

The Factors Influencing Relapse in Patients Presenting to the Emergency Department with COPD Exacerbation

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SUMMARY

Objectives

Chronic Obstructive Pulmonary Disease (COPD) is associated with high mortality and morbidity and is projected to be the third most common cause of death worldwide by 2020. For a variety of reasons, there is a drive to manage a greater number of individuals as outpatients. Preventing readmissions can reduce associated morbidity and subsequent healthcare costs.

Methods

The aim of the present study was to determine the factors affecting the relapse of COPD exacerbated patients in the emergency department (ED). This study combines data from two prospective cohort studies. Patients included in the study were above 18 years of age, had a previous diagnosis of COPD, and presented to the ED for the treatment of acute exacerbation. All the information relevant to the study was collected during the patient's visit to the ED. Relapse was defined as an unscheduled visit to an ED or primary physician within 2 weeks of initial ED visit for worsening COPD symptoms. Telephone follow-up was done on all patients at the end of 2 weeks.

Results

The cohort consists of 196 patients. Relapse rate in this study was 27%. Mean respiratory rate, exacerbations in previous year, home nebulator therapy, home oxygen therapy, admission to intensive care or hospital ward due to COPD exacerbation, previous intubation and abnormal chest x-ray were associated with increased re-visit in univariate analysis. However, after multivariate analysis, exacerbations in previous year (OR: 1.08, 95%CI: 1.01–1.15) and abnormal chest X-ray (OR: 2.5, 95%CI: 1.10–6.11) were still significant.

Conclusions

In conclusion, the number of ED visits previous year and abnormal chest x-ray can predict the revisit of a COPD exacerbated patient within 14 days of an ED visit.

Key words: Emergency medicine; COPD; relapse.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic disorder characterized by irreversible airway obstruction and is an important problem of public health. COPD mainly

occurs due to cigarette smoking, environmental and occupational exposure. This is a costly disease due to frequent exacerbations in addition to being a major cause of mortality and morbidity.^[1] Exacerbation of COPD is one of the most

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common reasons for presenting to emergency departments (ED). Some of those patients repeatedly present to EDs with continuing complaints. Medical doctors have restricted parameters concerning which patient will present to hospital with unending complaints and increasing dyspnea. Although it has been reported in various studies that the patients would be presenting to hospital again in case of frequent hospital visit within previous year and increasing dyspnea, there are not any objective parameters.^[2]

The present study is designed to research the factors influencing relapse in patients diagnosed with COPD and presenting to the emergency department with exacerbation.

Materials and Methods

This prospective cross sectional and clinical study was conducted through the data collected during two separate time periods in Akdeniz University, Faculty of Medicine Hospital, Emergency Department between November 2007-May 2008 and December 2011-July 2012. The study included the patients over 18, presenting to ED with COPD acute attack and who were later discharged. Exacerbation of COPD as an acute event was considered as defined in GOLD 2013 guidelines 'a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.'^[3] The patients with the suspicion of active pulmonary tuberculosis, with cystic fibrosis diagnosis, with a diagnosed bronchiectasis history, and with lung cancer were excluded from the study.

The form used in the study included the following information: age, gender, date of presenting, cigarette use (past smoker, still smoker, non-smoker), vital findings upon arrival and departure from ED (blood pressure, oxygen saturation, respiratory rate, pulse wave velocity, temperature), whether arterial blood gas (ABG) values are abnormal or not ($\text{pH} < 7.35$ or $\text{PaO}_2 > 60$ mmHg or $\text{PCO}_2 > 45$ mmHg accepted as abnormal), co-morbid conditions (Hypertension, Diabetes Mellitus, Coronary Heart Disease, Congestive Heart Failure, Chronic Renal Failure, Chronic Liver Disease), oxygen and nebulizer therapy receiving at home or not, history of hospitalization or intensive care requirements, having been intubated or not, systemic steroid use, number of presenting to ED during the last one year, body mass index, chest radiography abnormality (previous or recent changes in chest radiography accepted as abnormal), treatment in ED (β_2 mimetic, ipratropium bromide, steroid and dose), presence of Anthonisen criteria, possible factor inducing exacerbation (infection, wrong drug use), discharge with an unknown reason or pre-hospitalization treatment (antibiotic treatment, steroid treatment), discharge/hospitalization status, telephone numbers.

Anthonisen criteria are a classification used for the severity of COPD exacerbation. Those criteria are divided into two as major and minor. Increased dyspnea, increased sputum volume, and increased sputum purulence are considered as major criteria. Minor criteria are the presence of an upper respiratory tract infection in the past 5 days, fever without any other apparent cause, increased cough or wheezing. Type I have all three major criteria, and Type II exhibit two major criteria, Type III exacerbations (mild) have one major criterion plus one of the minor criteria.

