British Journal of Medicine & Medical Research
5(2): 221-234, 2015, Article no.BJMMR.2015.023
ISSN: 2231-0614

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Cohort Study of Factors Contributing to Mortality Two Months after Exacerbation of COPD According to Patient Destination from Emergency Department

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Authors' contributions

This work was carried out in collaboration between all authors. Authors MB and JMQ conceived the study and participated in its design and coordination. Author MB drafted and approved the final version of the manuscript. Authors CM, XP, JF, CE, SV and AS participated in the acquisition of data, helped in the interpretation of the results and revised the manuscript critically for important intellectual content. Authors MB and NT supported the statistical analysis. All authors critically reviewed the manuscript. All of them read and approved the final manuscript.

Article Information

DOI:10.9734/BJMMR/2015/11853
Editor(s):
(1) Jimmy T. Efird, Department of Public Health, Epidemiology and Outcomes Research East Carolina Heart Institute, Brody School of Medicine, Greenville, North Carolina, USA.
Reviewers:
(1) Anonymous, Dicle University, Turkey.
(2) Anonymous, Moh Bakirköy Sadi Konuk Training and Research Hospital, Turkey.
(3) Anonymous, Ladoke Akintola University of Technology, Nigeria.
Peer review History: http://www.sciencedomain.org/review-history.php?iid=661&id=12&aid=5995

Original Research Article

Received 6th June 2014
Accepted 25th July 2014
Published 8th September 2014

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ABSTRACT

Background: We aimed to determine the mortality two months after exacerbation of chronic obstructive pulmonary disease (eCOPD) and to identify factors associated with mortality, comparing patients admitted to wards and those discharged to home from the emergency department.
Methods: This prospective multicentre study included all consecutive patients presenting with eCOPD at emergency departments in 16 public hospitals in Spain. Clinical variables were recorded from a standardized questionnaire**.** Independent predictors of mortality were modelled by logistic regression analysis. The calibration and discriminative power of the models for the two groups (discharged and admitted) were estimated by the Hosmer-Lemeshow test and the area under the curve (AUC), respectively. Bootstrap methods were applied for internal validation.
Results: 2487 patients were included; 1537 (62%) of these were admitted to wards. A total of 155 (6.2%; 95% CI: 5.2% - 7.1%) patients had died at 2 months: mortality was four times higher in patients admitted than in patients discharged. Age ≥ 80 years, Charlson score >2, and pronounced dyspnoea were independent factors for mortality in both groups; in admitted patients, Glasgow scale, baseline treatments for COPD, previous heart disease, complications during hospitalization, and corticoids at discharge were also independent factors.
Conclusions: In eCOPD, age, comorbidities, and dyspnoea are important for short-term prognosis in both patients admitted to wards and those discharged to home. In patients admitted to wards, the severity of baseline disease and eCOPD and corticoid treatment affect the short-term prognosis.

Keywords: Fatal prognosis; dyspnoea; comorbidity; destination.

1. INTRODUCTION

In most developed countries, the exacerbation of chronic obstructive pulmonary disease (eCOPD) is among the most common reasons for hospitalization; [1,2] eCOPDs accelerate declines in patients' pulmonary function and quality of life and have a negative impact on survival [3,4]. Reported hospital mortality for patients with eCOPD requiring hospitalization ranges from 2.5% to 30% [5,6].

Various clinical factors are associated with short-term fatal outcome in patients with eCOPD [7,8]. The degree of dyspnoea or fatigue and baseline treatment have been analyzed less. Furthermore, most studies have evaluated the factors associated with mortality or other outcomes in hospitalized patients; [5,9] few have followed up patients discharged to home [10]. Patients attended at the emergency department (ED) for eCOPD who are not hospitalized because of their clinical condition or other factors could have other disease-related parameters or other patient-related factors that affect short-term prognosis. Mortality is one of the most objective and easiest outcomes to identify. In general, eCOPD is considered to take up to about 8 weeks until it is completely under control and any exacerbation of disease after this period would be considered a relapse or new eCOPD [11].

Given the scant evidence for some of these questions, within the context of a collaborative study, [12,13] we aimed to identify factors independently associated with mortality in patients attended in hospital EDs for eCOPD and to determine whether mortality and associated factors differed between patients discharged to home and those who were hospitalized.

2. METHODS

This prospective, observational, multicenter cohort study was carried out in 16 public hospitals from different regions in Spain, as reported elsewhere [12]. The institutional review board of the Parc Taulí and the respective boards of the other 15 hospitals approved the study, and all patients or their caregivers provided informed consent.

We included all consecutive adult patients with COPD who presented with eCOPD at the ED from June 2008 through September 2010. Patients were eligible for the study if they presented to the ED of any of the participating hospitals with symptoms consistent with eCOPD. COPD was confirmed if the patient had a forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) quotient <70%. Exacerbation was defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnoea,

cough, and/or sputum that was beyond normal day-to-day variations and may have warranted a change in regular medication. Apart from patients with known COPD, we included patients whose clinical history suggested COPD, provided spirometry confirmed the suspicion approximately two months later.

