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Severity and Outcomes of hospitalized community-acquired pneumonia in COPD Patients

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a frequent comorbidity in patients with community acquired pneumonia (CAP).We investigated the impact of COPD on outcomes of CAP patients.

Methods: We prospectively studied the clinical presentation of 1379 patients admitted with CAP during a 4 year-period. A comparative analysis of disease severity and

course was performed between 212 patients with COPD, as confirmed by spirometry, and 1167 non-COPD patients.

Results: COPD patients (median FEV_1 = 47.7±16.3 % predicted) were older and more likely received previous antibiotics (37.1% vs. 28.3%, p<0.01) than those without COPD. They presented with more severe respiratory failure, (PaO_2/FIO2 (270.4 vs. 287.8, p<0.01) and more severe pneumonia (PSI, 118.3 vs. 108.5; p<0.001). However, COPD patients had less multilobar infiltration (44 (21%) vs. 349 (30%), p<0.01) and less pulmonary complications (24 [14%] vs. 241 [24%]; p<0.01). A total of 89 patients (6.5%) died within 30 days. COPD patients had not different 30-days mortality rate compared to non-COPD patients (9 patients [4.2%] vs. 81[7%], p=0.14).

Conclusions: Despite worse clinical presentation COPD patients had a similar mortality compared to non-COPD patients. Previous antibiotic treatment and the decreased incidence pulmonary complications in COPD may account for these findings.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a frequent comorbidity in patients hospitalized with community acquired pneumonia (CAP), which may be explained mainly by the altered local and systemic immunity associated with this condition [1, 2]. Although this respiratory disease is a clear risk factor for CAP, it has not been shown to be a risk factor for mortality (4, 5, 6). Accordingly, COPD has not been included as one of the five main comorbidities determining the risk of death in the pneumonia severity index (PSI) [3].

A number of clinical and epidemiological studies have been carried out in order to determine the influence of COPD on the mortality of CAP with conflicting results. Whereas two studies do not support COPD as a risk factor for death[4, 5], two other studies did show an excess mortality of CAP in patients with COPD[6, 7]. Another study in patients with severe CAP treated at an ICU also showed an increased risk of mortality[8]. One of the main problems of these studies is the lack of spirometric confirmation of COPD in some[6, 8].

Thus, the aim of this prospective study was to determine whether COPD is a risk factor for pulmonary complications and death in patients hospitalized due to CAP. For that purpose, we selected COPD patients with a diagnosis confirmed by spirometry.

METHODS

Patients

We prospectively studied 1379 consecutive adults patients hospitalized with CAP during from 2004 to 2008 in an 850-bed tertiary care university hospital in Barcelona, Spain. Of these, 212 patients with CAP had COPD confirmed by spirometry performed prior to admission. Sixty patients were completely excluded from the study since despite a history of COPD no previous spirometry had been performed. Absence of COPD was confirmed by previous spirometry and or clinical history (N=1167). Moreover, we also excluded those smoking patients on inhaled corticosteroids (ICS) medication but without asthma to ensure the exclusion of not clearly diagnosed COPD.

Inclusion criteria were patients with a new radiographic infiltrate and at least two clinical symptoms suggestive of lower respiratory infection. We excluded patients with severe immunosuppression (patients with neutropenia after chemotherapy or bone marrow transplantation, solid-organ transplantation, HIV-infection, corticosteroid treatment > 20 mg prednisone-equivalent / day for 2 weeks or more) and those with nosocomial pneumonia.

The study protocol was approved by the Ethical Committee of the hospital and all patients or their next of kin gave informed consent (Registro: 2007/3543)

Definitions

We defined COPD according to the ATS/ERS criteria [9].

The classification of COPD severity was based on GOLD criteria: GOLD stage 1 was defined as a FEV_1 > 80%, GOLD stage 2 as FEV_1 predicted between 50% -80%, GOLD stage 3 as FEV_1 predicted between 30% - 50% and GOLD stage 4 as FEV_1 predicted < 30%[10].

