

# Long-Term Outcome and Predictors of Survival in Patients Hospitalized For an Acute Exacerbation of Chronic Obstructive Pulmonary Disease

## Kronik Obstrüktif Akciğer Hastalığı Akut Alevlenme İçin Hastaneye Yatırılan Hastalarda Uzun Dönem Sonuçlar ve Sağlık Belirteçleri

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**ABSTRACT Objective:** Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a major cause of hospitalizations, and associated with a greater risk of mortality in subsequent years. This study aimed to determine potential determinants of survival in a group of patients hospitalized for AECOPD. **Material and Methods:** A retrospective cohort study of 193 patients hospitalized for an AECOPD between the years 2002 and 2004 was performed. Patients' demographics, comorbidities, clinical, laboratory data on admission were recorded. In-hospital mortality was determined. Patients were followed-up for four years after discharge. **Results:** The mean age was  $65.49 \pm 8.85$  and 94.8% of the patients were males. In-hospital mortality rate was 5.2%. Twenty six patients (13.5%) were admitted to the intensive care unit (ICU). The mortality rates were 15.5%, 23.8%, 32.1%, and 36.8% 1st, 2nd, 3rd and 4th years, respectively. Cox regression analysis showed that increased age (HR 1.04; 95% CI, 1.01-1.07), lower BMI (HR 0.89; 95% CI, 0.84-0.94), GOLD stage IV (HR 2.74; 95% CI, 1.31-5.70), cor pulmonale (HR 3.53; 95% CI, 2.15-5.80) and ICU admission (HR 3.21; 95% CI, 1.84-5.61) were independently related to mortality. **Conclusion:** Advanced age, severe COPD, lower BMI, cor pulmonale, and ICU admission were independently associated with mortality after hospitalization for an acute exacerbation. With this regional data from Turkey, it has been concluded that it is useful to have lung function test data for COPD patients and to evaluate the disease stage as the predictors of mortality after acute exacerbations.

**Key Words:** Pulmonary disease, chronic obstructive; hospitalization; survival; intensive care; disease progression

**ÖZET Amaç:** Kronik obstrüktif akciğer hastalığı (KOA) alevlenmesi hastaneye yatışların başlıca nedenidir ve sonraki yıllarda daha yüksek mortalite riskiyle ilişkilidir. Bu çalışma KOAH alevlenmesi için hastaneye yatırılan bir hasta grubunda sağkalımın olası belirleyicilerini değerlendirmeyi amaçladı. **Gereç ve Yöntemler:** KOAH alevlenme için 2002-2004 yılları arasında hastaneye yatırılan 193 hastadan oluşan retrospektif kohort çalışması yapıldı. Hastaların demografik özellikleri, ek hastalıkları, başvuru sırasındaki klinik ve laboratuvar veriler kaydedildi. Hastane içi mortalite belirlendi. Hastalar taburcu olduktan sonra dört yıl izlendi. **Bulgular:** Yaş ortalaması  $65.49 \pm 8.85$  idi, hastaların %94.8'i erkekti. Hastane-içi mortalite oranı %5.2 idi. Yirmi altı hasta (%13.5) yoğun bakım ünitesine (YBÜ) yatırıldı. Mortalite oranları 1., 2., 3. ve 4. yılda sırasıyla %15.5, %23.8, %32.1 ve %36.8 bulundu. Cox regresyon analizinde ileri yaş (HR 1.04; 95% CI, 1.01-1.07), düşük beden kitle indeksi (HR 0.89; 95% CI, 0.84-0.94), GOLD evre IV (HR 2.74; 95% CI, 1.31-5.70), kor pulmonale (HR 3.53; 95% CI, 2.15-5.80) ve YBÜ'ye yatış (HR 3.21; 95% CI, 1.84-5.61) mortalite ile bağımsız olarak ilişkilidiler. **Sonuç:** İleri yaş, ağır KOAH, düşük beden kitle indeksi, kor pulmonale ve YBÜ'ye yatış, alevlenme nedeniyle hospitalizasyon sonrası mortaliteyle bağımsız olarak ilişkilidiler. Türkiye'ye ait bu bölgesel veri ile, KOAH'lı hastalarda solunum fonksiyon testleri verisine sahip olmanın ve hastalık evresini değerlendirmen alevlenmeler sonrasında mortaliteyi belirlemede yararlı olduğu sonucuna varılmıştır.

