

# One-year and long-term mortality in patients hospitalized for chronic obstructive pulmonary disease

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**Background:** Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide. Identifying potentially-modifiable predictors of mortality could help optimize COPD patient management. The aim of this study is to determine long-term mortality following hospitalization due to acute exacerbations of COPD (AECOPD), as well as AECOPD mortality predictors.

**Methods:** We conducted a retrospective study by reviewing the medical records of all patients admitted with AECOPD in the University Hospital Complex of Santiago de Compostela in 2007 and 2008. In order to identify variables independently associated with mortality, we conducted a multivariate Cox proportional hazard regression analysis including those variables which proved to be significant in the univariate analysis.

**Results:** Seven hundred and fifty seven patients were assessed. Patient mean age was 74.8 years and males accounted for 77% of all patients. Mean stay was 12.2 days. Three point six percent of all patients required intensive care. As for mortality rates, 1-year mortality was 26.2%, and 5-year mortality was 64.3%. In both scenarios, the most frequent causes of death were respiratory and cardiovascular disorders. Factors independently associated with mortality were older age, hospitalization by internal medicine (IMU), length of stay, the need for mechanical ventilation (MV) or noninvasive mechanical ventilation (NIV), early readmission, and history of atrial fibrillation (AF) and dementia.

**Conclusions:** In patients with COPD, age, exacerbation severity and comorbidity have long-term prognostic significance.

**Keywords:** Chronic obstructive pulmonary disease (COPD); exacerbation; hospitalization; long-term mortality

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## Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide (1). Recurrent in the course of the disease, acute exacerbations of COPD (AECOPD) worsen baseline symptoms, impair pulmonary function over time and increase the likelihood of new exacerbations (2,3). Initially, increased mortality had been attributed to baseline disease severity. However, recent studies have shown that AECOPD increase short-term and long-term mortality risk, especially those exacerbations requiring hospitalization (4). Other prognostic factors include age, several comorbidities, the need for oxygen therapy at home, previous hospitalization due to AECOPD, exacerbation severity and a number of physiological and laboratory parameters, such as anemia and hypercapnia (5-8). Nevertheless, these factors vary across studies, probably due to differences in analyzed populations, collected variables and statistical methods. Thus, identifying potentially-modifiable predictors of mortality could help optimize both therapeutic strategies and COPD patient management upon discharge.

The aim of this study is to determine long-term mortality following hospitalization due to AECOPD, as well as AECOPD mortality predictors.

## Methods

We conducted a retrospective study by reviewing the medical records of all patients admitted with AECOPD in the University Hospital Complex of Santiago de Compostela in 2007 and 2008. Data were retrieved from the hospital database, and included the first admission of all patients admitted to the Internal Medicine (IMU) and Pneumology Units in the study period. The study sample includes 757 patients, whose baseline characteristics, comorbidities and AECOPD characteristics during hospitalization were recorded.

COPD diagnosis and baseline severity were defined following GOLD criteria (9). In those cases with no spirometry available, COPD diagnosis was accepted by consensus of the research team for patients with a smoking history and clinical and radiological characteristics consistent with such diagnostic hypothesis (10-12). Patients who had quit smoking at least 1 year before the moment of admission were considered former smokers (13). Alcohol users were sorted into four different categories: those consuming over one gram alcohol per day (regular drinkers) (14), those consuming less than one gram alcohol per day

(occasional drinkers); those who quit at least 1 year before (former drinkers) (15) and never drinkers. Comorbidities registered include atrial fibrillation (AF), arterial hypertension (HTN), ischemic heart disease (IHD), cancer, cerebrovascular accident (CVA), dementia, chronic kidney disease (CKD) and liver disease. Comorbidity was assessed with the Charlson Index (16), and categorized into three groups: patients scoring “zero”, “1 or 2”, and “over 2” points, respectively. COPD baseline therapy was noted: short-acting and long-acting beta2-agonist inhalers, oral or inhaled corticosteroids, anticholinergics, theophylline, oxygen therapy and noninvasive mechanical ventilation (NIV) at home. The use of at least 5 mg prednisone per day for at least 3 months in a row was considered chronic steroid therapy (17).

Weekends were defined as the period between Friday midnight and Sunday midnight (18). Early readmission was defined as that occurring within 15 days upon discharge (19).