Alcohol abuse was considered in cases with current intake of at least 80 g/d of alcohol in males and 60g/d in females [11]. Pulmonary complications were defined as parapneumonic pleural effusion, complicated parapneumonic pleural effusion and empyema requiring chest drainage, lung abscess, and acute respiratory distress syndrome (ARDS) at presentation or developed during the first days of hospitalization. Systemic complications were defined as the presence of renal failure and/or septic shock at presentation or developed during the first days of hospitalization [12].

Mortality was evaluated 30 days after hospital admission, during follow up.

Data collection

Demographic data, coexisting conditions, clinical information and laboratory values were collected at admission. The PSI was used to assess severity of pneumonia on admission [3].

Radiography evaluated the number of lobes involved, the presence of cavitations, atelectasis and pleural effusions.

Follow up variables were as follows: septic shock, need for invasive mechanical ventilation, pulmonary and systemic complications, systemic steroid treatment, previous antibiotic treatment in the last month, antibiotic treatment as well as duration of treatment, length of hospital stay (LOS) and 30-day mortality.

Samples for microbiological investigation were collected following a standard protocol: (1) blood cultures; (2) urine for *Streptococcus pneumoniae* and *Legionella pneumophila* antigen detection; (3) sputum in all patients when possible; 4) tracheobronchial aspirates in all intubated patients; (5) pleural fluid by thoracocentesis and (6) paired serology when possible to detect seroconversion (ie, a fourfold increase in immunoglobulin G (IgG) titres) for *C. pneumoniae* and *L. pneumophila* >1:128, *C. burnetii* >1:80, and respiratory viruses (ie, influenza viruses A and B, parainfluenza viruses 1–3, respiratory syncytial virus, adenovirus).

Statistical Analysis

Categorical variables were described with counts and percentages. For continuous variables the mean and standard deviation (SD) were presented. Relationships between categorical variables were studied using the chi-square test or Fisher's exact test when necessary. The comparison of continuous variables between two groups was carried out using the Student's t test for unpaired data once normality was demonstrated (Kolmogorov-Smirnov test); otherwise, the nonparametric test (Mann-Whitney U test) was used.

The associations of the variables in general characteristics, severity of pneumonia, microbiological diagnosis and evolution of CAP with outcomes were assessed by using the following logistic regression models[13, 14]:

First analysis is based on multivariate logistic regression model with COPD as response and PCR and LOS as covariates and Men, ICU admission, Diabetes Mellitus, Pneumonia previous year, Smoking, Alcohol, Previous antibiotic, Corticoids inhalers, Previous corticoids therapy, FINE Classes IV+V, CURB-65 ≥3, Mechanical ventilation, Shock, Multilobar involvement, Atelectasis, Diagnosis, Systemic Complications, Pulmonary Complications and Corticoids therapy as factors.

Second analysis is based on multivariate logistic regression model with Pulmonary Complications as response and PCR as covariate and Men, Diabetes Mellitus, Pneumonia previous year, COPD severity, Smoking, Alcohol, Previous antibiotic, Corticoids inhalers, Previous corticoids therapy, FINE Classes IV+V, CURB-65 ≥3, Diagnosis and Corticoids therapy as factors.

Third analysis is based on multivariate logistic regression model with Systemic Complications as response and PCR as covariate and Men, Diabetes Mellitus, Pneumonia previous year, COPD severity, Smoking, Alcohol, Previous antibiotic, Corticoids inhalers, Previous corticoids therapy, FINE Classes IV+V, CURB-65 ≥3, Diagnosis and Corticoids therapy as factors.

Fourth analysis is based on multivariate logistic regression model with Mortality as response and PCR and LOS as covariates and Men, ICU admission, Diabetes Mellitus, Pneumonia previous year, COPD severity, Smoking, Alcohol, Previous

antibiotic, Corticoids inhalers, Previous corticoids therapy, FINE Classes IV+V, CURB-65 ≥3, Mechanical ventilation, Shock, Multilobar involvement, Atelectasis, Diagnosis and Corticoids therapy as factors.