We also excluded all patients admitted for processes other than eCOPD that might have caused the exacerbation (airflow limitation): pneumonia, heart failure, pneumothorax, pulmonary embolism, or any obstructive or restrictive lung disease other than COPD.

Duly trained research staff recorded the following variables: age; sex; residence (home or long-term care centre); the presence of oedema in the lower limbs; gasometric parameters (PaCO2, pH, PaO2) and respiratory rate (RR); Glasgow Coma Scale; FEV_1 prior to the eCOPD; whether the patient was hospitalized or was discharged to home; the presence of complications during the hospital stay (e.g., diabetic decompensation, atrial fibrillation, thrombosis, cardiorespiratory arrest, pneumonia, need for intubation or mechanical ventilation, acute renal failure, heart failure); Charlson score, which is calculated taking into account certain comorbidities and is a predictor of overall mortality [14]; the number of hospital admissions for COPD in the last 12 months; a history of chronic arrhythmia in treatment or arrhythmia onset coinciding with the episode of eCOPD; diabetes mellitus, or other heart disease within the last year (e.g., ischemic heart disease, valvular disease, cardiomyopathy); chronic home oxygen therapy (CHOT) or noninvasive mechanical ventilation (NIMV); and stable drug therapy before eCOPD. In addition to recording whether patients were on diuretics or oral corticoids, we defined the following mutually exclusive categories: aerosol or nebulized therapy (short-acting B2 agonists and/or short-acting anticholinergics) with or without any other treatment, triple therapy (inhaled corticosteroids, long-acting anticholinergics and long-acting B2-agonists without aerosol therapy), double therapy A (inhaled corticosteroids and long-acting B2-agonists without aerosol therapy), double therapy B (inhaled long-acting anticholinergics and B2-agonists without aerosol therapy), monotherapy (inhaled long-acting anticholinergics or B2-agonists or corticosteroids without aerosol therapy) and others. We also recorded the administration and/or prescription of antibiotics and oral corticoids.

Approximately 24 hours after admission to hospital ward or discharge, we questioned patients about their degree of dyspnoea prior to the episode by means of the Modified Medical Research Council (mMRC) dyspnoea scale, which is scored from 0 (absence of dyspnoea except during strenuous exercise) to 4 (dyspnoea that impedes leaving the house or occurs on activities like getting dressed). [15] The mMRC is included in the estimation of diverse prognostic indices for COPD [16,17].

Finally, we recorded information from telephone interviews and medical records about readmissions to any hospital for eCOPD or other reasons; in patients who died, we recorded the date of death whether it occurred in the ED, in the hospital ward, or after discharge during the follow-up period. The follow-up period was set at 70 days after discharge to home, whether from the ED or ward.

2.1 Statistical Analysis

For the analyses, we took into account only each patient's first episode during the recruitment period. None of the missing responses was imputed, except in the cases described previously [12].

The main variable was accumulated mortality from any cause from the time of arrival at the ED to the end of the follow-up period in two groups of patients: those discharged to home and those remaining in the hospital for more than 48 hours.

We applied bivariate techniques to analyze the possible association of each explicative variable with mortality in each group. We used the chi-square test or Fisher's exact test, as appropriate.

Afterward, we used forward stepwise logistic regression and then the enter method to determine whether the factors were independently associated with mortality in the two groups, obtaining the adjusted odds ratios with their respective 95% confidence intervals (CI). To find the adjusted model with the greatest discriminative power, the models included the variables that were statistically significant ($p<0.05$) in the bivariate analysis as well as other variables considered clinically relevant, provided their p-value was less than 0.2. To analyze the goodness of fit of the models, we used the Hosmer-Lemeshow test [18]. To measure the discriminative power of the model, we estimated the area under the curve (AUC) of the receiver

operating characteristic curve and its 95% CI. [19] Finally, we used bootstrapping (1000 samples) to internally validate the results obtained in the multivariate model [20].

Statistical significance was set at 5%. All statistical analyses were done with SPSS Statistics 20 (IBM software) and with R v.2.15.3.

3. RESULTS

Of the 3276 eCOPD attended in the ED, 789 were excluded for the reasons shown in (Fig. 1). Thus, 2487 patients were analyzed; 1537 (62%) were admitted to wards (mean hospital stay, 7.7±6.2 days) and 950 (38%) were discharged to home. Patients' mean age was 72.8±93.7 years; 2267 (91%) were men, and 629 (25.3%) were older than 79 years of age.
As is shown in (Table 1), between the two groups analyzed there were significant differences in the Charlson score, in some variables related to the baseline severity of the COPD (previous combination of inhaled or aerosol treatments for COPD, treatment with diuretics or CHOT or NIMV, FEV_1, and number of previous admissions for COPD), as well as in the variables related to the severity of the eCOPD at arrival (oedema in the lower limbs, Glasgow score, pCO_2, pH, pO_2, respiratory rate) or the percentage of later admissions for COPD. A significantly higher percentage of patients in the group of hospitalized patients received antibiotics or oral corticoids compared to the group of patients discharged to home.