Vital signs and arterial blood gas values were obtained upon patient arrival to the Emergency Department (ED). In those cases where no blood gas was determined, a record of O<sub>2</sub> saturation by pulse oximetry was obtained. Data from the CBC and serum biochemistry tests conducted on the first sample obtained upon arrival to the hospital were recorded. Anemia was defined as per WHO criteria: hemoglobin (Hb) <13 g/dL in males and Hb <12 g/dL in females (20).

Causes of death were retrieved from patient clinical records, both for deaths during the admissions studied and in subsequent admissions. We reviewed the death certificates of patients in doubtful cases, as well as the death certificates of those who died at home. Cause of death was sorted as follows: (I) respiratory causes: AECOPD (ICD-10 DJ440/DJ441), respiratory failure (DJ96) and lower respiratory tract infection (DJ12-DJ18); (II) cardiovascular causes: acute coronary syndrome (ACS) (DI21), heart failure (DI50), CVA (DI61-DI63), and pulmonary embolism (DI26); (III) cancer; (IV) other causes, including septic shock (DR57) and aspiration (DJ69) (21); (V) unknown origin (DR98, DR99).

## Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

As a retrospective study, formal consent is not required.

### Statistical analysis

Data obtained were expressed as mean values  $\pm$  standard deviation (SD) for continuous variables, and as frequencies and percentages for categorical variables. Continuous variables were compared with either Student's *t*-test or with Wilcoxon's test; as for categorical variables, they were compared with the chi-squared and Fisher's exact tests. In order to identify variables independently associated with 1-year mortality, we conducted a Cox regression including those variables with  $P \leq 0.05$  in the univariate analysis. We considered statistically significant those variables associated with  $P < 0.05$ . Data were analyzed with SPSS 15.

### Results

Seven hundred and fifty seven patients were assessed; 77% were males and mean age was 74.8 years (SD 11.2). Mean stay was 12.2 days (SD 9.1), and 3.6% of all patients required intensive care. Patient baseline characteristics are shown in *Table 1*. Acute exacerbation characteristics and complementary test results are shown in *Table 2*.

Hospital mortality rate was 4.8%, and the most frequent cause of death were respiratory disorders. One-year mortality rate was 26.2%, due to respiratory causes (52%), cardiovascular causes (19.6%), cancer (7.2%), other (18%) and unknown causes (3%). Five-year mortality rate was 64.3%, with the following causes: respiratory (49.1%), cardiovascular (20.1%), cancer (9.7%), other (19.2%) and unknown causes (1.6%). Factors significantly associated with increased mortality within the year following hospitalization for AECOPD included older age ( $P=0.001$ ), COPD baseline severity ( $P=0.001$ ), comorbidities such as AF ( $P=0.006$ ), HTN ( $P=0.01$ ), IHD ( $P=0.005$ ), CVA ( $P=0.02$ ), dementia ( $P=0.03$ ) and KCD ( $P=0.01$ ), comorbidity index ( $P=0.03$ ), and the need for oxygen therapy at home ( $P=0.001$ ) and hospitalization due to AECOPD the year before the first admission in the study period ( $P=0.03$ ). Other mortality-related factors were prolonged mean stay ( $P < 0.0001$ ), hospitalization by IMU ( $P < 0.0001$ ), anemia ( $P < 0.0001$ ), and the need for MV (NIV:  $P=0.03$ ; MV:  $P < 0.0001$ ). Factors associated with 5-year mortality were age ( $P < 0.0001$ ), baseline COPD severity ( $P < 0.0001$ ), AF ( $P=0.002$ ), IHD ( $P=0.02$ ), dementia ( $P=0.004$ ), CKD ( $P=0.0001$ ), comorbidity index ( $P=0.003$ ), the need for oxygen therapy at home ( $P=0.001$ ), hospitalization due to AECOPD the year before ( $P=0.02$ ), prolonged mean stay ( $P < 0.0001$ ), hospitalization by IMU ( $P < 0.0001$ ), anemia ( $P < 0.0001$ ) or

atelectasis ( $P=0.01$ ), as well as the need for NIV ( $P=0.04$ ).

Factors independently associated with 1-year mortality in multivariate analysis were older age (HRR 1.05), length of stay (HRR 1.04), the need for MV (HRR 2.68), early readmission (HRR 2.32), and history of AF (HRR 1.54) and dementia (HRR 2.44) (*Table 3*); those associated with 5-year mortality were older age (HRR 1.04), hospitalization by IMU (HRR 1.41), prolonged mean stay (HRR 1.03), the need for NIV (HRR 1.38), and history of AF (HRR 1.37) and dementia (HRR 2.79) (*Table 4*).

