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Original Article

30-day Readmission After an Acute Exacerbation of Chronic Obstructive Pulmonary Disease is Associated with Cardiovascular Comorbidity

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Abstract

OBJECTIVE: Readmission after hospitalization for a chronic disease is a major concern of interest for health care quality. Our aim was to investigate the predictors and rates of early readmission after an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in a tertiary care hospital.

MATERIAL AND METHODS: Over a 3-year period, patients hospitalized in our pulmonary disease clinic with a diagnosis of chronic obstructive pulmonary disease (COPD) and who had an index hospitalization for AECOPD were included. Readmission was defined as rehospitalization within 30 days of AECOPD discharge. Demographics, comorbidities, exacerbations, prior intensive care unit (ICU) stay, and long-term oxygen therapy (LTOT), blood eosinophil count, and antibiotic and/or steroid treatment at the index AECOPD admission were recorded.

RESULTS: Fifty-two (17.3%) readmissions occurred in 300 patients. Readmissions were due to AECOPD in 46.2%, pneumonia in 19.2%, and cardiovascular disease in 15.4% patients. Twenty-one (40%) of the readmitted patients were frequent exacerbators. After adjusting for individual and clinical predictors, the odds ratio for readmission was 2.11 (95% CI, 1.07-4.15, $P = .03$) for those with congestive heart failure, 3.30 (95% CI, 1.05-9.75, $P = .04$) for those with arrhythmia, and 1.99 (95% CI, 1.04-3.81, $P = .04$) for LTOT users prior to AECOPD.

CONCLUSION: A significant majority of patients readmitted after an AECOPD mainly suffered from recurrent AECOPD. Associated congestive heart failure, arrhythmia, and prior LTOT were risk factors identified for early AECOPD readmissions in our study. Better recognition of readmission risk factors might help to reduce readmission rates of AECOPD.

KEYWORDS: Chronic obstructive pulmonary diseases, acute exacerbation, readmission, discharge, rehospitalization
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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease and is the sixth leading cause of disability-adjusted life years (DALYs) lost globally.[1] The worldwide prevalence of COPD has been reported to be between 8.4% and 15.0%. In Turkey, the prevalence is between 5.3% and 19.1%, and it is the third leading cause of DALYs.[2-4] COPD exacerbations are the major determinants of future risk and survival. A substantial portion of COPD patients suffer exacerbations.[5] Different cohorts have reported that nearly 50% of COPD patients suffered at least one exacerbation up to 3-year follow-up.[6,7]

Hospital admissions due to COPD exacerbations account for approximately 30% of the costs related to the disease, and 1 in 5 COPD patients is rehospitalized within 30 days of discharge, mainly due to a new acute exacerbation of COPD (AECOPD).[8-10] Given this economic burden and the prognostic importance of exacerbations in COPD, defining the traits relating to specific susceptibility for readmission after an AECOPD, and thus predicting readmission risk, have become areas of interest recently.[11]

The rate of 30-day readmission after an index AECOPD was reported as approximately 20% in a database study in the United States.[12,13] However, there are geographical differences and lower rates have been reported, such as 10% in the United Kingdom.[14] Many factors are reported to be associated with the risk of readmission within 30 days, including age, ethnicity, comorbidity burden (congestive heart failure, chronic renal insufficiency, diabetes, depression, anxiety), length of hospital stay, discharging facility, insurance type, and income.[12,15] Recently, in a study including 1 622 983 participants, comorbidity has been reported as the strongest predictor of 30-day readmissions.[16] Previous exacerbation and hospitalizations have also been defined as risk factors,[17] and interventions targeting decreasing the rehospitalization risk would be an important point of COPD care.

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Currently, 30-day readmission and death rates in patients hospitalized with AECOPD have been hot topics, studied extensively in different countries. Avoiding early readmissions has become a major healthcare priority. In the USA, the Hospital Readmissions Reduction Program (HRRP) has been developed and implemented to control readmissions due to chronic diseases.[10,18,19] However, there is no comprehensive investigation on this topic in Turkey, where a readmission program has not been applied yet. Therefore, in this study, we aimed to determine the rates and predictors of early COPD readmissions in patients hospitalized with AECOPD in an academic facility—a teaching hospital located in the western part of Turkey—and thus take a picture of how COPD care is provided in our country.