**Anahtar Kelimeler:** Kronik obstrüktif akciğer hastalığı; hastaneye yatış; sağkalım; yoğun bakım; hastalığın ilerlemesi

Chronic obstructive pulmonary disease (COPD) is a major and increasing cause of morbidity and mortality in countries at all levels of economic development.<sup>1-3</sup> It has been estimated that COPD which ranked fifth as the cause of death in 2002 will become the fourth leading cause of death by the year 2030.<sup>4</sup> Internationally, COPD is projected to be the fifth among the conditions with a high burden to society.<sup>5</sup>

Patients with COPD experience acute exacerbations characterized by a change in baseline dyspnea, cough, and/or sputum production that is beyond normal day-to-day variations, it is acute in onset, and may warrant a change in regular medication.<sup>6</sup> COPD exacerbations can range from increased symptoms to hospitalizations, respiratory failure and death. Hospitalizations for acute exacerbations represent a significant part of socioeconomic burden related to COPD.<sup>2,7</sup> Previous studies have estimated in-hospital mortality to range from 4% to 30% for the acute exacerbations of COPD.<sup>8-10</sup> Hospitalization for acute exacerbations is also associated with a greater risk of mortality in subsequent years, since it usually occurs in the advanced phase of disease. Despite the increasing hospitalization rate for COPD, available data on long-term survival after hospitalization for acute exacerbations of COPD is limited. The long-term outcome have been evaluated in previous studies with different end-points, and some of these follow-up studies investigated directly the prognosis of COPD patients requiring admission to the intensive care unit (ICU) which is usually believed to be poor.<sup>7-15</sup> One year mortality after hospitalization for acute exacerbation of COPD have been reported to range between 22% and 59%.<sup>6,9,11,12</sup> The 2-year mortality rates were found to be 35.6-49 %, and the reported mortality rates in 3 years were 49-61.2%.<sup>7,11,13,15</sup> Studies on acute exacerbation of COPD have also investigated factors related to mortality. Some characteristics reported as risk factors are older age, low body mass index (BMI), other comorbidities, prior functional status, cardiac factors, severity of illness, serum albumin level, PaCO<sub>2</sub> and PaO<sub>2</sub>.<sup>11-13</sup> The impact of exacerbations is significant on the quality of life and prognosis of patients with COPD. COPD prevalence, and risk factors may vary across countries,<sup>4</sup> and also

health care system facilities have considerable differences. Through the implementations of the extended knowledge on the exacerbation outcomes, the potential predictors of mortality after an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) should be taken into account when making health-care decisions in these patients, and having regional data on the long-term outcome of COPD exacerbations would be beneficial.

The purpose of this study was to assess the long-term outcomes and to determine potential determinants of survival in a group of patients admitted for acute exacerbation of COPD in Turkey. To do so, we conducted a retrospective cohort study by obtaining the information from the discharge reports and all COPD patients hospitalized for acute exacerbation were included. The follow-up period was four years.

## MATERIAL AND METHODS

### PATIENTS

We consecutively included all patients with COPD who were hospitalized in the Pulmonary Disease Department of a university hospital for an exacerbation between January 2002 and January 2004. COPD diagnosis was made according to the criteria set by Global Initiative for Obstructive Lung Disease (GOLD) (the fixed ratio, postbronchodilator FEV<sub>1</sub>/FVC < 0.7, to define airflow limitation).

An exacerbation was defined as the presence of an increase in at least two of the three following symptoms: dyspnea, cough, and sputum purulence severe enough to warrant hospital admission. Each patient was included only once in the study, even if the patient had been hospitalized more than once. Patients with a history of asthma, active pulmonary tuberculosis, cystic fibrosis, bronchiectasis, lung cancer, hospitalization for causes other than COPD exacerbation were excluded from the study, as well as patients who had no previous pulmonary function tests confirming airflow obstruction in a stable condition. Patient recruitment, data and outcome collection were performed according to the Helsinki II Declaration.