A total of 155 (6.2%; 95% CI: 5.2% - 7.1%) patients died; 57 (37%) of these died in the hospital. The accumulated mortality was 2.2% (95% CI: 1.3% - 3.1%) in patients discharged to home from the ED and 8.7% (95% CI: 7.3% - 10.1%) in patients admitted to the wards.

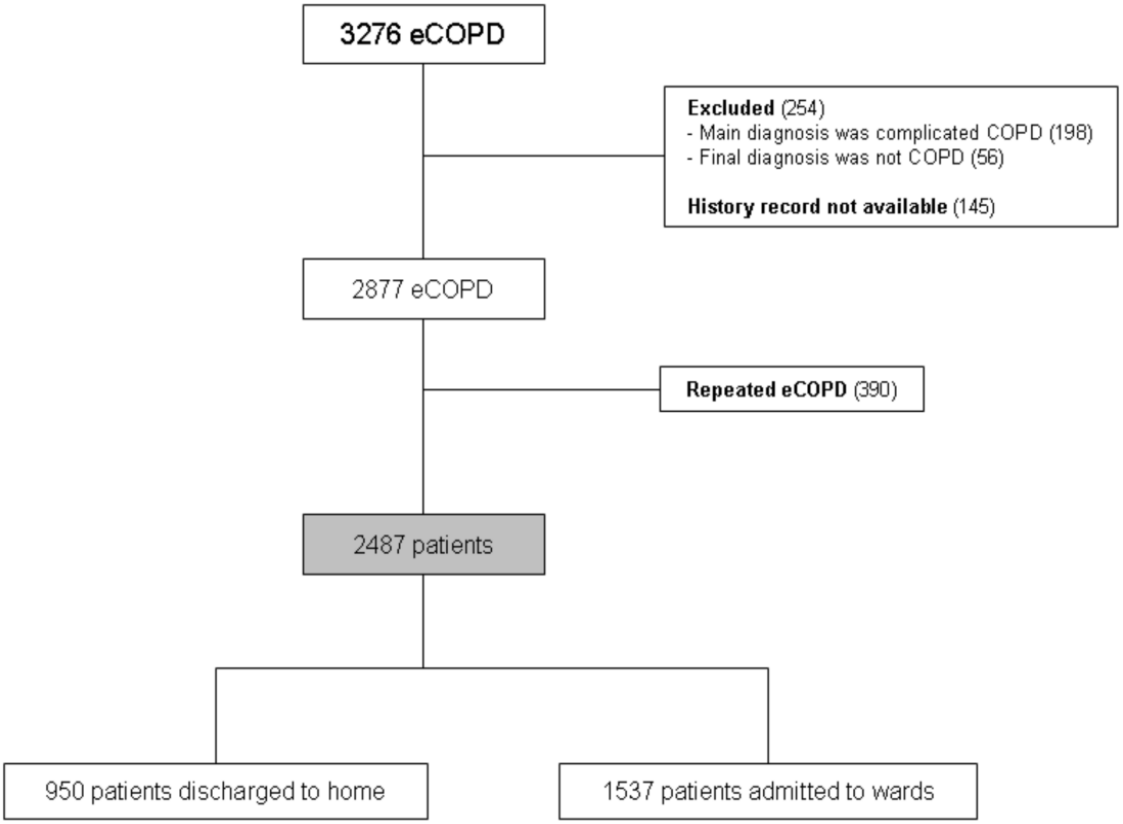

Fig. 1. Flow diagram of eCOPD (exacerbations) attended and patients analyzed in the study

