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# Education is Essential: Risk Factors for Frequent Hospitalization in Patients with COPD

**Hakan Arik, Sinem Ermin*, Özgür Batum, Ufuk Yilmaz**

Department of Chest Diseases, Dr. Suat Seren Chest Disease and Thoracic Surgery Training and Research Hospital, University of Health Sciences, Izmir, Turkey.

*sinemozsari@yahoo.com*

***Corresponding Author:** Sinem Ermin, Department of Chest Diseases, Dr. Suat Seren Chest Disease and Thoracic Surgery Training and Research Hospital, University of Health Sciences, Izmir, Turkey.*

## Abstract

***Introduction:*** *Chronic Obstructive Pulmonary Disease (COPD) is a common disease characterized by acute exacerbations requiring hospitalization.*

***Objectives And Methods:*** *The aim of this study was to determine the characteristics of patients hospitalized with acute exacerbation of COPD and the risk factors associated with frequent hospitalization.*

*This study was conducted with 113 patients hospitalized with acute exacerbation of COPD between 2015 - 2017.*

***Results:*** *There were 59(52.2%) patients in the frequent hospitalization group, and 54(47.8%) patients in the non-frequent hospitalization group. There were 34(64%) patients under 65 years of age, and 25(42%) patients over 65 years of age in the frequent hospitalization group. There were 19(36%) patients under 65 years of age, and 35(58%) patients over 65 years of age in the non-frequent hospitalization group(p=0.017). There were 46(46.9%) literate patients, and 13(86.7%) illiterate patients in the frequent hospitalization group. There were 52(53.1%) literate patients, and 2(13.3%) illiterate patients in the non-frequent hospitalization group(p=0.010). There was a significant difference between the two groups in terms of Long-Term Oxygen Therapy (LTOT), BIPAPtherapy and nebulizer treatment before hospitalization (p=0.001,p=0.001,p=0.000). mMRC score, duration of COPD, forced expiratory volume in one secondand forced expiratory flow between 25% and 75% of vital capacity were significant(p=0.000,p=0.14, p=0.041, p=0.034).*

*Multivariate analysis indicated that the risk of frequent hospitalization increased in illiterate patients and in patients receiving nebulizer treatment.*

***Conclusion:*** P*atients with COPD who are illiterate or receive nebulizer treatment are at serious risk of hospitalization. This group of patients should be followed with special care to reduce hospitalizations.*

**Keywords:** *COPD, frequent hospitalization, risk, mortality*

## Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the major causes of morbidity and mortality across the world. It is characterized by persistent airflow restrictions and respiratory symptoms due to airway and/or alveolar abnormalities caused by serious exposure to harmful particles or gases. It is preventable and treatablebut is a common disease (1). Patients complain of cough, sputum, shortness of breath, wheezing, and chest distress. COPD is characterized by acute exacerbations that accelerate lung function loss and affect morbidity and mortality in a negative way. As the disease progresses, the frequency and severity of exacerbations may increase, and thus,the quality of life may deteriorate (2).

Acute exacerbations are the most important reason for hospitalization. This increases both the morbidity and mortality and the health costs in patients. Determining

the risk factors for frequent hospitalization is important for preventing hospitalization. However, the risk factors differ between countries (3,4,5,6,7). The socioeconomic, ethnic and climatic characteristics of patient group or their countries may cause the emergence of different risk factors.

The aim of this study was to determine the characteristics of patients hospitalized with acute exacerbation of COPD and the risk factors associated with frequent hospitalization.

## Materials and Methods

113 patients who were admitted to the Chest Disease Clinic of Dr. SuatSeren, Chest Diseases and Surgery Training and Research Hospital due to acute exacerbation of COPD between March 2015 and March 2017 were included in this prospective study.

COPD is defined as a disease that is characterized by persistent respiratory complaints and airway obstruction caused by exposure to harmful gases and particles such as cigarette, smoke generated by a tandoor oven, and biomass.

An acute exacerbation of COPD is defined as an increase that requires admission to the hospital, medication change or hospitalization rather than usual daily changes in respiratory complaints (shortness of breath, cough, and amount and purulence of sputum) in a case diagnosed by COPD.

While patients with COPD with two or more exacerbations in the past one year constituted the frequent hospitalization group, patients hospitalized for the first time constituted the non-frequent hospitalization group.

The socio-demographic data (age, gender, occupation, Body Mass Index (BMI), livingconditions, education status, income status, smoking history), past medical history data (comorbid diseases, duration of COPD, medications used, long-term oxygen therapy (LTOT), BiPAP therapy, nebulizer use, number of hospitalizations due to acute exacerbation of COPD during past one year, respiratory function and blood test results), admission complaints and mMRC scores were recorded by benefiting from the patients and the Electronic Patient Record System. The GOLD Strategy (2015) groups appropriate for the stabilization period were identified.