Variables that showed a significant result univariately ($p<0.1$) were included in the corresponding multivariate logistic regression backward stepwise model to determine which of them were independently related to prognosis. The Hosmer-Lemeshow goodness-of-fit test was performed to assess the overall fit of the models[13].

All analyses were performed with SPSS 16 for Windows, considering statistically significant a 2-side p-value<0.05.

RESULTS

Clinical characteristics

We identified 1379 patients hospitalized with CAP with a mean age of 70 years (SD ±17). The main characteristics of the patients, comorbidities and disease presentation are shown in the online data supplement (table 1).

Of the study population, 770 (56%) were smokers (271 ex-smokers and 499 current smokers) and 130 (9%) were living in nursing homes. 928 (67%) patients belonged to high risk classes (PSI classes IV+V). The most frequent comorbidities were lung disease, chronic heart failure and neurological disease (table 1).

COPD was confirmed by spirometry in 212 patients (15%). The mean FEV_1 was 48% (SD ± 16). The classification of COPD patients into GOLD stages was as follows: n=13 (6%) stage 1, n=78 (37%) stage 2, n=98 (46%) stage 3 and n=23 (11%) patients stage 4.

The differences in baseline characteristics between COPD and non-COPD patients are summarized in [***Table 1].*** COPD patients with CAP were significantly more likely to be men, less likely to reside in nursing homes, and were more likely to have a history of malignancy and high alcohol consumption. The rate of pneumonia in the previous year was also higher (71 [34%] vs. 198 [18%], $p<0.01$). COPD patients were more frequently on antibiotics before admission (76 [37%] vs. 322 [28%], $p=0.01$), inhaled corticoids (ICS) (137 [65%] vs. 148 [13%], $p<0.01$) and previous oral steroids (27 [13%] vs. 49 [4 %], $p<0.01$).

TABLE 1. Clinical characteristics of the study population stratified according to the presence or absence of COPD.

Variable	COPD (N=212)	Non-COPD (N=1167)	p-value
Age, years	73.4±8.8	69.4±17.9	0.49
Men	191 (90.1)	635 (54.4)	**<0.01**
Nursing home resident	12 (5.7)	118 (10.2)	**0.04**
ICU admission	21 (9.9)	125 (10.7)	0.73
Mechanical Ventilation	10(4.7)	61 (5.2)	0.76
Non Invasive Mechanical Ventilation	16 (7.5)	45 (3.9)	**0.02**
PSI	118.3±34.1	108.5±36.9	**<0.01**
FINE Classes IV+V	159 (75.4)	769 (65.9)	**0.01**
CURB-65 ≥3	55 (27.5)	286 (25.7)	0.60
Comorbid Conditions			
Heart failure	56 (26.4)	267 (23.0)	0.28
Chronic liver disease	12 (5.7)	48 (4.1)	0.32
Malignancy	28 (13.2)	66 (5.7)	**<0.01**
Renal failure	19 (9.0)	78 (6.7)	0.24
Neurological disease	46 (21.7)	318 (27.2)	0.09
Diabetes Mellitus	55 (25.9)	234 (20.2)	0.06
Pneumonia previous year	71 (33.8)	198 (17.5)	**<0.01**
COPD severity			
Mild	13 (6.1)	-	
Moderate	78 (36.8)	-	
Severe	98 (46.2)	-	
Very severe	23 (10.8)	-	
History of smoking	202 (95.3)	568 (48.7)	**<0.01**
History of alcohol	63 (34.2)	197 (17.9)	**<0.01**
Previous antibiotic in the last month	76 (37.1)	322 (28.3)	**0.01**
Previous inhaled corticoid therapy	137 (64.9)	148 (12.9)	**<0.01**
Previous oral corticoid therapy	27 (12.9)	49 (4.2)	**<0.01**
Physical and Laboratory data			
FEV_1 (% of predicted), median	47.7±16.3	-	
Confusion	51 (24.2)	326 (28.1)	0.24
Respiratory rate>30/min	89 (43.4)	385 (34.4)	**0.01**
Systolic blood pressure < 90mmHg	9 (4.3)	61 (5.3)	0.56
Heart rate>120/min	27 (12.8)	161 (13.9)	0.67
Fever	157 (75.1)	960 (82.9)	**0.01**
Temperature>39 °C	18 (8.5)	148 (12.8)	0.08
PaO_2/FiO_2< 250	270.4±67.6	287.8±72.3	**<0.01**
C-RP, mg/dl	17.4±12.3	20.5±17.6	**<0.01**

Continuous numbers represent mean ± SD, categorical numbers represent n (%). Abbreviations. ICU: intensive care units; C-RP: C-reactive protein. History of smoking includes former and current smoking habit. Similarly, history of alcohol includes former and current alcohol habit.