Table 1. Descriptive and bivariate statistics of all variables, by destination

		Discharged to home (n=950)		Admitted to wards (n=1537)		p-value
		n	Col%	n	Col%	
Age*	<80	705	74.3	1152	75.0	0.712
	≥80	244	25.7	385	25.0	
Sex*	Male	872	91.8	1395	90.9	0.466
	Female	78	8.2	139	9.1	
Residence*	At home	825	98.4	1377	97.4	0.097
	Long-term care	13	1.6	37	2.6	
Charlson Comorbidity Index	≤2	674	70.9	1012	65.8	0.008
	>2	276	29.1	525	34.2	
Diabetes*	No	756	80.0	1181	77.5	0.141
	Yes	189	20.0	343	22.5	
Heart disease*	No	752	79.9	1179	77.3	0.120
	Yes	189	20.1	347	22.7	
Arrhythmia under treatment*	No	775	82.6	1241	81.5	0.476
	Yes	163	17.4	282	18.5	
Previous treatment for COPD*	Aerosol therapy	68	7.3	137	9.1	<0.001
	Triple therapy	405	43.7	773	51.1	
	Double therapy A	168	18.1	238	15.7	
	Double therapy B	42	4.5	51	3.4	
	Monotherapy	122	13.2	118	7.8	
	Other	122	13.2	196	13.0	
Previous treatment with oral corticosteroid*	No	871	94.3	1410	93.9	0.695
	Yes	53	5.7	92	6.1	
Previous treatment with diuretics*	No	646	69.8	982	65.6	0.031
	Yes	279	30.2	515	34.4	
Previous treatment with CHOT or NIMV*	No	679	72.6	935	61.5	<0.001
	Yes	256	27.4	585	38.5	
FEV_1*	≥50	316	42.7	403	30.3	<0.001
	<50	424	57.3	926	69.7	
Number of hospital admissions in the previous 12 months for COPD*	0	625	67.1	810	53.3	<0.001
	1	190	20.4	347	22.8	
	>1	117	12.6	362	23.8	
mMRC Dyspnoea*	0, 1, 2	504	60.6	784	55.8	0.065
	3	238	28.6	434	30.9	
	4	90	10.8	186	13.2	
Lower limb oedema*	No	769	84.9	1127	79.0	<0.001
	Yes	137	15.1	299	21.0	
Glasgow*	15 (normal)	939	98.8	1476	96.2	<0.001
	<15 (altered)	11	1.2	59	3.8	
pCO2 at arrival*	<46	519	69.3	713	50.7	<0.001
	46 to 55	165	22.0	319	22.7	
	56 to 65	48	6.4	193	13.7	
	>65	17	2.3	180	12.8	
pH at arrival*	>7.34	813	95.5	1178	81.6	<0.001
	7.26 to 7.34	36	4.2	214	14.8	
	<7.26	2	0.2	52	3.6	
pO2 at arrival*	>60	593	70.2	541	37.8	<0.001
	46 to 60	211	25.0	636	44.4	
	<46	41	4.9	256	17.9	
Respiratory rate at arrival*	<20	209	56.0	165	20.2	<0.001
	20 to 24	365	35.3	630	54.9	
	>24	234	8.7	664	24.9	
Complications	No			1322	86.0	
	Yes			215	14.0	
Antibiotics prescribed*	No	203	22.0	94	6.2	<0.001
	Yes	720	78.0	1414	93.8	
Oral corticosteroid prescribed*	No	301	32.5	168	11.1	<0.001
	Yes	624	67.5	1341	88.9	
Re-admitted*	No	765	80.5	1036	70.0	<0.001
	Yes, for COPD	151	15.9	381	25.7	
	Yes, for others	34	3.6	63	4.3	

*COPD: Chronic Obstructive Pulmonary Disease; CHOT: chronic home oxygen therapy; NIMV: noninvasive mechanical ventilation; FEV1: forced expiratory volume in one second; mMRC: Modified Medical Research Council. * Numbers do not add up because of missing data in some patients*

As shown in (Table 2), in patients discharged to home, the only variables associated with short-term mortality were age ≥ 80 years, residing in a long-term care facility, the Charlson Index, the mMRC scale, abnormal pH at admission to the ED, and readmission for other causes. Observed mortality was unrelated to antibiotic prescription or oral corticoid prescription. In the regression analysis, only age ≥ 80 years, Charlson score >2, and grade 4 on the mMRC were independent explanatory factors of short-term mortality with estimated OR ≥ 4 (Fig. 2). These three variables discriminated mortality with an AUC=84% (95%CI: 75%-94%) (Fig. 3). The Hosmer-Lemeshow test showed the model had good calibration (p=0.165).

In patients admitted to the wards, the variables associated with short-term mortality were age ≥ 80 years, baseline FEV1 <50, admission for COPD in the previous 12 months, baseline dyspnoea on the mMRC, oedema in the lower limbs, altered Glasgow score, elevated pCO2, abnormal pH, tachypnoea on arrival at the ED, and complications during the hospital stay. The following co-morbidities were also significantly associated with mortality: Charlson score >2, diabetes, heart disease, and arrhythmia. Baseline treatment for COPD was also associated. Mortality was significantly lower in patients treated with corticoids and was also higher in patients who were readmitted for COPD or for other causes.

For patients admitted to the wards, independent risk factors were age ≥ 80 years, Charlson score >2, previous heart disease, baseline treatment with CHOT or NIMV or with aerosol therapy, mMRC 4, altered Glasgow score, and complications during the hospital stay; the prescription and/or administration of corticoids at any point in the period analyzed was a protective factor that reduced the probability of death by 60% (30% - 80%). (Fig. 2) shows that dyspnoea on minimal exertion (mMRC=4) had the strongest association (OR 3.6; 95%CI: 2.0-6.3). The Hosmer-Lemeshow test showed the model had good calibration (p=0.396) with an AUC of 80% (95%CI: 76%-84%) (Fig. 3).

(Table 3) shows the results of bootstrap analyses for internal validation of the complete models.