The best PFT results in past 6 months were evaluated. The mMRC score was determined before exacerbation, which required admission to the hospital. Blood tests (hemogram, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), blood urea nitrogen (BUN), creatinine, AST, ALT, pro-brain natriuretic peptide (proBNP)) were studied on the day of hospital admission.

Statistical analyzes were performed using the PASW Statistics 18.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The distributions of categorical variables were evaluated by the Chi-square Test. Nonparametric methods were used to compare groups. Differences between groups were investigated by the Mann-Whitney U test. The cut-off values for continuous variables, which were found to be significant for frequent hospitalization, were calculated using the Receiver Operating Characteristic (ROC) Curve Method.Binary Logistic Regression Analysis was used for multivariate analysis. In all statistical tests, the Type I error was set to 0.05. A p-value of $<0.05$ was considered statistically significant.

## Results

113 patients hospitalized with acute exacerbation of COPD were included in the study. There were 59 (52.2%) patients in the frequent hospitalization group, and 54 (47.8%) patients in the non-frequent hospitalization group. The median value of the number of hospitalizations in past one year was 3 (2-9) in the frequent hospitalization group. 53 (46.9%) patients were ≤ 65 years of age, and 60 (53.1%) patients were > 65 years. There were 34 (64%) patients under 65 years of age, and 25 (42%) patients over 65 years of age in the frequent hospitalization group. There were 19 (36%) patients under 65 years of age, and 35 (58%) patients over 65 years of age in the non-frequent hospitalization group *(p=0.017)*.In the present study, 102 (90.3%) of the patientswere male and 11 (9.7%) were female. There were 53 (52%) male patients in the frequent hospitalization group, and 49 (48%) male patients in the non-frequent hospitalization group. There were 6 (55%) female patients in the frequent hospitalization group, and 5 (45%) female patients in the non-frequent hospitalization group. 20 (17.7%) of the patients were living alone at home whereas 93 (82.3%) were living with two or more close relatives. There were 7 (35%) patients living alone in the frequent hospitalization group, and

13 (65%) patients living alone in the non-frequent hospitalization group.There were 52(55.9%) patients living with two or more close relatives in the frequent hospitalization group, and 41 (44.1%) patients living with two or more close relatives in the non-frequent hospitalization group. There were 46 (46.9%) literate patients, and 13 (86.7%) illiterate patients in the frequent hospitalization group. There were 52 (53.1%) literate patients, and 2 (13.3%) illiterate patients in the non-frequent hospitalization group *(p=0.010).* All socio-demographic characteristics of our patients are shown in table-1.

**Table 1.** *Socio-demographic characteristics of patient groups*

| | | COPD hospitalization group | | | | |
|---|---|---|---|---|---|---|
| | | frequent hospitalization | | non-frequent hospitalization | | |
| | | ***n*** | ***%*** | ***n*** | ***%*** | ***P*** |
| ***Age*** | *≤65* | 34 | 64% | 19 | 36% | ***0,017**** |
| | *>65* | 25 | 42% | 35 | 58% | |
| ***Sex*** | *Man* | 53 | 52% | 49 | 48% | 0,870 |
| | *Women* | 6 | 55% | 5 | 45% | |
| | *< 18,50* | 9 | 56% | 7 | 44% | |
| ***BMI*** | *18,50 - 24,99* | 28 | 51% | 27 | 49% | 0,931 |
| | *25,00+* | 22 | 52% | 20 | 48% | |
| ***relatives in the same home*** | *1* | *7* | *35%* | *13* | *65%* | 0,112 |
| | *≥2* | *52* | *55,9%* | *41* | *44,1%* | |
| ***Incomestatus*** | *<570 $* | 26 | 63% | 15 | 37% | 0,109 |
| | *≥570 $* | 33 | 46% | 39 | 54% | |
| ***Educationstatus*** | *illiterate* | 13 | 86,7% | 2 | 13,3% | ***0,010**** |
| | *literate* | 46 | 46,9% | 52 | 53,1% | |

*BMI: Body massindex, *: statisticallysignificant*

There were 6 (32%) patients with the GOLD Group C in the frequent hospitalization group, and 13 (68%) patients with the GOLD Group C in the non-frequent hospitalization group. There were 53 (57%) patients with the GOLD Group D in the frequent hospitalization group and 40 (43%) patients with the GOLD Group D in the non-frequent hospitalization group *(p=0.043).* Accordingly, there were more patients with the GOLD Group C in the non-frequent hospitalization group,and more patients with the GOLD group D in the frequent hospitalization group*(p=0.043).*There was no significant difference between the two groups in terms of cigarette smoking status, blood test results, and admission complaints (p>0.05).