MATERIAL AND METHODS

Study Design/Population

The study was designed as a retrospective cohort. Local Ethics Committee approval (Approval number: 2018/14-36) was obtained from Dokuz Eylül University Faculty of Medicine ethics committee before the study, and the study was conducted according to the principles of the Declaration of Helsinki. Patients aged between 45 and 80 years who were hospitalized in our pulmonary disease clinic with a diagnosis code of COPD (ICD-10 codes of J44, J44.0, J44.1, J44.8, and J44.9) between January 1, 2014, and December 31, 2017, were screened from our hospital's electronic database archive. The medical records of these patients were evaluated for coherence with AECOPD. COPD diagnosis was confirmed according to the GOLD 2017 criteria[1] and AECOPD was described as an acute worsening of respiratory symptoms (dyspnea, increase in sputum volume, and sputum purulence) beyond daily variations, requiring additional treatment. The study population only included hospitalized patients, and thus, AECOPDs were classified as severe.[2]

A total number of 939 patients were screened. Five hundred seven patients were excluded due to lack of accessible adequate information (absence of respiratory symptom history and/or verifying spirometry, a clearly defined AECOPD admission record) or incompatible ICD codes checked from the medical records. Exclusion criteria were death during the index AECOPD hospitalization, hospitalization with indications other than AECOPD (pleural effusion, pneumothorax, pulmonary embolism, pulmonary edema, cardiac and metabolic diseases, and surgical procedures) and co-existing chronic respiratory diseases (asthma/asthma-COPD overlap and active tuberculosis). Finally, 300 patients of the initial 939 were involved in the analysis (Figure 1). Written informed consent was not obtained from the patients, because the study was retrospective and used anonymous data which did not identify individual patients.

MAIN POINTS

- Patients with COPD had a 17.3% rate of 30-day readmission after an AECOPD, in this study.
- The prevalence of frequent exacerbators was 40% among readmitted patients.
- Acute exacerbations (46.2%), pneumonia (19.2%), and cardiovascular diseases (15.4%) were the most common causes.
- Congestive heart failure, arrhythmia, and prior long-term oxygen use increased the risk of readmission by 2-fold.

As multiple COPD admissions and readmissions may have occurred during the study period, only the last admission for AECOPD of an individual patient was included in the analysis. Readmission reasons and risk factors (predictors) were addressed.

Risk Factors

Risk factors were determined as patient and clinical characteristics. Patient characteristics were demographics (age, gender, and smoking status), and comorbidities (congestive heart failure, hypertension, coronary artery disease, arrhythmias, diabetes mellitus, renal failure, and lung cancer). Among clinical characteristics, there were the severity indices such as prior intensive care unit (ICU) stay (both requiring invasive or non-invasive ventilation support), long-term oxygen therapy (LTOT), and severe disease (exacerbation history); and admission characteristics including blood eosinophil count, need for ICU, and treatment (antibiotic, quinolone/beta lactam+beta lactamase inhibitor and/or parenteral steroid, 0.5 mg/day, both for up to 10 days) given in the index AECOPD admission.

LTOT therapy data were self-reported and/or recorded in the database. Frequent exacerbation was defined as having ≥ 1 hospitalization for AECOPD or 2 COPD exacerbations during the previous year.[2] Absolute eosinophil counts were taken from the complete blood counts measured at index admission. The need for antibiotic and/or steroid treatments were obtained from the electronic records.

Outcome

Readmission was defined as presenting to the emergency service within 30 days of AECOPD discharge for any reason, and readmission to the hospital. Patients who stayed in emergency service for more than 24 hours and were discharged home were also counted as being readmitted.