### Discussion

Mid-term and long-term mortality of patients admitted for AECOPD to our hospital are mainly due to respiratory and cardiovascular causes. Mortality risk factors include older age, length of stay, the need for MV, hospitalization by the IMU, early readmission, AF and dementia.

In our sample, both hospital mortality and one-year mortality rates are similar to those in previous studies (5,7). However, our 5-year mortality rate is lower to that referred by other authors. Chung *et al.* report a 74% mortality rate following hospitalization due to AECOPD requiring NIV (22), and the rate reported is 76% for patients with AECOPD requiring admission to the ICU (23); 5-year mortality is 73% in the study by Steinmetz (24) and 79% in that by Gudmundsson (21). The difference could be explained by the fact that some of these studies only include patients admitted to the ICU or treated with NIV, probably due to the more severe nature of AECOPD. Thus, they could result in increased mortality in spite of more intensive patient management. However, Gudmundsson's patients, admitted to Pneumology Units, show higher mortality rates even if younger, and the study by Steinmetz includes both hospitalized patients and outpatients, a priori with apparently less severe exacerbations.

Indications for NIV include respiratory acidosis and severe dyspnea with clinical signs of muscle fatigue or increased work of breathing (10). NIV has been shown to effectively treat respiratory failure from various causes, including AECOPD (25,26). In fact, previous studies and international guidelines on COPD clearly suggest the use of noninvasive ventilation (NIV) as the first-line choice for hospitalized patients with severe AECOPD (10,27-31). However, patients treated with NIV in our study show higher long-term mortality, leaving the impression that these results support the concept that the use of NIV for AECOPD may be a dangerous approach instead of a beneficial one.

**Table 1** Patient baseline characteristics

Characteristics	1-year survival			5-year survival		
	No [198]	Yes [559]	P	No [485]	Yes [269]	P
Age (mean $\pm$ SD)	78.9 (8.8)	73.3 (11.6)	0.001	77.4 (9.9)	69.9 (11.8)	<0.0001
Gender (male), n (%)	154 (77.8)	431 (77.1)	0.800	377 (77.7)	206 (76.6)	0.70
Tobacco use, n (%)			0.600			0.10
Never smokers	47 (32.4)	127 (29.1)		110 (29.6)	63 (30.1)	
Active smokers	33 (22.8)	111 (25.4)		81 (21.8)	62 (29.7)	
Former smokers	65 (44.8)	199 (45.5)		180 (48.5)	84 (40.2)	
OH use, n (%)			0.400			0.70
Regular drinkers	54 (40.6)	157 (41.6)		127 (39.7)	83 (43.9)	
Occasional drinkers	6 (4.5)	18 (4.8)		14 (4.4)	10 (5.3)	
Never drinkers	22 (16.5)	42 (11.1)		42 (13.1)	22 (11.6)	
Former drinkers	51 (38.3)	160 (42.4)		137 (42.8)	74 (39.2)	
GOLD, n (%)			0.001			<0.0001
I	16 (11.6)	65 (17.9)		39 (12.0)	42 (24.4)	
II	47 (34.1)	159 (43.8)		130 (39.9)	75 (43.6)	
III	4 (2.9)	8 (2.2)		9 (2.8)	3 (1.7)	
IV	71 (51.4)	131 (36.1)		148 (45.4)	52 (30.2)	
FEV <sub>1</sub> (mean $\pm$ SD)	1.3 (1.29)	1.39 (0.94)	0.500	1.34 (1.14)	1.41 (0.84)	0.60
Comorbidities, n (%)						
AF/flutter	64 (32.3)	126 (22.5)	0.006	140 (28.9)	50 (18.6)	0.002
HTN	114 (57.6)	265 (47.5)	0.010	243 (50.2)	133 (49.4)	0.80
DM	44 (22.3)	265 (47.5)	0.400	111 (23.0)	73 (27.1)	0.20
IHD	55 (27.8)	102 (18.3)	0.005	113 (23.3)	44 (16.5)	0.02
Cancer	32 (16.2)	69 (12.3)	0.100	69 (14.2)	32 (11.9)	0.30
CVA	27 (13.7)	46 (8.2)	0.020	53 (11.0)	20 (7.4)	0.10
Dementia	14 (7.1)	19 (3.8)	0.030	29 (6.0)	4 (1.5)	0.004
CKD	25 (12.7)	40 (7.2)	0.010	55 (11.4)	10 (3.7)	<0.0001
Liver disease	14 (1.8)	38 (5.0)	0.800	35 (7.2)	17 (6.3)	0.60
Charlson, n (%)			0.030			0.003
0	2 (1.0)	5 (0.9)		4 (0.8)	3 (1.1)	
1–2	57 (28.8)	212 (37.9)		154 (31.8)	114 (42.4)	
>2	139 (70.2)	342 (61.2)		327 (67.4)	152 (56.5)	