Non COPD patients chronically using ICS before admission (n, 148) were mainly affected by asthma (39%) bronchiectasis (15%), interstitial lung diseases

(12%) and other chronic respiratory disorders, such as bronchial hyper-responsiveness or TB sequelae. Twelve smoking patients on ICS medication but without asthma were excluded from the study. Similarly, non COPD patients that had previously been administered oral steroids (n, 49) were mostly affected by a chronic non-COPD respiratory disease (57%) such as asthma or bronchiectasis, or by other chronic diseases such as neurologic (31%) or a previous neoplastic disease (18%).

COPD patients had a higher mean PSI (118 vs. 109, $p<0.01$) but a similar proportion of CURB-65 score≥3. They had a worse clinical presentation (respiratory rate, respiratory failure) at admission, but less fever and CRP levels (table 2). Likewise, radiographic extension was lower (multilobar infiltrates in 44 patients [21%] vs. 349 [30%], $p=0.01$), and pleural effusions (19 patients [11%] vs. 168 [16%], $p=0.07$) and empyema (0 vs. 4%, $p=0.01$) were less frequent in COPD patients.

Etiological diagnosis

Microbiological diagnosis was achieved in 537 (46%) patients. Blood cultures were diagnostic in 153 patients (16%), with 19 (12%) having COPD. The most frequent microorganism in both groups was *Streptococcus pneumoniae.* Patients with COPD had more infections attributable to *Pseudomonas aeruginosa* but less *L. pneumophila* than non-COPD patients ($p<0.01$ and $p=0.04$ respectively) [***Table 2***].

TABLE 2. Microbiological diagnosis according to COPD

Microorganisms	COPD (N=212)	Non-COPD (N=1167)	p-value
No Diagnosis	117 (55.2)	630 (54.0)	0.74
Diagnosis	95 (44.8)	537 (46.0)	
Streptococcus pneumoniae	36 (37.9)	230 (42.8)	0.37
** Virus,spp	13 (13.7)	67 (12.5)	0.74
Legionella pneumophila	2 (2.1)	42 (7.8)	**0.04**
Staphylococcus aureus	0 (0.0)	17 (3.2)	0.08
Chlamydophila pneumoniae	2 (2.1)	22 (4.1)	0.35
Mycoplasma pneumoniae	2 (2.1)	18 (3.4)	0.52
Haemophilus influenzae	1 (1.1)	12 (2.2)	0.45
Pseudomonas aeruginosa	7 (7.4)	5 (0.9)	**<0.01**
Klebsiella pneumoniae	0 (0.0)	5 (0.9)	1.00
Moraxella catarrhalis	0 (0.0)	2 (0.4)	1.00
Escherichia coli	2 (2.1)	7 (1.3)	0.54
Others	12 (12.6)	42 (7.8)	0.12
Polymicrobial pneumonia*	18 (18.9)	68 (12.7)	0.10

Note: Data are expressed as n (%).

* 2 microorganisms were found in 16 patients and 3 microorganisms were found in 2 patients in the COPD group; 2 microorganisms were found in 61 patients and 3 microorganisms were found in 7 patients in the non-COPD group.

** Virus spp.: Influenza A, influenza B, parainfluenza virus, respiratory syncytial virus (RSV) and adenovirus.

No specific microorganisms were significantly associated with pulmonary complications in the course of CAP, except for a trend towards a higher frequency of *P. aeruginosa* [5 cases (3%) vs 7 (1.5%)].