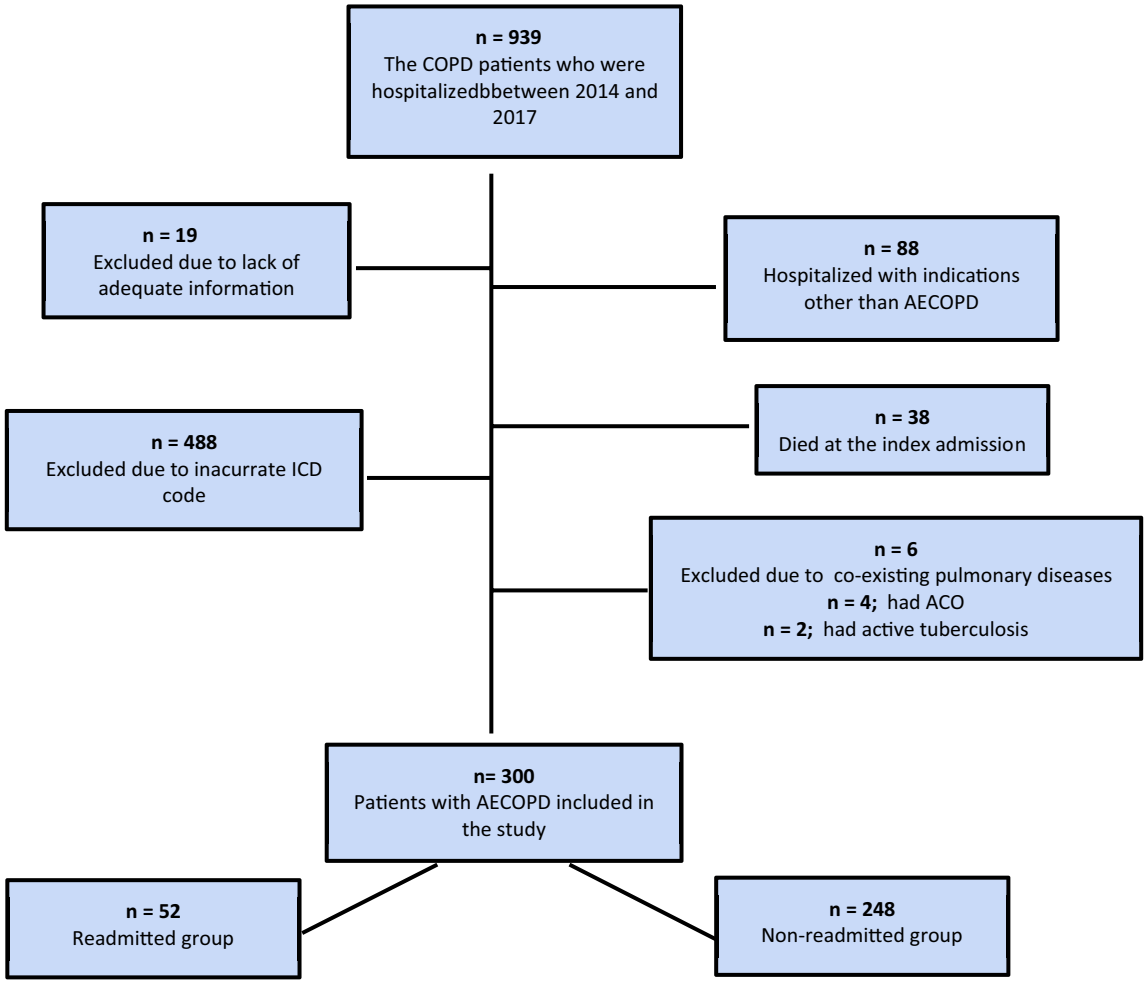
Statistical Analysis

Data were analyzed with SPSS software version 22.0 (IBM SPSS Corp.; Armonk, NY, USA). We used mean and standard deviation or median and minimum-maximum values according to the distribution of the data. Parametric evaluations with the Student's *t*-test, and evaluations of nonparametric values with the Mann–Whitney *U*-test, were performed. Categorical data were evaluated by chi-square or Fisher's exact test. To investigate trends in the 30-day readmission rate after AECOPD, we constructed adjusted logistic regression models in the multivariable models; we adjusted for age, sex, and cardiovascular comorbidities. The relationship between independent variables was evaluated by Pearson correlation analysis. A *P*-value $< .05$ was considered significant.

RESULTS

Study Population

A total of 300 patients were included in the analysis. More than 50% (488) of the screened patients had to be excluded



COPD: Chronic obstructive pulmonary disease
ACO: Asthma and chronic obstructive pulmonary disease overlap syndrome
AECOPD: Acute exacerbation of chronic obstructive pulmonary disease
ICD: International statistical classification of diseases and related health problems

Figure 1. The algorithm of study population inclusion.

due to over diagnosis or misdiagnosis of COPD. Fifty-two (17.3%) of them were found to be readmitted within the first 30 days. The mean age of the participants was 73.11 ± 10.06 years and the majority of them were male (*n* = 215, 71%). Both readmitted patients and those not readmitted were similar in age and sex (*P* = .14, *P* = .36, respectively). One hundred eighteen (83.3%) patients were ex- or current smokers. There was no significant relationship between the other demographic features including smoking status and early readmission (Table 1).

Readmission Causes

Early readmissions were mainly due to respiratory diseases (*n* = 34, 65.4%). Of the 52 readmissions, 46.2% were hospitalized due to COPD exacerbation, 19.2% due to pneumonia, 15.4% due to cardiovascular diseases, 1.9% due to lung cancer, and 17.3% due to other causes (femur fracture, fall, etc.). Associated cardiovascular diseases were not more in COPD patients readmitted for cardiovascular diseases than in the ones readmitted due to other causes (*P* = .65).