## CLINICAL DATA

Patients' data were collected retrospectively. We reviewed 209 patients' hospital records, and 193 of them were eligible for the analysis since their clinical data were complete. We obtained information regarding survival status and survival time. The age, gender, smoking status and the severity of COPD were documented. Active smoking status was defined as having smoked within the last 6 months. The information about the disease duration (years), comorbidities, the number of previous hospitalizations and/or ICU admissions with an acute exacerbation of COPD and the use of home oxygen therapy were also noted. Baseline severity of disease was defined by the GOLD 2003 criteria upon pulmonary function tests performed in a stable condition within the previous year before admission. Postbronchodilator FEV1 measurements were used to stage the patients. Comorbidities were quantified according to previously validated Charlson index.<sup>16</sup> The following variables on admission were recorded; body mass index (BMI), arterial blood gas measurements, hematocrit, serum albumin levels, chest roentgenogram findings (with consolidation/without consolidation). Cor pulmonale was defined as the presence of two or more of the following criteria: 1. right ventricular hypertrophy or right atrial enlargement on the ECG; 2. enlarged pulmonary arteries on the chest radiograph; and 3. pedal edema. During the hospital stay, the need for transfer to the ICU was recorded. Arterial blood gas measurements prior to the discharge from the hospital were also collected to determine reversible hypercapnia.

## OUTCOME AND FOLLOW-UP

In-hospital mortality was determined for each patient, if patients died during hospital stay, their date of death was recorded and verified by hospital records. Patients were followed-up for four years after discharge from the hospital by review of the clinical records, telephone contacts, and death registration records. If patients died after hospital discharge, their date of death was verified from hospital records or the death records of the city in which they lived. The information on the survival

status and survival time of all subjects were collected, and confirmed in this way.

## Statistical analysis

The statistical analysis were performed using statistical software package (SPSS for Windows, version 11.0; SPSS Inc; Chicago, IL.) Shapiro-Wilk test was used for testing for normality. Demographic and baseline clinical characteristics were presented as mean  $\pm$  SD (standard deviation) for normally distributed continuous variables (age, FEV1/FVC%, hematocrit, albumin), and median (25-75% percentiles) for non-normally distributed continuous variables (smoking pack/year, disease duration/year, Charlson index, BMI, FEV1%, FEV1 (L), FVC(%), FVC(L), pH, pA02, pAC02) and as percentage of the group for categorical variables. Comparisons between groups were made by using the independent sample t test, Mann-Whitney U test and chi-square test. Kaplan-Meier method was used to evaluate the prognosis, and the survival time was calculated with this method. The Cox proportional hazards model was used to investigate the effects of clinical variables on survival. Age, number of previous hospitalizations, duration of disease, Charlson index, BMI, FEV1, arterial blood gas measurements (pH, PaO2, paCO2), hematocrit, urea and albumin levels were included as continuous variables in the model, and the smoking status, prior ICU admission, use of home oxygen therapy, presence of cor pulmonale, severity of disease, ICU admission, and invasive mechanical ventilation were included as categorical variables. Only statistically significant variables were included into the Cox proportional hazards model. Hazard ratios (HR) were calculated. Results of the analysis were presented in terms of the estimated HRs with corresponding 95% confidence intervals. p values less than 0.05 were considered as statistically significant.

## RESULTS

Between January of 2002 and January 2004, 193 patients hospitalized for an acute exacerbation of COPD were included in the study. Patient demographics and medical history characteristics are listed in Table 1. The mean age was  $65.49 \pm 8.85$ . Most patients were elderly, and the study group

mainly consisted of male patients (n: 183, 94.8%). One-hundred sixty eight patients (87%) were either current smokers or ex-smokers. Comorbid conditions were present in 55.4% of the study group. Majority of comorbid diseases were cardiovascular diseases. According to GOLD criteria, our hospitalized patients had moderate to very severe disease; 159 of them (82.4%) were classified as having severe to very severe COPD. One-hundred eleven patients (57.5%) had prior history of hospitalization for an acute exacerbation of COPD. One third of the study group were using home oxygen. The clinical and laboratory data on admission are shown in Table 1. In arterial blood gas measurements on admission, hypoxemia was a common condition as well as hypercapnia. Forty two patients (21.8%) had hypoalbuminemia. One-hundred and sixty five patients (85.5%) received antibiotic therapy, and 66 patients (34.2%) were treated with systemic corticosteroids during hospital stay. Twenty six patients (13.5%) were admitted to ICU, 25 patients had NIMV and seven of them needed invasive mechanical ventilation. When the characteristics of ICU patients and non-ICU patients were compared, ICU patients had significantly lower pH, PaO<sub>2</sub>, and higher PaCO<sub>2</sub> values (Table 2). Seventeen patients were treated with NIMV on the ward.