**Table 1** (continued)

Table 1 (continued)

Characteristics	1-year survival			5-year survival		
	No [198]	Yes [559]	P	No [485]	Yes [269]	P
Baseline therapy, n (%)						
Inhaled Ach	117 (64.6)	305 (60.9)	0.300	284 (63.5)	138 (59.5)	0.30
SABA	55 (30.6)	175 (35.0)	0.200	144 (32.3)	84 (36.4)	0.20
LABA	109 (60.6)	284 (56.8)	0.300	260 (58.3)	131 (56.7)	0.60
Inhaled corticosteroids	114 (63.3)	296 (59.2)	0.300	273 (61.2)	135 (58.4)	0.40
Theophylline	11 (6.1)	25 (5.0)	0.500	26 (5.8)	10 (4.3)	0.40
Oral corticosteroids	8 (4.4)	26 (5.2)	0.600	22 (4.9)	12 (5.2)	0.80
O <sub>2</sub> therapy at home	69 (35.0)	127 (22.8)	0.001	144 (29.8)	50 (18.6)	0.001
NIV at home	16 (8.2)	42 (7.6)	0.700	43 (9.0)	15 (5.6)	0.10
Hospitalization due to AECOPD-previous year, n (%)	66 (33.3)	143 (25.6)	0.030	148 (30.5)	61 (22.7)	0.02
Emergency due to AECOPD-previous year, n (%)	67 (33.8)	217 (38.8%)	0.200	192 (39.6)	92 (34.2)	0.10

OH, alcohol; AF, atrial fibrillation; HTN, hypertension; DM, diabetes mellitus; IHD, ischemic heart disease; CVA, cerebrovascular accident; CKD, chronic kidney disease; Ach, anticholinergics; SABA, short-acting beta2 agonists; LABA, long-acting beta2 agonists; NIV, noninvasive ventilation.

Other authors also refer this finding, which could be related to inadequate indication of NIV or to greater exacerbation severity. Greater baseline severity of patients may also influence, as it is the case of those patients not considered subsidiary of MV due to comorbidities and treated with NIV.

Factors such as old age and underlying diseases may influence the decision to intubate or not to intubate some patients, thus assuming a worse prognosis in these cases (32). Besides, patients requiring NIV are known to have poor prognosis (33-35).

Possible reasons to explain our seemingly contradictory results could include: PCO<sub>2</sub> high levels, suggesting AECOPD severity; the history of NIV therapy, suggesting higher COPD baseline severity; and a number of indicators of the overall health condition could explain the worse prognosis and the high long-term mortality risk in those patients treated with NIV and admitted for AECOPD (36-40). In our study, over half of all patients with ventilatory support were classified as stage IV in the GOLD classification and ranked high on the Charlson scale. Severe AECOPD may require admission to the ICU and the use of MV, especially with ineffective NIV (41), and subsequent complications due to AECOPD severity or decompensation. So, patient characteristics and the decision to put them or not into particular care seem to

influence prognosis, and not NIV per se.

Patients hospitalized for AECOPD with prolonged stay show higher hospital and long-term mortality rates (5,42), possibly due to the contribution by other factors justifying worse prognosis, such as nosocomial infections, thromboembolic disease and decompensation of underlying diseases (43-45). Prolonged stays may help identify frailer patients potentially requiring more careful attention, either due to COPD baseline severity or due to AECOPD severity (46,47). These factors may also contribute to a higher mortality risk (4). In our sample, both anemia and underlying diseases, as well as older age and indicators of higher AECOPD severity, such as admission to the ICU or the need for MV, were predictors of higher long-term mortality, although not all of them were confirmed by multivariate analysis.

According to a recent study, mortality risk increases over time in a 3-year follow-up period for those patients readmitted within the first month after discharge (2). The number of comorbidities, advanced age, respiratory acidosis and the need for NIV are factors directly associated with the probability of early readmission following AECOPD discharge (48,49). These factors were also associated with long-term mortality in our sample.

