Chronic Obstructive Pulmonary Disease in COVID-19 Patients: A Risk Factor for Worse Outcomes?

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Abstract

Introduction: Early meta-analysis suggested that chronic obstructive pulmonary disease (COPD) was a risk factor for severe forms of coronavirus disease-2019 (COVID-19), however, reported COPD incidence was very low. We aimed to compare the population of COPD patients admitted to the hospital with patients without COPD.

Methods: *The study cohort included patients admitted with COVID-19 from March to July of 2020. The patients with a previous diagnosis of COPD were compared with patients without this diagnosis.*

Results: *A total of 194 patients were included, 28 (14%) had COPD. COPD patients were significantly older than non-COPD patients. There was no difference in sex distribution, the prevalence of hypertension and diabetes mellitus and medical therapy administered between both groups. A previous diagnosis of COPD did not correlate with a higher need for invasive mechanical ventilation (p=0,378), death (p=0,396), readmission at 3 months (p=0,76) or death at 3 months (p=0,315).*

Discussion: *We report a higher number of COPD patients than previous works, with a prevalence similar to that expected in the Lisbon region and, therefore, these patients do not seem to be at higher risk for the hospital admission. In this cohort study, we didn't find an association between COPD and the severity of SARS-CoV-2 infection.*

Keywords: *SARS-CoV-2; COVID-19; chronic obstructive pulmonary disease; pandemic.*

Abbreviations

COVID-19: coronavirus disease 19

COPD: chronic obstructive pulmonary

ACE-2: angiotensin-converting enzyme II

HFNC: high flow nasal cannula

NIV: non-invasive mechanical ventilation

IMV: invasive mechanical ventilation

ECMO: extracorporeal membrane oxygenation

SARS: severe acute respiratory syndrome

MERS: Middle East respiratory syndrome

Introduction

Prior knowledge about the contribution of bacterial and viral infections in exacerbations of chronic obstructive pulmonary disease (COPD) may suggest that these patients are at risk for severe forms of coronavirus disease 2019 (COVID-19) **(**1,2**)**. Furthermore, the symptoms of SARS-CoV-2 infection may mimic an acute exacerbation of COPD possibly postponing a correct diagnosis or even causing a delay in a patient seeking medical attention **(3)**. It is widely known that SARS-CoV-2 uses the angiotensin-converting enzyme II (ACE-2) as the cellular entry receptor. There is evidence proposing that active cigarette smoking and COPD upregulate ACE-2 expression in the lower airways, which is another factor potentially contributing to the severity of COVID-19 **(4)**. Two early meta-analyses, including main studies carried out in China, suggested that COVID-19 infection is associated with significant severity and mortality in COPD patients. However, the reported incidence of COPD among COVID-19 patients was very low compared with estimates of the prevalence of these conditions in the general population. **(**3,5**)**. A larger case series of 20133 patients in the UK found COPD as a comorbidity in 5.4% of the patients **(6)** and a recent review of 168 patients in Spain reported a COPD prevalence of 7.1% **(7)**.

With this paper, we aimed to characterize the population of COPD patients admitted to a Central Hospital in Lisbon and to compare morbidity and mortality outcomes with patients without COPD.

Methods

This was a retrospective single-center study carried out at the Infectious Disease Department of Centro Hospitalar e Universitário de Lisboa Central (Lisbon, Portugal). The study cohort included patients admitted with COVID-19 from March to July of 2020. Patients whose admission criteria were not directly related to the severity of the SARS-CoV-2 infection (social vulnerability, impossibility of isolation from cohabitants, surgical cases, and other less frequent situations) were excluded. The patients with a previous diagnosis of COPD were selected and a comparative analysis was carried out between this group and the patients without this diagnosis. The following clinical and socio-demographic data were collected from electronic records: age, sex, smoking status (non-smoker, active smoker and former smoker), co-morbidities as arterial hypertension, diabetes *mellitus* and previous diagnosis of COPD, duration of the admission stay, specific therapy and antibiotics administrated, type of respiratory support and the outcome (death or hospital discharge).