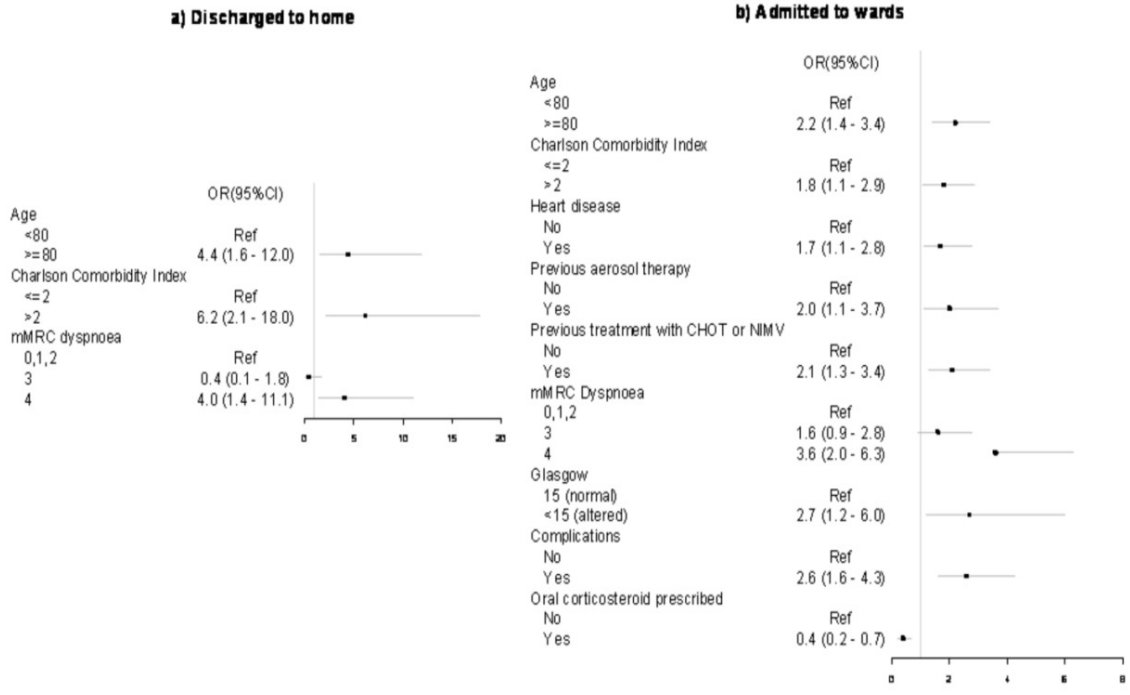

Fig. 2. Logistic regression models for 2-month mortality after an eCOPD

Table 2. Descriptive and bivariate statistics of death according to all variables, stratified by destination

		Discharged to home (n=950)					Admitted to wards (n=1537)				
		Death									
		No (n=929)		Yes (n=21)		p-value	No (n=1403)		Yes (n=134)		p-value
		n	Row%	n	Row%		n	Row%	n	Row%	
Age*	<80	698	99.0	7	1.0	<0.001	1071	93.0	81	7.0	<0.001
	>=80	230	94.3	14	5.7		332	86.2	53	13.8	
Sex*	Male	852	97.7	20	2.3	0.560	1270	91.0	125	9.0	0.322
	Female	77	98.7	1	1.3		130	93.5	9	6.5	
Residence*	At home	808	97.9	17	2.1	0.001	1270	92.2	107	7.8	0.940
	Long-term care	11	84.6	2	15.4		34	91.9	3	8.1	
Charlson Comorbidity Index	<=2	667	99.0	7	1.0	<0.001	948	93.7	64	6.3	<0.001
	>2	262	94.9	14	5.1		455	86.7	70	13.3	
Diabetes*	No	740	97.9	16	2.1	0.659	1090	92.3	91	7.7	0.014
	Yes	184	97.4	5	2.6		302	88.0	41	12.0	
Heart disease*	No	734	97.6	18	2.4	0.502	1097	93.0	82	7.0	<0.001
	Yes	186	98.4	3	1.6		296	85.3	51	14.7	
Arrhythmia under treatment*	No	756	97.5	19	2.5	0.337	1147	92.4	94	7.6	0.001
	Yes	161	98.8	2	1.2		243	86.2	39	13.8	
Previous treatment for COPD*	Aerosol therapy	66	97.1	2	2.9	0.596	116	84.7	21	15.3	0.032
	Triple therapy	396	97.8	9	2.2		713	92.2	60	7.8	
	Double therapy A	166	98.8	2	1.2		213	89.5	25	10.5	
	Double therapyB	42	100.0	0	0.0		49	96.1	2	3.9	
	Monotherapy	117	95.9	5	4.1		109	92.4	9	7.6	
	Others	119	97.5	3	2.5		183	93.4	13	6.6	
Previous treatment with oral corticosteroids*	No	851	97.7	20	2.3	0.846	1301	92.3	109	7.7	<0.001
	Yes	52	98.1	1	1.9		72	78.3	20	21.7	
Previous treatment with diuretics*	No	631	97.7	15	2.3	0.872	921	93.8	61	6.2	<0.001
	Yes	273	97.8	6	2.2		449	87.2	66	12.8	
Previous treatment with CHOT or NIMV*	No	664	97.8	15	2.2	0.901	891	95.3	44	4.7	<0.001
	Yes	250	97.7	6	2.3		498	85.1	87	14.9	
FEV_1*	>=50	310	98.1	6	1.9	0.532	378	93.8	25	6.2	0.047
	<50	413	97.4	11	2.6		838	90.5	88	9.5	
Number of hospital admissions in the previous 12 months for COPD*	0	611	97.8	14	2.2	0.418	754	93.1	56	6.9	0.031
	1	184	96.8	6	3.2		309	89.0	38	11.0	

Table 2 continued.....