The patients were using different inhaler treatments. There were 39 patients (57%) using ICS (Inhale corticosteroid) + LABA (Long-acting beta agonist) + LAMA (Long-acting muscarinic agonist) combination treatment in the frequent hospitalization group; but 30 patients (44%) in the non-frequent group were using ICS + LABA + LAMA. There was only one patient in both two groups using LABA + LAMA treatment. Pharmacological treatments were summarized in table-2. There was no significant difference between the two groups in terms of types of pharmacological treatment (*p*>0.05).

**Table 2.** *Pharmacological treatment of patient groups*

| | | COPD hospitalization group | | | | |
|---|---|---|---|---|---|---|
| | | frequent hospitalization | | non-frequent hospitalization | | |
| | | ***n*** | ***%*** | ***n*** | ***%*** | **P** |
| ***ICS-LABA + LAMA*** | *Var* | 39 | 56,5% | 30 | 43,5% | 0,339 |
| | *Yok* | 20 | 45,5% | 24 | 54,5% | |
| ***ICS-LABA + Methylxanthines*** | *Var* | 6 | 66,7% | 3 | 33,3% | 0,494 |
| | *Yok* | 53 | 51,0% | 51 | 49,0% | |
| ***ICS-LABA*** | *Var* | 9 | 40,9% | 13 | 59,1% | 0,345 |
| | *Yok* | 50 | 54,9% | 41 | 45,1% | |
| ***ICS-LABA + LAMA + Methylxanthines*** | *Var* | 6 | 66,7% | 3 | 33,3% | 0,494 |
| | *Yok* | 53 | 51,0% | 51 | 49,0% | |
| ***LABA + LAMA*** | *Var* | 1 | 50,0% | 1 | 50,0% | N/A |
| | *Yok* | 58 | 52,3% | 53 | 47,7% | |

*ICS: Inhale corticosteroid, LABA: Long-acting beta agonist, LAMA: Long-acting muscarinic agonist*

34 (71%) patients from the frequent hospitalization group, and 14 (29%) patients from the non-frequent hospitalization group received LTOT *(p=0.001)*. 22 (81%) patients from the frequent hospitalization group, and 5 (19%) patients from the non-frequent hospitalization group received BiPAP therapy *(p=0.001).*41 (71%) patients from the frequent hospitalization group, and 17 (29%) patients from the non-frequent hospitalization group used a nebulizer *(p=0.000)* (Table-3).

**Table 3.** *Device use of patientgroups*

| | | COPD hospitalization group | | | | |
|---|---|---|---|---|---|---|
| | | frequent hospitalization | | non-frequent hospitalization | | |
| | | ***n*** | ***%*** | ***n*** | ***%*** | **P** |
| ***LTOT**** | *Var* | 34 | 71% | 14 | 29% | ***0,001**** |
| | *Yok* | 25 | 38% | 40 | 62% | |
| ***BIPAP ***** | *Var* | 22 | 81% | 5 | 19% | ***0,001**** |
| | *Yok* | 37 | 43% | 49 | 57% | |
| ***Nebulizeruse*** | *Var* | 41 | 71% | 17 | 29% | ***0,000**** |
| | *Yok* | 18 | 33% | 37 | 67% | |

*LTOT: Longtermoxygentherapy, BIPAP: Bilevel Positive Airway Pressure, *: statisticallysignificant*

There was a significant difference between the two groups in terms of the duration of COPD *(p=0.014)* andmMRCscore *(p=0.000).*The median mMRC score was 3 for the frequent hospitalization group, and 2.5 for the non-frequent hospitalization group. Moreover, there was a significant difference between the two groups in terms of $FEV_1$ (lt) and FEF25-75 (lt) *(p=0.041* and *p=0.034, respectively).*All variables and their median values are shown in table-4.

**Table 4.** *Median values of the clinical continuity variables of the groups*

| | COPD hospitalizationgroup | | | | |
|---|---|---|---|---|---|
| | frequent hospitalization | | non-frequent hospitalization | | |
| | Median (min-max) | | Median (min-max) | | *P* |
| ***Age*** | 64 | (47-86) | 67,5 (46 | -85) | 0,087 |
| ***Presence of COPD*** | 10 (1-25) | | 5 (1-30) | | **0,014*** |
| ***Smokinghistory (package-year)*** | 50 (20-120) | | 50 (10-165) | | 0,887 |
| ***mMRC*** | 3 (0-4) | | 2,5 (0-4) | | **0,000*** |
| ***$FEV_1$ (lt)*** | 0,8 (0,4-2,47) | | 0,9 (0,3-2,59) | | **0,041*** |
| ***FEF25-75 (lt)*** | 0,41 (0,15-1,36) | | 0,45 (0,09-1,66) | | **0,034*** |

*MMRC: Modified Medical Research Council, $FEV_1$: Forced expiratory volume in one second, FEF 25-75: The forced expiratory flow between 25% and 75% of vital capacity, *: statistically significant*

In the Univariate Analysis made for the COPD patient group, it was determined that being <65 years of age, being illiterate, being GOLD Group D, USOT, BIPAP or nebulizer use, presence of long-term COPD, high mMRC score, low $FEV_1$, and low FEF25-75 were determined to be risk factors for hospitalization.