### IN-HOSPITAL MORTALITY AND SURVIVAL

In-hospital mortality rate was 5.2% (n= 10). Among 10 patients, eight of them (80%) admitted to the ICU during the hospital stay. In-hospital mortality rate was 30.8% for the patients transferred to the ICU (n= 26). The overall mortality rates were 15.5 %, 23.8%, 32.1%, and 36.8% in 1st, 2nd, 3rd and 4th years, respectively. The differences in baseline characteristics and clinical data between survivors and nonsurvivors are listed in Table 3. The significant parameters were lower BMI and FEV<sub>1</sub>, the presence of cor pulmonale, arrhythmias, uremia, hypoalbuminemia, low PaO<sub>2</sub> and high PaCO<sub>2</sub> levels on admission, the need for ICU admission, and the presence of hypercapnia at discharge. The median survival time was 60 months . The Kaplan-Meier cumulative survival plot of the patients was shown in Figure1. The

**TABLE 1:** Patient characteristics: demographics, and laboratory data on admission.

Characteristics	
Age,year	65.49 ± 8.85
Male/Female,n	183 / 10
Smoking history,n(%)	
Nonsmoker	25(%12.9)
Current	73(%37.8)
Ex-smoker	95(%49.2)
Smoking pack-year	40(29.5-60)
Severity of COPD (GOLD),n(%)	
Stage 2	34 (%17.6)
Stage 3	73 (%37.8)
Stage 4	86 (%44.6)
Disease duration,year	6(3-10)
Comorbidity,n(%)	107 (%55.4)
Cardiovascular,n(%)	87 (%45.1)
Hypertension,n(%)	57 (%29.5)
Diabetes Mellitus,n(%)	23 (%11.9)
Other comorbidity,n(%)	25 (%12.9)
Charlson index ,n(%)	2(1-2)
Prior hospitalization for AECOPD,n(%)	111 (%57.5)
Prior admissions to ICU,n(%)	15 (%7.8)
Use of home oxygen therapy,n(%)	56 (%29.0)
BMI, kg/m <sup>2</sup>	23.74(21.36-26.61)
FEV <sub>1</sub> % predicted	32(24.50-45)
FEV <sub>1</sub> (L)	0.89(0.69-1.21)
FVC % predicted	50(39-61)
FVC (L)	1.72(1.40-2.19)
FEV <sub>1</sub> /FVC%	53.84 ± 9.08
pH	7.40(7.36-7.43)
PaO <sub>2</sub> ,mmHg	48.2(39.3-60.6)
PaCO <sub>2</sub> ,mmHg	46.4(37.8-55.6)
Hematocrit,%	45.90 ± 7.01
Albumin,mg/dl	3.90 ± 0.56
ECG right heart strain,n(%)	50(%25.9)
Cor pulmonale,n(%)	71 (%36.8)
Arrhythmias,n(%)	49 (%25.4)

Data are presented, as mean ± Standard deviation and median (25-75% percentiles), n(%).

overall mortality rate increased by the severity of the disease at the end of the study, as it was 26.4%, 34.2% and 50% for stages 2, 3 and 4, respectively. For the ICU patients, the mortality rates were 46.1%, 61.5%, 69.2%, and 73% in 1st, 2nd, 3rd and 4th years, respectively. Kaplan-Meier survival curves for ICU and non-ICU patients were plotted in Figure 2. The median survival time for ICU patients was calculated as 12.3 months and it was 60 months for non-ICU patients (p< 0.001).