		Discharged to home (n=950)					Admitted to wards (n=1.537)				
		Death									
		No (n=929)		Yes (n=21)		p-value	No (n=1403)		Yes (n=134)		p-value
		n	Row%	n	Row%		n	Row%	n	Row%	
mMRC Dyspnoea*	0, 1, 2	496	98.4	8	1.6	**<0.001**	753	96.0	31	4.0	**<0.001**
	3	236	99.2	2	0.8		399	91.9	35	8.1	
	4	81	90.0	9	10.0		144	77.4	42	22.6	
Lower limb oedema*	No	753	97.9	16	2.1	0.538	1037	92.0	90	8.0	**0.043**
	Yes	133	97.1	4	2.9		264	88.3	35	11.7	
Glasgow*	15 (normal)	919	97.9	20	2.1	0.118	1360	92.1	116	7.9	**<0.001**
	<15 (altered)	10	90.9	1	9.1		42	71.2	17	28.8	
pCO2 at arrival*	<46	508	97.9	11	2.1	0.302	670	94.0	43	6.0	**0.001**
	46 to 55	160	97.0	5	3.0		288	90.3	31	9.7	
	56 to 65	45	93.8	3	6.3		176	91.2	17	8.8	
	>65	17	100.0	0	0.0		153	85.0	27	15.0	
pH at arrival*	>7.34	796	97.9	17	2.1	**<0.001**	1088	92.4	90	7.6	**0.027**
	7.26 to 7.34	34	94.4	2	5.6		192	89.7	22	10.3	
	<7.26	0	0.0	2	100.0		43	82.7	9	17.3	
pO2 at arrival*	>60	578	97.5	15	2.5	0.992	487	90.0	54	10.0	0.062
	46 to 60	206	97.6	5	2.4		595	93.6	41	6.4	
	<46	40	97.6	1	2.4		231	90.2	25	9.8	
Respiratory rate at arrival*	<20	207	99.0	2	1.0	0.321	156	94.5	9	5.5	**0.005**
	20 to 24	356	97.5	9	2.5		586	93.0	44	7.0	
	>24	227	97.0	7	3.0		588	88.6	76	11.4	
Complications	No						1228	92.9	94	7.1	**<0.001**
	Yes						175	81.4	40	18.6	
Antibiotics prescribed*	No	199	98.0	4	2.0	0.742	83	88.3	11	11.7	0.140
	Yes	703	97.6	17	2.4		1308	92.5	106	7.5	
Oral corticosteroids prescribed*	No	294	97.7	7	2.3	0.937	139	82.7	29	17.3	**<0.001**
	Yes	610	97.8	14	2.2		1253	93.4	88	6.6	
Re-admitted*	No	750	98.0	15	2.0	**0.028**	1005	97.0	31	3.0	**<0.001**
	Yes, for COPD	148	98.0	3	2.0		344	90.3	37	9.7	
	Yes. for others	31	91.2	3	8.8		54	85.7	9	14.3	

*COPD: Chronic Obstructive Pulmonary Disease; CHOT: chronic home oxygen therapy; NIMV: noninvasive mechanical ventilation; FEV1: forced expiratory volume in one second; mMRC: Modified Medical Research Council.; * Numbers do not add up because of missing data in some patients*