With regards to the chronic use of ICS we observed that *Legionella spp.* was less frequent among patients using ICS (3 cases [2%] vs. 41 [8%], p=0.02) while *P. aeuriginosa* was more frequent (6 cases [5%] vs. 6 [1%], p=0.01).

Disease evolution

Pulmonary complications

COPD patients less frequently developed pulmonary complications (24 patients [14%] vs. 241 [24%], p<0.01). They less frequently presented multilobar involvement (44 [21%] vs. 349 [30%] p=0.01), empyema (0 vs. 41 [4%], p=0.01) and a trend to less pleural effusion (19 [11%] vs. 168 [16], p=0.07) [**Table 3**].

TABLE 3. Complications and outcomes of CAP in patients with and without COPD

Variable	COPD (N=212)	Non-COPD (N=1167)	p-value
Systemic Complications	25 (14.3)	190 (18.6)	0.17
Pulmonary complications	24 (14.0)	241 (23.6)	**0.01**
Acute Respiratory Distress	1 (0.6)	23 (2.3)	0,15
Empyema	0 (0.0)	41 (4.0)	**0.01**
Pleural effusion	19 (11.0)	168 (16.5)	0.07
Septic shock	4 (2.3)	42 (4.1)	0.34
LOS, days	10.2±8.8	10.3±9.5	0.49
Mortality	9 (4.2)	81 (7.0)	0.14

Note: Data are expressed as mean±SD or n (%).

Pulmonary complications were more frequent in patients admitted to the ICU (n, 49 [18%] vs. 61 [7%], p<0.01), and in nursing home patients (33 [13%] vs. 76 [8%], p=0.03), and in those with higher CRP levels at admission (23.9±29.3 mg/dl vs. 18.9±11.8 mg/dl, p<0.01).

In univariate analysis, diabtes mellitus, COPD mild/moderate, a history of previous pneumonia in the previous year, previous chronic therapy with ICS and systemic steroids were associated with less pulmonary complications, while an increased CRP at admission and a known microbiological etiology were associated with more respiratory complications [**Table 2 of online supplement data**].

Multivariate analysis revealed that increasing CRP values (+1 mg/dl, OR: 1.02, 95% CI: 1.00 to 1.03) and a known microbiological etiology (OR: 1.6, 95% CI: 1.1 to 2.1) were risk factors for pulmonary complications while diabetes mellitus (OR: 0.62, 95% CI: 0.41 to 0.95) and chronic use of ICS were protective factors (OR: 0.54, 95% CI: 0.35 to 0.84) [**Table 2 of online supplement data**].

Systemic complications

COPD and non COPD patients developed a similar rate of systemic complications [25 cases (14%) vs. 190 (19%), p=0.17].

Systemic complications were more frequent in patients admitted to the ICU (27% vs. 6%, p<0.01) and in those requiring mechanical ventilation (15% vs. 2%, p<0.01). They had higher PSI (IV-V, 87% vs. 62%, p<0.01) and CURB-65 (≥3, 51% vs. 21%) classes, were more frequently men (66% vs. 58%, p=0.03), alcohol abusers (26% vs. 19%, p=0.02), and more renal failure (13% vs. 6%, p<0.01).

At univariate analysis, a history of previous pneumonia in the previous year, prior antibiotic use and ICS use were associated with less systemic complications. By contrast, men, alcohol abuse, an increased CRP at admission, higher PSI (IV-V), higuer CURB-65 (≥3), a known microbiological etiology and previous intake of oral corticoid therapy were associated with increased systemic complications. COPD severity was not associated with the development of systemic complications. [**Table 3 of online supplement data].**

Multivariate analysis showed that classification into PSI class IV or V (OR: 2.7, 95% CI: 1.7 to 4.4), CURB-65≥3 (OR: 2.8, 95% CI: 1.9 to 4.1) and increasing CRP values (+1 mg/dl, OR: 1.03, 95% CI: 1.01 to 1.04) were predictors of systemic complications **[Table 3 of online supplement data].**

Outcomes

No differences were observed in ICU admission (21 [10%] vs. 125 [11%], p=0.73) and in LOS (10.2±8.8 days vs. 10.3±9.5 days, p=0,49) between patients with and without COPD.

