findings should help to delineate a subset of COPD patients that could benefit best from an active interventional program[25-28] with the aim of lowering hospital readmission rates and costs. A prospective interventional study incorporating these findings is warranted.

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