**TABLE 2:** Comparison of the ICU and non-ICU patients on hospital admission.

Characteristics	ICU patients (n:26)	Non-ICU patients (n:167)	P value
Age, year	64.92±8.43	65.58±8.94	0.726
Disease duration, year	7.50 (4-10)	6 (3-10)	0.850
Charlson index	1(1-2)	2 (1-2)	0.414
BMI, kg/m <sup>2</sup>	24.29 (20.83-28.10)	23.73 (21.42-26.50)	0.803
FEV1, %predicted	30 (22-47)	32 (26-44.50)	0.427
pH	7.33 (7.28-7.40)	7.41 (7.38-7.43)	<0.001
PaO <sub>2</sub> mmHg	35.3 (32.8-46.6)	51 (40.8-62.3)	<0.001
PaCO <sub>2</sub> mmHg	59.7 (51.6-64.6)	44 (37.4-53.3)	<0.001

Data are presented, as mean ± standard deviation, and median values (25-75% percentiles).

BMI: Body mass index; ICU: Intensive care unit.

**TABLE 3:** Differences in baseline characteristics and clinical data between survivors and nonsurvivors

Variables	Survivors (n:116)	Nonsurvivors (n:77)	p value
Age, year	64.61±8.65	66.81±9.05	0.094
Male/Female,n	113/3	70/7	0.092
Duration of disease,year	6 (3-10)	8 (4-10)	0.234
Smoker/ES /NS,n	38/63/15	35/32/10	0.17
Smoking pack-yea	40 (20-60)	40 (30-60)	0.326
Severity of COPD,n			
Stage2/3/4	25/48/43	9/25/43	0.027
Charlson Index	1.5 (1-2)	2 (1-2)	0.724
Use of home oxygen,n	85/31	52/25	0.421
BMI kg/m <sup>2</sup>	24.78 (22.76-27.92)	22.83 (20.31-25)	0.001
FEV1 L	0.93 (0.73-1.29)	0.84 (0.65-1.02)	0.014
PaO <sub>2</sub> mmHg	54.1 (40.7)	43.2 (37.4-51.7)	0.001
PaCO <sub>2</sub> mmHg	41.8 (37-53.1)	51 (41-59.9)	<0.001
Hypercapnia at discharge,n	85/31	37/40	<0.001
Arrhythmias	94/22	50/27	0.018
Cor pulmonale,n	88/28	34/43	<0.001
Uremia,n	91/25	47/30	0.010
Hypoalbuminemia,n	9/17	52/25	0.004
ICU admission,n	109/7	58/19	<0.001

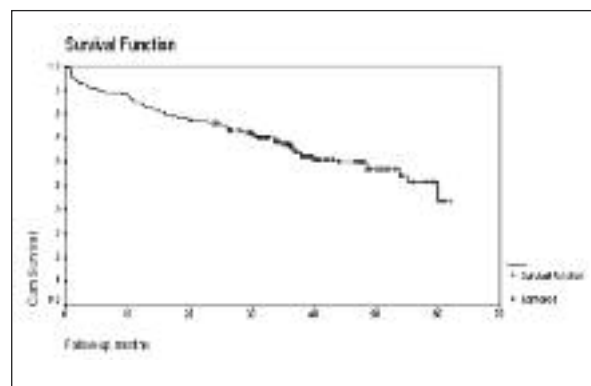
ES: exsmoker; NS: nonsmoker

Continuous variables are presented as mean ± standard deviation, and median values (25-75% percentiles).

Cox regression analysis showed that increased age (HR1.04; 95% CI, 1.01-1.07), lower BMI (HR 0.89; 95% CI, 0.84-0.94), GOLD stage IV (HR 2.74; 95% CI, 1.31-5.70), cor pulmonale (HR 3.53; 95% CI, 2.15-5.80), ICU admission (HR 3.21; 95% CI, 1.84-5.61) were independently related to mortality (Table 4).