A total of 9 patients with COPD died compared to 81 patients without COPD. COPD patients had not different mortality rate compared to the other CAP patients (4.2% vs. 7%, p=0.14). After exclusion of nursing home patients from groups, the mortality rates were 8 (4%) and 57 (5.4%), respectively (p=0.52).

In univariate analysis, the variables significantly associated with mortality at 30 days included admission to the ICU, smoking, alcohol, PSI class IV-V, CURB-65 ≥3, mechanical ventilation, shock, multilobar infiltrates, corticosteroid systemic therapy during hospitalization and LOS, [***Table 4***].

TABLE 4. Significant predictors of 30-day mortality from CAP at univariate and multivariate analysis.

Variable	Univariate			Multivariate		
	OR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
ICU admission	2.3	(1.3 to 3.9)	**<0.01**	-	-	
Smoking	0.58	(0.38 to 0.89)	**0.01**	0.51	(0.32 to 0.83)	**0.01**
Alcohol	0.54	(0.27 to 1.05)	**0.07**	-	-	
FINE Classes IV+V	23.6	(5.8 to 96.1)	**<0.01**	25.4	(3.5 to 187.3)	**<0.01**
CURB-65 ≥3	4.7	(2.9 to 7.4)	**<0.01**	2.5	(1.6 to 4.1)	**<0.01**
Mechanical ventilation	5.3	(2.9 to 9.6)	**<0.01**	4.2	(2.2 to 8.2)	**<0.01**
Shock	3.8	(2.1 to 6.8)	**<0.01**	-	-	
Multilobar involvement	1.7	(1.1 to 2.7)	**0.01**	-	-	
Systemic corticosteroids	2.3	(1.4 to 3.6)	**<0.01**	-	-	
LOS, days (+1)	1.02	(1.00 to 1.03)	**0.04**	-	-	

Note: LOS: Length of hospital stay; *CI = confidence interval; OR = odds ratio. Hosmer-Lemeshow goodness-of-fit test, p=0.36.*

Multivariate regression analysis revealed mechanical ventilation (OR: 4.2, 95% CI: 2.2 to 8.2), PSI class IV-V (OR: 25.4, 95% CI: 3.5 to 187.3), CURB-65 ≥3 (OR: 2.5, 95% CI: 1.6 to 4.1) and non-smoking (OR: 0.51, 95% CI: 0.32 to 0.83) to be independently associated with death [***Table 4***].

Neither COPD nor the severity of COPD as defined with the classification in Gold stages (I+II vs. III+IV) was significantly associated with mortality either in the univariate or multivariate analyses.

DISCUSSION

In this study, patients with COPD and CAP did not differ in mortality rate from those without COPD. In fact, although COPD patients presented with more severe pneumonia as reflected by significantly higher PSI scores, a trend towards an even lower mortality in COPD patients was observed.

The impact of COPD in patients hospitalized with CAP is controversial. In one prospective Spanish study, the mortality was 8% which did not seem to be in excess of the rates reported for the general population[4]. Accordingly, in a sub analysis of a randomized clinical trial, the mortality was 8% and not increased in patients with COPD hospitalized with CAP. However, patient number was limited and the proportion of COPD patients was higher than usual (57%)[5]. In a large series of nonresponding CAP patients, Menendez et al [12] found that COPD was a protective factor against treatment failure to initial antibiotics. Accordingly, it has recently been reported that in a series including thousands of hospitalized CAP patients the mortality of COPD was the lowest (10%) compared with several other co morbidities with a mortality of up to 25%[15]. Conversely, in a retrospective observational study from the USA, including 744 patients, 215 of whom had COPD, there was a significantly higher 30- and 90-day mortality in COPD patients compared to those without COPD (10.6 versus 8.7%) [6]. Likewise, in a prospective multicenter study including 710 patients (244 with COPD), COPD was an independent risk factor for mortality in patients with CAP (OR=2.62)[7].