10 variables (age, education status, LTOT, BIPAP therapy, nebulizer use, GOLD group, duration of COPD, mMRC score, $FEV_1$, FEF25-75), which were found to be significant according to Univariate Analysis results, were included in the Multivariate Analysis. It was found that illiteracy *(OR=8.227; 95% CI: 1.595-42.438)* and nebulizer use *(OR=5.131; 95% CI: 2.183-12.064)* were associated with frequent hospitalization (Table-5).

**Table 5.** *Multivariate logistic regression analysis*

| Variables | OddsRatio | % 95 CI | |
|---|---|---|---|
| | | Minvalue | Maxvalue |
| ***Illiteracy*** | 8,227 | 1,595 | 42,438 |
| ***Nebulizeruse*** | 5,131 | 2,183 | 12,064 |

*CI; Confidenceinterval*

## Discussion

According to the Univariate Analysis, being under 65 years of age, illiteracy, GOLD Group D, use of LTOT, BiPAP, or nebulizer, prolonged presence of COPD, high mMRC score, low $FEV_1$ and low FEF25-75 were determined as risk factors for frequent hospitalization in our patients with COPD. According to the Multivariate Analysis, the risk of frequent hospitalization due to acute exacerbation of COPD was 8.2 times higher in illiterate patients and was 5.1 times higher in patients receiving nebulizer treatment.

In a study of Katayoon et al., high PaCO2, low $FEV_1$, oral and/or inhaled corticosteroid use, high dose steroid therapy, low BMI, needing someone else for personal care, active cigarette smoking, LTOT, hospitalization ≥5 days, presence of COPD ≥5 years, comorbid diseases, high mMRCscore andadvanced age were identified as risk factors for hospitalization or recurrent hospitalization in patients with COPD (8). In our study, low $FEV_1$, LTOT, presence of COPD >10 years and highmMRCscores were found to be associated with frequent hospitalization. However, comorbid diseases, BMI and active cigarette smoking were not found to be associated with frequent hospitalization. In this study, hospitalization rates were higher in patients under 65 years of age.This result may be due to the number of patients.

In a study of Emily et al. on 354 COPD patients with GOLD stage 3-4, they found that the presence of asthma diagnosis, low FEF25-75 and high mMRC scores were independent risk factors for frequent exacerbations (3).

In a study of Judith et al., the number of hospital admissions due to COPD in the past year being ≥3, low $FEV_1$, oral corticosteroid use and inadequate use of LTOT were identified as risk factors for frequent hospital admissions (4).

Studies reported that LTOT was a risk factor for frequent hospitalization (5,6,7). In our study, the use of LTOT, BiPAP, or nebulizer was found to be associated with frequent hospitalization. In previous studies, the use of BiPAP and nebulizer was not investigated as a risk factor. The use of LTOT, BiPAP, and nebulizer indicates respiratory insufficiency, higher dose treatment, and thus, advanced COPD. Therefore, the need for hospitalization arises frequently. In previous studies, it was also reported that low $FEV_1$and active cigarette smoking were not associated with frequent hospitalization. Similar to our study, Kessler et al. (6) found that active cigarette smoking was not related to frequent hospitalization. Kessler et al. also determined that chronic hypercapnic respiratory failure and pulmonary hypertension (PaCO2>44 mmHg and mean pulmonary artery pressure>18 mmHg)were risk factors for frequent hospitalization due to acute exacerbation of COPD (6). Low $FEV_1$was found to be associated with frequent hospitalization in some studies (9,10,11,12) but was not found to be associated with frequent hospitalization in other studies (6,13,14). In our study, we concluded that low $FEV_1$may increase the number of hospitalizations.

In a case-control study of Radisaet al.,they determined that advanced age (>65), respiratory tract comorbidities, long hospital stay, CRP<10 mg/dL and low $FEV_1$/FVC ratio were significant risk factors for severe acute exacerbations of COPD requiring hospitalization (15).

## Conclusion

Consequently, patients with COPD who are illiterate or receive nebulizer treatment are at serious risk of hospitalization. This group of patients should be followed with special care to reduce hospitalization.

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