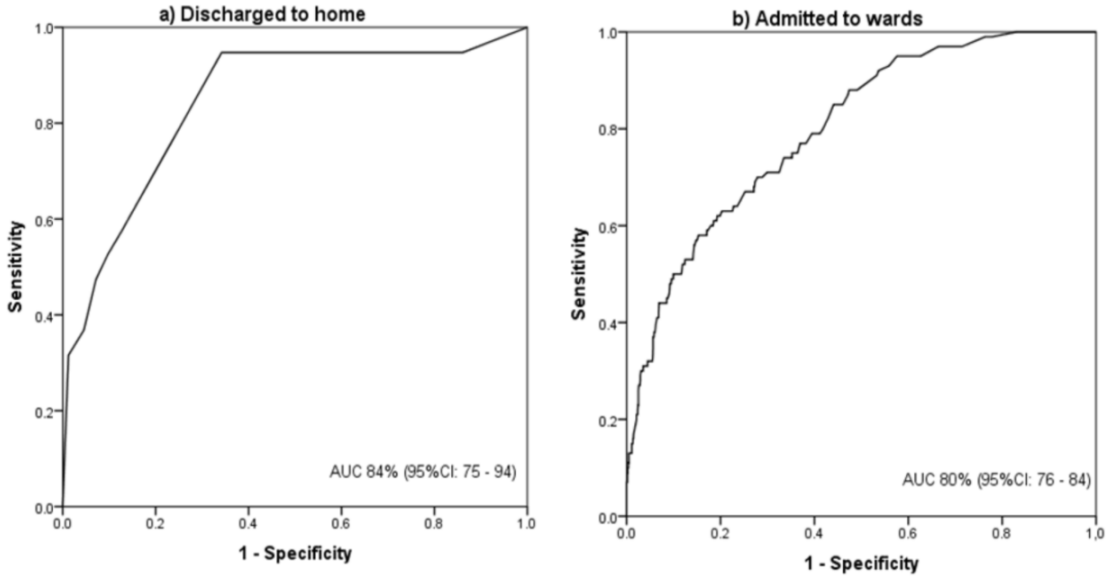

Fig. 3. ROC curve of regression models according to destination

Table 3. Internal validation of the logistic regression models with bootstrap methods

	Discharged to home		Admitted to wards	
	OR	**CI 95%**	**OR**	**CI 95%**
Age (≥ 80)	4.44	0.95-20.68	2.15	1.34-3.45
Charlson Comorbidity Index (> 2)	6.18	0.34-112.22	1.81	1.10-3.00
Heart disease (Yes)			1.73	1.04–2.90
Previous aerosol therapy (Yes)			1.96	0.97-3.97
Previous treatment with CHOT or NIMV (Yes)			2.10	1.25-3.50
mMRC Dyspnoea (3)	0.36	0.00-19420.38	1.61	0.95–2.74
mMRC Dyspnoea (4)	3.96	1.25-12.53	3.58	1.95-6.57
Glasgow (<15 altered)			2.69	1.18-6.14
Complications (Yes)			2.60	1.60-4.30
Oral corticosteroid prescribed (Yes)			0.38	0.22-0.67

CHOT: chronic home oxygen therapy; NIMV: noninvasive mechanical ventilation; mMRC: Modified Medical Research Council

4. DISCUSSION

In this nationwide study of COPD, the short-term mortality due to any cause in patients attended at EDs for eCOPD was 6.2% overall: 2.2% in patients discharged to home and 8.7% in patients admitted to hospital wards. In patients discharged to home from the ED, the strongest predictors of short-term mortality were age ≥ 80 years, Charlson score, and mMRC prior to eCOPD; these three factors accounted for 84% of the mortality in these patients. In patients admitted to hospital wards from the ED, about 80% of the mortality is explained by these three factors together with previous heart disease, baseline treatment with CHOT/NIMV or aerosol therapy, altered Glasgow score on arrival at the ED, certain complications, and corticoid treatment.

In our study, the accumulated mortality rate due to any cause is slightly higher than rates reported by other authors for similar follow-up periods, although direct comparisons are difficult due to the heterogeneity of follow-up periods and the type and time in which mortality is analyzed, as Singanayagam et al.[8] point out in their review. More recently, in a context similar to our study, Almagro et al. [10] found 4.5% mortality 90 days after discharge. Matkovic et al. [21] reported 3% mortality from respiratory causes within 30 days in patients admitted to wards. The nationwide Spanish study (AUDIPOC) of patients admitted to wards reported 6.9% mortality in 90 days [22].

The strongest association with short-term mortality was baseline mMRC score. Patients who scored 4 (dyspnoea on minimal exertion) had up to three times higher probability of death compared to those who scored 0 to 3, independently of other factors. Interestingly, patients' own assessments of their severity through the mMRC was more reliable at predicting fatal outcome than other parameters commonly used to evaluate the severity of baseline disease, such as FEV_1 or previous admissions [23], especially when dyspnoea was very pronounced. This observation was noted in a previous study with a longer follow-up period, although other authors found dissimilar results using other scales to measure dyspnoea. [24] In fact, the mMRC dyspnoea score is one of the parameters used in the Body-Mass Index, Airflow Obstruction, Dyspnoea, and Exercise (BODE) and Age, Dyspnoea, and Airflow Obstruction (ADO) indices, as well as in the new Global Initiative for Chronic Lung Disease (GOLD) classification of the severity of COPD [25,16]. We had no data on BMI or walking test results; in ordinary clinical practice, these parameters are not routinely recorded in the ED or during the hospital stay or immediately after discharge to home. The interviews with patients enabled us to obtain information about their perception of the severity of their dyspnoea prior to the eCOPD. In fact, the degree of dyspnoea might be related not only to the severity of the baseline disease, but also to BMI or to habitual physical activity or to cardiorespiratory diseases that had no independent effects in our study [26]. Thus, it is not possible to rule out confounding factors.

Another strong short-term prognostic factor was treatment with CHOT or NIMV. In fact, the stepped care recommended in the previous GOLD guidelines for stable patients, which is common in routine practice, called for CHOT in advanced stages of COPD (stage D) [27]. Likewise, the Glasgow score on arrival at the ED was clearly related with mortality, although this factor may have had a greater impact on the immediate mortality during the hospital stay, since it is correlated with the degree of decompensation during the first few hours. In fact, mortality in patients with altered Glasgow score was 28.8%, and half of these died in the hospital (data not shown).