## DISCUSSION

The present study confirms that most patients with an acute exacerbation of COPD survived their hospital stay (hospital mortality rate of 5.2%), and the



**FIGURE 1:** Survival curve of 193 patients hospitalized for acute exacerbation.



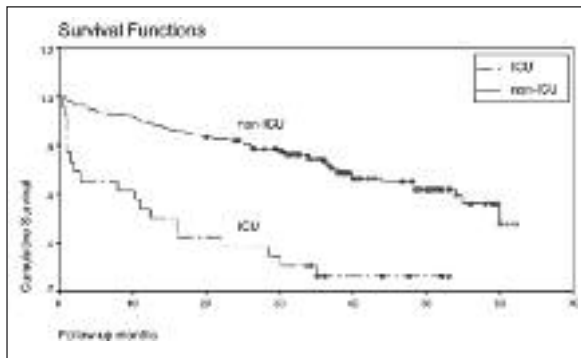


FIGURE 2: Kaplan-Meier survival curves for ICU and non-ICU patients .

mortality rates continued to increase substantially in one (15.5%), 2 (23.8%), 3 (32.1%) and four years (36.8%) after discharge. The follow-up time is one of the longest periods for that group of patients in the literature. The results of this study support the previous findings from studies investigating predictive factors of mortality after hospital discharge, and also contributes to the long-term outcome data. Advanced age, severe COPD, lower BMI, the presence of cor pulmonale, and the need for the ICU admission were associated with increased mortality risk.

In-hospital mortality rate of patients with acute exacerbation of COPD has been reported to be between 2.5% and 30%.<sup>9,10</sup> Patil et al. reported the lowest in-hospital mortality rate of 2.5% based on a nationwide sample of patients.<sup>9</sup> For the patients admitted to the ICU with an acute exacerbation of COPD, mortality was 30% during the hospital stay.<sup>9</sup> In previous reports, the mortality rate has been found between 6.4% and 8.3%.<sup>12,13,17</sup> In-hospital mortality rate of our patients requiring

the ICU admission (30.8%) is similar to other studies.<sup>10,15,18</sup>

The mortality rates following hospitalization for an acute exacerbation of COPD were found to be slightly lower compared to other long-term survival studies. However, the difference between our results and the results of these long-term survival studies may be related to the patient population, and the data collection method. The highest mortality rates at subsequent years after hospital discharge have been reported for patients admitted to the ICU for an acute exacerbation of COPD. Seneff et al. found mortality as 59% one year after hospitalization in patients aged 65 years or older admitted to an ICU with an acute exacerbation of COPD.<sup>10</sup> The mortality rates in one, three and five years were found as 42.7%, 61.2% and 75.9% for patients treated in the ICU for acute exacerbation of COPD by Ai-Ping et al.<sup>16</sup> The largest study on survival after hospital admission for acute exacerbation of COPD was performed by Connors et al., and they reported that mortality rates one year and two years after discharge were 43% and 49%, in a cohort of 1016 patients.<sup>11</sup> However, the high mortality rates in first year were the result of the patient population consisted of seriously ill, hypercapnic patients ( $\text{PaCO}_2 \geq 50$  mmHg). Our department is one of the largest pneumology ward in the capital of the country, besides its academic function. Therefore, this patient population is representative of general pulmonary practices. With regard to patient population, the following studies were similar to our study, as they investigated long-term outcomes in patients hospitalized for an acute exacerbation of COPD to the pneumology wards of

TABLE 4: Cox proportional hazard analysis for factors associated with mortality.

Variables	B	Wald	HR	95%CI	p value
Age,yrs	0.04	7.41	1.04	1.01-1.07	0.006
BMI kg/m <sup>2</sup>	-0.11	14.22	0.89	0.84-0.94	<0.001
GOLD Stage II			1		
GOLD Stage III	0.58	2.20	1.8	0.82-3.91	0.13
GOLD Stage IV	1.00	7.29	2.74	1.31-5.7	0.007
Cor pulmonale	1.26	24.95	3.53	2.15-5.80	<0.001
ICU admission	1.16	16.87	3.21	1.82-5.61	<0.001

B: beta coefficient, HR: hazard ratio, CI:confidence interval.

tertiary referral centers. Mortality in one year and two years was found as 22% and 35.6% by Almagro et al.<sup>7</sup> The 1-year mortality was 23% in the study of Groenewegen et al. for patients who admitted to the hospital with an acute exacerbation.<sup>12</sup> Gunen et al. reported 1-, 2- and 3-year mortality rates as 33%, 39% and 49%, respectively.<sup>13</sup>

In the present study, age was an independent predictor of mortality. In majority of other studies, age has been demonstrated as an important determinant of survival in COPD patients,<sup>11,12,19-23</sup> and older age has been found as a significant predictor of mortality in follow-up studies on stable COPD patients and on patients admitted to the hospital for an acute exacerbation.