**Table 2** Characteristics of acute exacerbation (univariate analysis)

Characteristics	1-year survival			5-year survival		
	NO [198]	YES [559]	P	NO [488]	YES [269]	P
Weekend admission, n (%)	47 (23.7)	112 (20.0)	0.200	107 (22.1)	51 (19.0)	0.30
Mean stay, n (SD)	16 (1.8)	11 (6.2)	<0.0001	13.6 (10.5)	9.8 (5.1)	<0.0001
Admission unit, n (%)			<0.0001			<0.0001
Pneumology	118 (22.2)	414 (77.8)		308 (58.1)	222 (41.9)	
Internal medicine	80 (35.6)	145 (64.4)		177 (79.0)	47 (21.0)	
Laboratory data						
Hb <12 mg/dL, n (%)	68 (34.3)	89 (16.1)	<0.0001	122 (25.4)	35 (13.1)	<0.0001
Platelets	247,755 [105,168]	25,0452 [103,966]	0.700	250,624 [106,384]	247,691 [99,385]	0.70
Leukocytes	11,695 [5,231]	11,600 [5,622]	0.800	11,569 [5,328]	11,662 [5,834]	0.80
Glucose	148 [77]	141 [63]	0.200	146 [73]	137 [55]	0.80
Urea	67.7 (39.2)	66 (36.1)	0.500	66 (38.0)	65 (35.0)	0.70
Creatinine	1.2 (0.6)	1.1 (0.7)	0.700	1.14 (0.6)	1.15 (0.8)	0.90
Total protein count	6.4 (0.6)	6.3 (0.7)	0.200	6.4 (0.6)	6.3 (0.7)	0.05
Albumin	3.8 (2.5)	3.9 (3.7)	0.700	3.9 (4.0)	3.6 (1.8)	0.20
Fibrinogen	482 (162.8)	243.8 (62.3)	0.300	459 (156.0)	446 (146.0)	0.40
Initial blood gas						
pH	7.4 (0.8)	7.4 (0.8)	0.200	7.4 (0.08)	7.4 (0.07)	0.10
PCO <sub>2</sub>	48 (15.5)	46.3 (15.8)	0.200	47.4 (16.1)	45.8 (15.0)	0.10
PO <sub>2</sub>	56.3 (14.3)	59 (20.4)	0.100	57 (16.3)	59 (15.0)	0.40
Bicarbonate	28.7 (5.8)	28.2 (5.6)	0.200	28.4 (5.8)	28.1 (5.4)	0.40
O <sub>2</sub> /FiO <sub>2</sub>	239 (57.2)	244 (62.3)	0.300	244 (61)	238 (59)	0.30
Chest radiograph, n (%)						
pleural effusion	20 (10.1)	83 (14.9)	0.090	66 (13.6)	37 (13.8)	0.90
Cardiomegaly	51 (25.8)	153 (27.4)	0.600	125 (25.8)	79 (29.4)	0.20
Atelectasis	14 (7.1)	26 (4.7)	0.200	33 (6.8)	7 (2.6)	0.01
Bronchiectasis	5 (2.5)	26 (4.7)	0.200	15 (3.1)	16 (5.9)	0.05
CHF/APE	0 (0)	7 (1.3)	0.100	4 (0.8)	4 (0.8)	0.60
Pneumonia	14 (7.1)	40 (7.2)	0.900	34 (7.0)	18 (6.7)	0.80
ICU, n (%)	17 (8.6)	10 (1.8)	0.090	22 (4.5)	5 (1.9)	0.05
ICU mean stay	14.7 (12.9)	8 (4.7)	0.0600	13.2 (11.8)	7.8 (5.4)	0.30
NIV, n (%)	39 (19.7)	75 (13.4)	0.0300	82 (16.9)	31 (11.5)	0.04
MV, n (%)	18 (9.1)	9 (1.6)	<0.0001	22 (4.5)	5 (1.9)	0.05
Antibiotic therapy, n (%)	178 (89.5)	489 (87.5)	0.300	431 (88.9)	234 (87.0)	0.40
Early readmission, n (%)	19 (10.1)	25 (4.5)	0.005	34 (7.2)	10 (3.7)	0.05
Late readmission, n (%)	87 (43.9)	287 (51.3)	0.070	250 (51.1)	123 (45.7)	0.12

CHF, congestive heart failure; APE, acute pulmonary edema; ICU, intensive care unit; NIV, noninvasive ventilation, MV, mechanical ventilation; Hb, hemoglobin.