The patients discharged from ED were called back after 15 days and were inquired whether they had visited any health institution with the same complaints and their responses were recorded.

First group data of the study were published in 'European Journal of Emergency Medicine' in 2010 and approval for use of some of the data was received from the concerning journal.^[2] Also, approval from Faculty of Medicine Research Ethics Committee was obtained for the second group data.

Statistical Analysis

Statistical analyses were performed with SPSS Statistics version 16.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were presented as mean \pm standard deviation; for non-normally distributed variables, median values and interquartile range were given; variable frequencies were stated as percentage. Normality distribution of variables was examined via both visual (histogram and probabilistic graphs) and analytic methods (Kolmogorov-Smirnov). In order for group comparison, Student t-test for normally distributed variables, Mann-Whitney U test for non-normally distributed variables, and χ^2 (Chi-square) tests for categorical variables were performed. In multivariate analysis, logistic regression analysis was performed by employing probable factors determined in previous analyses. The conditions of type I error level under 5% were accepted as statistically significant.

Results

The present study evaluated 196 patients. Development of relapse were observed in 54 (27%) of the patients. The study group consisted of 92 (47%) males, 104 (53%) females with a mean age of 67 ± 10 . Demographic details of the patients were displayed in Table 1.

Arterial blood gas values were normal in 107 (55%) and abnormal in 65 (34%) of the patients while in 24 (11%) of the patients arterial blood gas measurement was not demanded. As a result of co-morbid disease evaluation; it was established that of the patients 84 (43%) were with hypertension, 35 (18%) with diabetes mellitus, 41 (21%) with coronary

Table 1. Demographic attributes

Variables	Population	Relapse (+)	Relapse (-)	p
Number of patients	196	142	54	
Mean age (year±SD)	67±10	66±10	69±11	0.13
Sex				
Male	92	68	24	0.66
Female	104	74	30	
Respiratory rate/min	29±7	28±6	31±8	0.03
Body mass index (kg/m ²)		25±6.4	24±6.2	0.40
Exacerbation number in last year	2	2	4	0.00
Oxygen therapy at home	55/196	32/142	23/54	0.005
Nebulation therapy at home	94/196	59/142	34/54	0.007
Intensive care unit admission	47/196	26/142	21/54	0.003
Ward admission	136/196	92/142	44/54	0.024
Previous intubation	17/196	7/142	10/54	0.003
Chest X-ray	115/179	75/127	40/52	0.002
Antibiotic use	147/196	105/142	42/54	0.58

SD: Standard deviation.

Table 2. The variables included in logistic regression model in predicting relapse

Variables	OR ^a	(%95 CI)	p
Respiratory rate/min	1.05	0.99-1.11	0.06
Exacerbation number in last year	1.08	1.01-1.15	0.02
Oxygen therapy at home	0.64	0.22-1.84	0.41
Nebulation therapy at home	1.62	0.58-4.46	0.34
Intensive care unite admission	1.21	0.43-3.36	0.71
Ward admission	1.87	0.65-5.37	0.24
Previous intubation	1.24	0.27-5.70	0.77
Chest x-ray	2.59	1.10-6.11	0.02

OR: Odds ratio.

heart disease, 31 (16%) with congestive heart failure, 4(%) with chronic renal failure, 2 (2%) with chronic liver disease.

During discharge of the patients, 83 (42%) were prescribed modification in treatment, 45 (25%) were prescribed antibiotics, and 71 (36%) were prescribed systemic steroid. According to Anthonisen criteria which are used for the severity of symptoms,^[4] 45 patients type 1 (severe), 42 patients type 2 (moderate) and 109 patients were evaluated as type 3 (mild) exacerbation.

All in all, average respiratory rate, frequency of exacerbation in previous year, having oxygen and nebulizer therapy at home, having a previous history of hospitalization or inten-

sive care requirements, having been intubated due to COPD exacerbation, and chest radiography abnormality were found out to have relationship with relapse in univariate analysis. On the other hand, in multivariate analysis, frequency of exacerbation in previous year (OR:1.08, 95%CI: 1.01–1.15) and chest radiography abnormality (OR:2.5, 95%CI: 1.10–6.11) were significant (Table 2).

Discussion

As a result of the current study, increased application to ED due to COPD exacerbation within prior year and abnormality of chest radiography results found to be significant in

terms of relapse prediction.