Risk Factors

Comorbidities: The most common comorbidity in both groups was hypertension (*n* = 107, 35.7%).

Cardiovascular Diseases

Overall, 107 (35.7%) patients had hypertension, 61 (20.3%) had congestive heart failure, 53 (17.7%) had coronary artery disease, and 14 (4.7%) had arrhythmia.

Patients with coronary heart disease (*P* = .04), odds ratio 2.12 (95% CI, 1.02-4.39), congestive heart failure (*P* = .03), odds ratio 2.11 (95% CI, 1.07-4.15, *P* = .03), and arrhythmia (*P* = .04), odds ratio 3.30 (95% CI, 1.05-9.75) had significantly more readmission rates than others while adjusting for age, sex, and LTOT use (Table 2).

Renal Failure, Diabetes Mellitus, and Lung Cancer

The presence of diabetes mellitus was the second most common comorbidity in the study population (21.0%). There was no statistically significant difference for the presence of

Table 1. Risk Factors for Readmission after an Acute COPD Exacerbation in the Study Population

	Readmitted Group (*n* = 52)	Non-readmitted Group (*n* = 248)		
	n **(%)**	***n*** **(%)**	**OR (95% CI)**	***P***
Age (mean ± SD)	74.87 ± 9.06	72.75 ± 10.24	-	.14
Gender				
Male	40 (18.6)	175 (81.4)	1.39(0.69-2.80)	.36
Female	12 (14.1)	73 (85.9)		
Hypertension				
Yes	22 (20.6)	85 (79.4)	1.41 (0.77-2.59)	.27
No	30 (15.5)	163 (84.5)		
Coronary heart disease				
Yes	14 (26.4)	39 (73.6)	1.97 (0.98-3.98)	.05
No	38 (15.4)	209 (84.6)		
Congestive heart failure				
Yes	17 (27.9)	44 (72.1)	2.25 (1.16-4.38)	.02
No	35 (14.6)	204 (85.4)		
Arrhythmia				
Yes	6 (40.0)	9 (60.0)	3.46 (1.18-10.2)	.03
No	46 (16.1)	239 (83.9)		
Lung cancer				
Yes	2 (22.2)	7 (77.8)	1.38 (0.28-6.83)	.66
No	50 (17.2)	241 (82.8)		
Smoking history				
Yes	33 (18.3)	147 (81.7)	1.39 (0.50-3.85)	.52
No	5 (13.9)	31 (86.1)		
Long- term oxygen therapy use				
Yes	19 (25.7)	55 (77.3)	2.02 (1.07-3.83)	.03
No	33 (14.6)	193 (85.4)		
Intensive care unit admission				
Yes	7 (18.9)	30 (81.1)	1.13 (0.47-2.73)	.79
No	45 (17.1)	218 (82.9)		
Antibiotic use				
Yes	48 (18.8)	207 (81.2)	2.38 (0.81-6.95)	.11
No	4 (8.9)	41 (91.1)		
Systemic steroid use				
Yes	43 (17.1)	208 (82.9)	0.92 (0.42-2.03)	.83
No	9 (18.4)	40 (81.6)		

Data are expressed as *n* (%) otherwise mentioned.
COPD, chronic obstructive pulmonary disease; SD, standard deviation.

diabetes mellitus (*P* = .44), chronic renal failure (*P* = .36), and lung cancer (*P* = .66) between the early readmission and the non-readmission groups.

Severity Indices

Prior ICU Stay: Prior ICU stay was determined in 37 patients (12.3%); 7 of them were in the readmission group. There was no statistically significant difference in terms of prior ICU need between the early readmission and the non-readmission groups (*P* = .786).

Long-Term Oxygen Treatment

Another feature investigated was prior LTOT prescription, which was used as an indicator of severity. Seventy-four (24.7%) patients were receiving long-term oxygen treatment. Early readmission rate was 1.96-fold (95% CI, 1.03-3.75, *P* = .042) more frequent in patients on LTOT (Table 2).