In both patients discharged to home and those admitted to the wards, age≥80 years and Charlson score were both independent explanatory factors for mortality, although the estimators of the OR were much higher in patients discharged to home from the ED. These results agree with those reported by Almagro et al. [10] in a study analyzing the role of comorbidities in 90-day mortality in patients with eCOPD admitted to internal medicine departments throughout Spain. The direct relation between COPD and certain cardiovascular diseases due to shared risk factors and pathophysiologic mechanisms has been well documented [28]. Our results corroborate that prior heart disease has an independent role in the short-term outcome of eCOPD that requires admission to the wards, although it is impossible to establish a cause-and-effect relationship based on our data.

Although patients admitted to wards had greater baseline COPD severity and more compromised condition on arrival at the ED than patients discharged to home, the treatment prescribed to both groups would theoretically follow the standards recommended in the current guidelines [27]. In the eCOPD phase, prescribing systemic corticoids in addition to the patient's usual treatment is considered the first-line treatment in the absence of contraindications. Our results corroborate the protective role of corticoids against short-term death in patients admitted to the wards; however, in patients discharged from the ED to home, neither antibiotics nor corticoids affected the short-term prognosis.

Furthermore, in patients admitted to the wards, treatment prior to the eCOPD was related to mortality. In fact, 15% of the patients admitted to the wards who received aerosol therapy died during the follow-up period; this treatment is indicated in patients in whom inhalers are considered insufficient to control their condition, so to a certain degree it reflects greater severity of the baseline COPD. It is also noteworthy that patients admitted to wards developed certain complications or concomitant processes that could also affect the control of the eCOPD and even favour death. Among these complications, the most common was diabetic decompensation or acute renal failure (data not shown). In fact, we found that these complications could increase the probability of death in the short term by 60% to over 300%.

Despite the importance of smoking as a direct cause of COPD and as a prognostic factor, we had no information about this variable. This is a limitation of our study. Quitting smoking is the

most efficacious measure for the prevention and treatment of COPD [29]. Nevertheless, we consider that the benefits of quitting smoking rarely affect short-term life expectancy. One recent study that included this variable found that smoking was not an independent prognostic factor for long-term outcome [30]. Another factor that might seem unusual in our study is the small proportion of women; however, the proportion of women in our study is in line with epidemiological data in our environment and does not reflect a selection bias. Women were latecomers to the smoking habit in our society, so at present COPD predominantly affects men [31]. Moreover, it seems that COPD is under diagnosed in women [32]. Although it seems that the mortality rates for women were lower than for men in both groups, these differences did not reach significance. In fact, there is little evidence about possible gender differences in COPD, and acquiring such evidence probably requires large cohorts from countries with high prevalence of COPD among women [33]. Finally, we did not take into consideration certain biomarkers related with the inflammatory process such as C-reactive protein or procalcitonin because they are not widely used in routine clinical practice; likewise, we did not consider hemodynamic alterations in the eCOPD because they have not proven specific [7,34].

This study provides new knowledge about the emergency treatment of eCOPD in hospitals through a large multicenter cohort that might be representative of the situation in Spain and other countries. Not only does it take into account patients admitted to wards, about whom many studies have been published, but it also analyzes the short-term prognosis in patients discharged to home. Furthermore, it incorporates the easily applied mMRC to measure the degree of dyspnoea in the stable phase, the most common treatments for eCOPD and the habitual treatments for COPD grouped according to the classification recommended by the most commonly used guidelines in our environment [35]. Moreover, given the importance of aids for decision making and prognostic assessment, this study shows that it is possible to explain short-term mortality in patients with eCOPD through variables that are readily available in routine clinical practice that do not require additional tests.

5. CONCLUSION

In conclusion, age ≥ 80 years, comorbidities, and mMRC should be considered important in determining the prognosis for survival in patients attended in hospitals for eCOPD, regardless of whether they are admitted to the wards or discharged to home. Moreover, in patients with eCOPD who require admission to wards, the severity of both the baseline disease and the eCOPD as well as corticoid treatment may determine the short-term prognosis.

CONSENT

All patients or their caregivers provided informed consent.

ETHICAL APPROVAL

The institutional review board of the Parc Taulí and the respective boards of the other hospitals approved the study.

ACKNOWLEDGMENTS

We are grateful for the support of the 16 participating hospitals, as well as the members of the various services, research, quality units, and medical records sections of these hospitals. We also gratefully acknowledge the patients who participated in the study. The authors also acknowledge the editorial assistance provided by John Giba.

This work was supported in part by grants from the Fondo de Investigación Sanitaria (PI06\1010, PI06\1017, PI06\714, PI06\0326, PI06\0664); and the thematic networks- Red IRYSS (Investigación en Resultados y Servicios Sanitarios (G03\220) and REDISSEC (Health Services Research on Chronic Diseases Network; RD12/0001/0007) – of the Instituto de Salud Carlos III.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=661&id=12&aid=5995