Relapse rate was established as 27% in the study. In the previous studies, relapse rates ranging from 22% to 32% were reported.^[5] Despite notable progress in health services, similar relapse rates have been observed since the last decade of 1980s.^[6]

Some studies showed that application to ED due to COPD exacerbation within prior year could be considered as a good parameter for relapse prediction.^[7,8] For instance, a study by Bhowmik et.al, reported that patients with 3 or more frequent exacerbations had higher levels of interleukin 6 (IL-6) and IL-8 in sputum and those patients also had more increased airway inflammation.^[9] Besides, another study by Gompertz et.al, displayed that in sputum of patients experiencing frequent inflammation, an anti-protease concentration called secretory leukoprotease inhibitor was at low level, which may explain the weakness of antibacterial and viral activities in patients being exposed to frequent inflammation.^[10] Also, in another study by Patel et.al, it was established that in the airways of patients presenting with frequent inflammation, bacterial colonization and IL-6 levels had been higher.^[11] These results might explain why relapse is more frequent in those patient group having increased inflammation and decreased inflammatory response. Global Initiative for Chronic Obstructive Lung Disease 2013 (GOLD 2013) Guidelines declared frequent exacerbation as a hospitalization criterion.^[3] In order to prevent relapse, the patients with frequent exacerbation should be assessed for hospitalization. In a study carried out with the patients hospitalized owing to COPD exacerbation and with pre-existent severe COPD, hospital mortality was found out to be very high.^[12] Even though it is difficult to reach the records about disease stages in ED conditions, the classification by GOLD 2013 might be indicative for medical doctors.

In a prospective study by Kim and colleagues, it was stated that respiratory rate predicted relapse during admission to ED.^[8] The study reported that average respiratory rate of patients per minute in relapse group (n=30) had been 25 while it had been 23 in non-relapse group (n=110). Though the results are statistically significant, clinical significance and indicative strength for medical doctors is debatable. Even though in our study average respiratory rate was significant in univariate analysis, no difference could be established between two groups in multivariate analysis. Dewan and colleagues found out in their retrospective study (n=107) that oxygen therapy at home and the frequency of exacerbation in prior year were the parameters which could predict relapse.^[13] Although utilizing oxygen therapy at home was significant in univariate analysis in our study, it was not significant in multivariate analysis. It might be thought that

the patients receiving oxygen therapy at home have advanced stage COPD and even that difference could not have been established due to the fact that those patients were hospitalized through ED more than others. As mentioned before, in the study by Dewan and colleagues, it was found out that first group or second group antibiotic intake had not influenced relapse. GOLD 2013 guidelines suggest that antibiotic should be prescribed in the case of increase in dyspnea, sputum volume, and sputum purulence and that the choice of the antibiotic should be based on the local bacterial resistance pattern.

In our study the antibiotic class was not recorded but usually second generation antibiotics were preferred; however, the findings displayed that they were ineffective on relapse.

In a prospective study evaluating the patients presenting to family physician due to COPD exacerbation and the examining the factors influencing relapse within 30 days, ischemic heart disease, the degree of dyspnea and, history of hospital admission due to exacerbation were found significant.^[14] However, the results in that study might have been affected by the foreseen period of 30 days. In our previous study related to COPD and relapse, the assessment performed by using two different visual analog scales for the degree of dyspnea including the time of ED admission and of pre-discharge showed that the degree of dyspnea was not significant in predicting relapse.^[2] Besides, in patients presenting to family physician and to ED due to COPD exacerbation, the severity of exacerbation might not be equal.

Because of the similar pace of COPD exacerbation rates during the last 30 years and high hospital bed occupancy rate during winter months when exacerbation density is high, establishment of observation units may be an effective alternative for the care period of those patients. In relation to that, in a study by Salazar and colleagues, inpatient treatment (n=1961) and follow-up at observation unit (n=545) were compared retrospectively and it revealed that the duration of hospital stay for inpatient treatment was 12 days while it was 3.4 days for follow-up at observation unit (p<0.001). In the same study, hospital admission rates for the second time within 10 days were 7% for inpatient treatment and 9.9% for follow-up at observation unit (p=0.02). Although in this study second time hospital admission was based on 10 days, very low level of relapse rate in both conditions and 3.4 days average stay duration in observation unit might be beneficial for the care process of those patients.^[15]

As a surprising result of this study, some of the objective parameters (respiratory rate at the time of presenting to ED, blood pressure, pulse rate, blood gas, chest radiography, body mass index) were not found useful in predicting relapse within two weeks. This might be explained by much more

hospitalization of patients with abnormal vital findings.

In conclusion, it might be said that the patients presenting to ED with COPD exacerbation, with frequent COPD exacerbation in previous year, and with abnormal chest radiography are more likely to have relapse. Hence, it will be advantageous for the ED physicians to keep this condition in mind during the caring of those patients.

Conflict of Interest

The authors declare that there is no potential conflicts of interest.

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