Frequent Exacerbations

Twenty-one (40%) patients among 52 readmitted patients had 2 AECOPDs or 1 AECOPD requiring hospitalization

Table 2. The Association Between Readmission after an Acute COPD Exacerbation Discharge and Risk Factors by Multivariate Analysis

	Model 1†		Model 2††		Model 3†††	
	P	OR (95 CI%)	*P*	OR (95 CI%)	*P*	OR (95 CI%)
Long-term oxygen use	.02	2.25 (1.16-4.35)	.04	1.96 (1.03-3.375)	.04	1.99 (1.04-3.81)
Coronary heart disease	.04	2.12 (1.02-4.39)	-	-	-	-
Congestive heart failure	-	-	.03	2.11 (1.07-4.15)	-	-
Arrhythmia	-	-	-	-	.04	3.30 (1.05-9.75)

†Model 1: Adjusted for age, sex, LTOT use, and CHD status by logistic regression.
††Model 2: Adjusted for age, sex, LTOT use, and CHF status by logistic regression.
†††Model 3: Adjusted for age, sex, LTOT use, and arrhythmia status by logistic regression.
COPD, chronic obstructive pulmonary disease.

during the previous year. Of the 24 patients who readmitted due to AECOPD, 13 (54%) patients were also frequent exacerbators.

Admission Characteristics

Absolute Eosinophil Counts: The mean absolute eosinophil count was 118.56/μL (± 14.6 SE) for the study population, of which 67 patients had absolute eosinophil count ≥ 200/μL at the index admission. The mean absolute eosinophil value measured at index hospitalization in the early readmission group was 67.60/μL (±19.81 SE), while it was 129.4/μL (±17.17 SE) in the non-readmission group (*P* = .38) (Table 3). Two patients in the readmission and 13 patients in the non-readmission groups were not included in the analysis due to lack of data.

ICU Admission, Antibiotic and/or Systemic Steroid Treatment at Index Hospitalization

Thirty-seven (12.3%) patients had a prior ICU admission before index AECOPD in their medical history (*P* = .76). Of the 300 cases in the study population, 251 (83.7%) were treated with antibiotics and 255 (85.0%) received systemic steroid therapy. Antibiotic and systemic steroid treatment were also not different between the groups (*P* = .11 and *P* = .83, respectively) (Table 1).

DISCUSSION

The 30-day readmission rate after an AECOPD discharge is one of the major global concerns. In this study, we aimed to determine the 30-day readmission rates and identify modifiable risk factors in a country in which HRRP is not implemented. We observed that repeated AECOPD was the most common reason for readmission, and congestive heart failure, arrhythmia and LTOT were the factors associated with readmission risk in patients with an index AECOPD, in our single-center study.

We found that the 30-day readmission rate after an AECOPD was 17.3% in our study. In a North-American study in which a national database was searched for early readmissions after an index AECOPD, the 30-day readmission rate was 19.1%.[12] However, in another study, for a population of 40-65 years of age, 30 days post-index hospitalization was found 8.25%.[20] Another study reported a decline in readmission rates from 20.0% to 19.2% between 2006 and 2012 in the USA when adjusted for patient demographics and comorbidities. The authors concluded that the readmission rate remained high in most national priority populations such as the elderly, women, racial/ethnic minorities, low-income and rural populations, and patients with chronic illnesses.[21] The HRRP in the USA was developed to penalize hospitals with higher 30-day readmission rates for 3 targeted conditions (acute myocardial infarction, heart failure, and pneumonia), and this was extended to include COPD, in 2015.[22] On the contrary, among Medicare beneficiaries, 30-day post-discharge mortality increased for heart failure and pneumonia.[23] Considering that a quartile of patients does not recover their lung function within 30 days following AECOPD, whether readmission might be protective for morbidity and mortality is such a dilemma in this high-risk period.[24] A workshop report focusing on the barriers to reducing COPD readmissions has currently been published to address the issue.[22] Although there is no HRRP in Turkey, a lower readmission rate after an AECOPD is regarded as a quality standard for hospitals.

The demographic features of our study population are consistent with the current literature in terms of age. We found the mean age of the study population to be 73.11. However, the majority of the participants were male (71%), which differs from some previous reports with female predominance.[12,21,25] In the European COPD audit, which also involved our country, the rate was also in favor of men (68.7%).[26] Male smoking prevalence in Turkey is higher than in any Western European country and among the highest in Central Asia.[27]

Table 3. Eosinophil Counts Derived from Peripheral Blood Counts of the Study Population

	Readmitted Group (*n* = 50)	Non-readmitted Group (*n* = 235)	Total (*n* = 285)	*P*
Eosinophil count at admission	67.60 (±19.81)/μL	129.40 (±17.2)/μL	118.56 (±14.6)/μL	.38
Eosinophil count at discharge	69.60 (±13.07)/μL	118.56 (±14.6)/μL	104.59 (±9.6)/μL	.93

*Data are expressed as mean ± standard deviation.