The most remarkable finding of this study was that the disease stage defined by GOLD criteria (recommends the use of postbronchodilator lung function measurements) was an independent predictor of long-term mortality in patients hospitalized for an acute exacerbation of COPD. Previous studies have demonstrated that lower levels of lung function lead to higher mortality.<sup>20,24</sup> In a large cohort of subjects followed up for 11 years, it was shown that GOLD classification system predicted the mortality, and risk of death increased by the disease severity.<sup>25</sup> In another study, rapid lung function decline was found to be associated with an increased risk of death in COPD patients. Among them, patients with GOLD stage 3 and 4 disease were more likely to be in the most rapidly declining quartile.<sup>26</sup> The present study showed that GOLD 4 patients had an increased risk of death during the follow-up time. With this data coming from Turkey, it can be emphasized that it is important to have previous lung function measurements to stage the study patients. So we could reliably stage COPD, and we found a strong relationship between the GOLD stage and outcome.

In our study, there was no influence of comorbidity on mortality expressed by Charlson comorbidity index, in contrast to a report by Almagro et al. which found the greater comorbidity index (Charlson index) was a significant predictor of mortality in a follow-up study after hospitalization for COPD.<sup>7</sup> This may be explained by our lower

Charlson index scores of 1.76 (as compared to 2.22 as reported by Almagro et al.), and it should be related to the retrospective data collection.

Another finding of our study was that lower BMI was an independent predictor of long-term mortality in COPD patients after an acute exacerbation. Several studies have shown that low BMI is a strong predictor of poor long-term survival in COPD.<sup>11,26,27</sup> Weight loss is prevalent among patients with COPD, 20% of those with a stable condition, and 35% of patients who are hospitalized.<sup>29,30</sup> Body mass index <25 kg/m<sup>2</sup> was demonstrated to be a threshold value below which the mortality risk was increased significantly by Schols and colleagues.<sup>27</sup>

In the present study, the presence of cor pulmonale was demonstrated to be associated with the mortality in this population. Cor pulmonale is a known factor of poor prognosis in COPD patients.<sup>31,32</sup> The appropriate treatment of cor pulmonale and follow-up of these patients should be performed carefully, since the long-term outcomes of patients who have cor pulmonale will be poor compared to others.

The need for the ICU admission has been shown to be a predictor of mortality in COPD patients hospitalized for an acute exacerbation in this study. For the ICU patients, the mortality rates were found to be 46.1%, 61.5%, 69.2%, and 73% in one, two, three and four years, respectively. The need for the ICU admission is a result of a severe exacerbation, and the prognosis of this group of patients is commonly believed to be poor.<sup>33</sup> Data on long-term survival after hospital discharge for this group of patients is limited. Seneff and colleagues reported the one year mortality as 59%, and they showed that mortality has doubled in one year after hospital discharge.<sup>10</sup> Breen et al. found the mortality rate in COPD patients treated in the ICU as 64% in three years.<sup>34</sup> The longest follow-up study so far reported a mortality rate of 75.9% in five years.<sup>15</sup> According to our results, patients who require admission to the ICU have significant in-hospital mortality, and the survivors from a severe acute exacerbation have an increased risk of mortality in the subsequent years.

The limitation of this study was that we could not be able to identify the specific cause of death, we only reported the overall death rates in this study. Despite that point, our follow-up rate was >90%, and the data we used mainly consisted of clinical and laboratory parameters which are routinely recorded in patient's chart in our department.

The results of this study demonstrate several factors that are useful to predict the long-term mortality after hospitalization for an acute exacerbation of COPD. Advanced age, severe COPD, lower BMI, the presence of cor pulmonale, and need for the ICU admission were independently as-

sociated with mortality. With this regional data from Turkey, it was aimed to emphasize the clinical importance of having lung function data for COPD patients and using a standardized method (GOLD) in order to stage the disease which is also a strong determinant of the long-term outcome after an acute exacerbation.

**Conflict of Interest Statement:** None of the authors have a conflict of interest to declare in relation to this work. Any private company was not involved in the data collection, the interpretation of the results and/or the redaction of the manuscript, and the authors had full access to the data.

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