**Table 3** Factors related to 1-year mortality following hospitalization due to AECOPD

Variables	Hazard ratio	95% CI	P value
Age	1.05	1.03–1.07	<0.0001
AF	1.54	1.01–2.35	0.0400
Dementia	2.44	1.08–5.49	0.0300
MV	2.68	1.16–6.15	0.0200
Mean stay	1.04	1.02–1.06	<0.0001
Early readmission	2.32	1.30–4.17	0.0050

AECOPD, acute exacerbations of COPD; AF, atrial fibrillation; MV, mechanical ventilation.

**Table 4** Factors related to 5-year mortality following hospitalization due to AECOPD

Variables	Hazard ratio	95% CI	P value
Age	1.04	1.02–1.05	<0.0001
AF	1.37	1.05–1.78	0.0200
Dementia	2.79	1.55–5.02	0.0010
NIV	1.38	1.03–1.86	0.0300
Mean stay	1.03	1.02–1.04	<0.0001
Admission to IMU	1.41	1.09–1.84	0.0090

AECOPD, acute exacerbations of COPD; AF, atrial fibrillation; NIV, non-invasive ventilation; IMU, Internal Medicine Unit.

Admission for AECOPD to the IMU is a long-term mortality risk factor compared to patient admission to the Pneumology Unit. These results seem real in our population, as they are adjusted for multiple factors. However, we cannot exclude potential impacts from other variables not analyzed in our study.

AF and IHD rates were higher in those patients admitted to the IMU. Both diseases are subject to decompensation with the beta<sub>2</sub>-agonists and the anticholinergics used to treat AECOPD, and complications therefrom could influence mortality (50). The contribution by these factors seems relevant in our patients, as both older age and AF were independently associated with mortality in our multivariate analysis.

Nevertheless, other authors report differences in respiratory disease management outcomes depending on the specialist staff providing the medical care (51,52), which could contribute to greater survival. In a recent study by Wijayarathne *et al.* (52), 1-year mortality was 10.7% in the

General Medicine group, and 6% in that of respiratory specialists. The difference seems relevant, being almost twice as much. However, it was not statistically significant, probably due to the reduced sample size. Other study with asthma patients objectively reports significant differences between specialists and general practitioners (53).

Patients with COPD have a significant prevalence of cognitive impairment (54), and patients with dementia have worse prognosis and shorter life expectancy (55). In spite of these data, little is known regarding how dementia is an additional risk for the worse prognosis of patients with COPD. A recent study has shown that dementia increases the risk of respiratory failure and hospital mortality in patients with COPD (56). Factors accounting for the higher long-term mortality risk could include weight loss and lower BMI as a result of poor diet and various catabolic problems in patients with dementia (57), as well as physical inactivity, deficiency in self-care and bronchial aspiration, which are frequent in these patients and are possible causes of mortality (58).

AF is the most common arrhythmia in the general population (59) and in patients with COPD, and the incidence of AF increases with decreasing FEV<sub>1</sub> (60). AF has an adverse impact on COPD prognosis and mortality (61); also, a recent study in patients with AF reported COPD to be independently associated with increased mortality from both cardiovascular and non-cardiovascular causes (62). The mechanism responsible for increased mortality in patients with AF and COPD seems not only related to the shared risk factors, such as tobacco use or age, but rather to thromboembolic events associated with FA and resulting from hypercoagulable states, and increased platelet aggregation, frequent in COPD (63,64), regardless of pulmonary HTN and prescribed treatment for underlying cardiovascular diseases (62). On the other hand, bleeding complications resulting from the use of anticoagulants, frequent in patients with AF and favored by age, comorbidities and polypharmacy, could influence the increased mortality of these patients (65). We have no reason to think the possible causes of higher mortality attributed to AF to differ therefrom in our patients.

Our study shows the prognostic significance of age, those factors related to AECOPD severity and a number of comorbidities for mortality risk. Nevertheless, the results should be interpreted with caution due to limitations, such as the lack of recorded information, inherent to retrospective studies, and the assumption that the information in the files reflects clinical practice. The

seemingly high number of never-smokers seems attributable to the fact that tobacco use is underreported in medical records, a rather common problem in our country, as we know from the data in other studies. Thus, patients are not considered smokers if no information on tobacco use has been recorded. Furthermore, as our data come from a single hospital, they might not be generalized to other populations.

In conclusion, long-term mortality rate of COPD patients is high, and patient age, AECOPD severity and a number of comorbidities influence prognosis.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. As a retrospective study, formal consent is not required.

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