We found that early readmissions were mostly due to respiratory causes (65.4%); COPD exacerbations were in the first place, with pneumonia, cardiovascular diseases, and lung cancer following behind. Respiratory diseases including COPD, respiratory failure, and pneumonia, have been reported as the most common readmission reasons in most previous studies.[10,12,28]

Several factors have been reported to be associated with AECOPD readmissions, including both patient and clinical factors.[12,29] A retrospective study also highlighted that variations in primary care services, hospital resources, and the specialty of the treating physicians did not affect AECOPD readmission rates.[14] The management of comorbidities is a cornerstone of good COPD care since comorbidities are related to hospitalizations, readmissions, and mortality.[30] This is assumed to be due to the fragility of patients with multiple medical conditions. However, a recent study pointed out that antibiotic and/or steroid treatments for COPD exacerbations were less used in patients with high comorbidity index. Therefore, failing to get appropriate therapy for AECOPD might be the reason for readmissions in patients with a high Charlson comorbidity index. Congestive heart failure, renal failure, psychiatric disorders, and diabetes are comorbidities observed to be associated with a high risk of readmission.[12,15] There are studies similar to ours, in which the common readmission diagnosis, after respiratory disease, was congestive heart failure.[12,20] We found that congestive heart failure increased readmission risk 2.11-fold and arrhythmia 3.30-fold and were the most influential parameters among the others investigated. Considering that nearly a quarter of the study population had these conditions, treatment and best management of these cardiac comorbidities should be a priority in controlling readmissions.

We also looked for the relationship between frequent exacerbation and early readmission risk as an individual patient factor. We found nearly half of the patients readmitted due to AECOPD were frequent exacerbators. A European COPD audit demonstrated that previous admissions were related to readmission risk.[26] Another study reported a 30-day readmission rate of 35.3% among the frequent exacerbator type, which remained likewise during a 5-year period with only a 0.6% decrease.[21]

Among the clinical factors that might be related to readmissions and previously not investigated was the effect of LTOT. We observed that being on LTOT increased readmission risk nearly 2-fold. A likely explanation of this is that advanced disease is associated with readmissions. Other clinical factors such as prior ICU stay and treatment patterns at the index admission had no effect on readmissions whereas the non-readmitted group had higher eosinophil counts, although this was statistically not significant. Similarly, a recent study from Turkey reported non-eosinophilic exacerbations had an increased risk of readmission in the first month.[31]

Limitations

The major limitation of our study is that the study population was chosen from a single center. This is also a problem of missing readmissions to another hospital. Another limitation of the study is that it relied on ICD codes, although an intensive search has been made to identify COPD, as well as to classify index AECOPD hospitalizations.

Strengths

To our knowledge, this is the first study examining this issue comprehensively in Turkey, and despite the single-center design, a significant number of patients were screened.

CONCLUSION

Early readmissions after an AECOPD are a burden to the healthcare system. The major reasons for readmissions are respiratory, followed by cardiovascular diseases. Among the previous risk factors associated with readmission, we found congestive heart failure and arrhythmia increased readmission risk, as well using LTOT, which has not been previously reported. To date, there are no algorithms to predict the risk of early readmission after an AECOPD. Besides, no AECOPD interventions have been observed to reduce readmission rates. Depending on national data, a national COPD-specific readmission reduction program may be developed to decrease readmission rates without increasing mortality.

The study was performed in Dokuz Eylül University Faculty of Medicine, Department of Pulmonary Diseases, Izmir, Turkey.

The preliminary results of the study were presented by Saliha Selin Ozuygur at the Turkish Thoracic Society Annual Congress, 2018, Antalya, Turkey.

Ethics Committee Approval: The study was approved by the ethics committee of Dokuz Eylül University Faculty of Medicine (July 19, 2018; 2018/18-37).

Peer Review: Externally peer-reviewed.

Author Contributions: Design - A.O.A.,S.S.U.; Resources - S.S.U., C.S., K.C.T.; Materials - A.O.A., K.C.T., S.S.U.; Data Collection and/or Processing - S.S.U., K.C.T.; Analysis and/or Interpretation - A.O.A., S.S.U., C.S. R.R.; Literature Review - A.O.A, S.S.U.; Writing - A.O.A, S.S.U, R.R.; Critical Review - R.R.

Conflict of Interest: The authors have no conflict of interest to declare.

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