Besides potential biases in study designs, there are at least three important factors that might account for the conflicting results. First, the definition of COPD was not regularly done using spirometric measurements before admission for CAP,

thus introducing a significant potential bias. Second, without spirometric measurements, no adjustment for COPD severity can be performed. Finally, inhaled and systemic steroids might fundamentally affect outcomes, however, variations in dosages and difficulties in documenting varying dosages over time make it extremely difficult to adequately control for this confounder[16]. And additional limitation of the study is the impossibility to have spirometry in non COPD patients prospectively admitted for CAP.

In our study, patients were only defined as COPD patients when spirometries were available before admission, and we excluded patients with a clinical history of COPD and without spirometry. This approach substantially increases the validity of the diagnosis. On the other hand, the availability of spirometries allowed the adjustment for COPD severity on multivariate analysis of complications and mortality. We made every effort to capture the history of inhaled and systemic steroid medications and included this confounder in the multivariate analysis as well. However, we could not exclude hidden effects of dosage variations over time. Overall, we believe that we have approached these potential confounders as closely as possible. In the non-COPD group COPD was discarded by a previous spirometry and or clinical history.

Patients with COPD had higher mean PSI classes at presentation but a similar CURB-65 score compared to patients without COPD, mainly because of older age and higher percentage of males and of comorbidities. Despite the higher PSI class, the mortality was lower. The same results were maintained when nursing home patients were excluded from the study. The paradox of more severe pneumonia in COPD patients by PSI score but with better clinical outcomes could reflect the fact that

possibly PSI is not a good marker of severity of CAP in COPD patients. Otherwise, the level of inflammatory response and the consequent lung injury could be better markers of disease severity in COPD patients.

Two main reasons may account for this finding. First, it may be related to the fact that COPD patients more frequently received antibiotics before admission which has been shown to be protective against severe CAP[17, 18]. Accordingly, it has also been demonstrated in a large series of 388406 CAP patients in Germany that death occurs mostly within the first day after admission [19]. On the other hand the absence of differences in mortality between COPD and non-COPD did not change when we stratified COPD patients according GOLD stages.

Second, despite a higher PSI in COPD patients, the extension of infiltrates and the amount of inflammatory response was lower. On the other hand, parameters of acute respiratory failure (respiratory rate and PaO_2/FIO_2 ratio) were more severely compromised in COPD patients. This pattern of findings is best explained by the view that COPD patients might already experience acute respiratory failure with less pulmonary extension of pneumonia because of the premorbid chronic respiratory compromise. Moreover, this disproportionate effect of mild inflammatory compromise may account for a dilution of COPD as a risk factor of death[20, 21].

In accordance with this interpretation, COPD patients had fewer pulmonary complications at admission. Previous treatment with ICS failed to be an independent protective factor against mortality, but it was a protective factor against the development of respiratory complications at admission and during hospitalization. Thus, we cannot discard the possibility that previous administration of ICS is not only

a “marker of COPD” but that may reduce lung inflammatory response resulting in less pulmonary complications[22]. In concordance with this hypothesis, different authors have clearly suggested that ICS could diminish CAP severity by modulating the local inflammatory response (lung microenvironment and macrophage activation[23] and subsequent organ dysfunction[24, 25] and, possibly, could even reduce mortality rate [26, 27]. Our data do not confirm an association of ICS with mortality, but the observed protective effect against pulmonary complications clearly confirms the hypothesis of a positive influence of ICS on CAP severity.

Adjunctive therapy with corticosteroids can cause an attenuation of the inflammation and may improve outcome [28]. Systemic steroids have an inhibitory effect on cytokine production, and have been proposed as a therapeutic option in pulmonary infection and severe sepsis, mainly in patients with adrenocortical insufficiency. In this study, the treatment with systemic steroids did not affect mortality.

In conclusion, this study showed comparable 30-day mortality between patients with spirometrically confirmed COPD and CAP and patients without COPD despite more severe pneumonia at admission (respiratory rate, respiratory failure, PSI). More frequent previous antibiotic treatment and the disproportion of amount of acute respiratory failure and radiographic extension in COPD patients are possible explanations for this paradox.

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