Categorical variables are presented as frequencies and percentages, and continuous variables as medians and interquartile ranges since all had skewed distributions. Categorical variables were compared with the use of the Chi-square test and continuous variables were compared with the Mann-Whitney test. All reported p-values are two-tailed, with a p-value <0.05 indicating statistical significance. Statistical analysis was performed with commercially available IBM SPSS software version 22 for Windows.

Results

A total of 194 patients were included (table 1). The median age was 65 years old (youngest 18, oldest 100), and the majority were males (69,6%, n=135). A previous diagnosis of COPD was identified in 28 patients (14% of the total).

The prescription of specific therapy (table 2) (hydroxychloroquine, lopinavir/ritonavir, remdesivir and corticotherapy) was the same in both groups, changing over time, according to the growing evidence available. Likewise, there were no differences in the antibiotic prescription.

All patients needed some kind of respiratory support: oxygen therapy, high flow nasal cannula (HFNC), non-invasive mechanical ventilation (NIV), invasive mechanical ventilation (IMV) or extracorporeal membrane oxygenation (ECMO). The patients received supportive treatment with oxygen therapy in an equal proportion between the groups, with a need for an equal median O2 output of 3L/min (2-5) (p=0,923). HFNC was used in 6 patients, 4 of them had no indication for IMV according to clinical decision and passed. Only 4 patients were treated with NIV, all had COPD and 2 of them were already on nocturnal home NIV. IMV was necessary for 43 patients (22,2% of the total), of which 8 had COPD, and this previous diagnosis did not correlate to an increased need for IMV (p=0,378). Only 3 patients were treated with ECMO, none of them had COPD and they all survived.

A summary of the outcomes is presented in Table 3. There were 169 hospital discharges (87% of the patients), the majority for their residences or previous home care facilities, 14 patients were referred for rehabilitation institutions.

Table 1. Patients' demographic and clinical characteristics

	Total n(%) n=194	COPD n(%) n=28	Non-COPD n(%) n=166	p value
Age	65 (50-81)	78 (68-83)	63 (49-79)	0,002
Gender male	135 (69,6%)	21 (75%)	114 (68,7%)	0,501
Smoking status				
Not smoker	153 (78,9%)	9 (32,1%)	144 (86,7%)	<0,0001
Former smoker	26 (13,4%)	11 (39,3%)	15 (9,1%)	<0,0001
Current smoker	15 (7,7%)	8 (28,6%)	7 (4,2%)	<0,0001
Hypertension	95 (49%)	13 (46,4%)	82 (49,4%)	0,881
Diabetes mellitus	47 (24,2%)	6 (21,4%)	41 (24,7%)	0,845

COPD inhaled treatment				
LAMA/LABA	-	9 (32,1%)	-	-
LABA/ICS	-	5 (17,9%)	-	-
LAMA/LABA/ICS	-	5 (17,9%)	-	-
LAMA	-	3 (10,7%)	-	-

COPD: chronic obstructive lung disease; LAMA: long-acting muscarinic receptor antagonists; LABA: long-acting beta-agonists; ICS: inhaled corticosteroids

Table 2. Prescription of antibiotics and specific therapy

	Total n(%) n=194	COPD n(%) n=28	Non-COPD n(%) n=166	p value
Antibiotics	83 (42,8%)	14 (50%)	69 (41,7%)	0,404
Specific therapy				
Hydroxychloroquine	74 (38,1%)	12 (42,9%)	62 (37,3%)	0,579
Lopinavir/ritonavir	28 (14,4%)	5 (21,4%)	23 (19,9%)	0,577
Remdesivir	21 (10,8%)	5 (17,9%)	16 (9,6%)	0,195
Corticotherapy	38 (19,6%)	8 (28,6%)	30 (18,1%)	0,195

COPD: chronic obstructive lung disease

Table 3. Outcomes

	Total n(%)	COPD n(%)	Non-COPD n(%)	p value
Median length of stay (days)	12 (7-22)	11,5 (6,5-20)	12 (7-22,3)	0,778
Deaths n (%)	25 (12,9%)	5 (17,9%)	20 (12%)	0,396
Post hospital discharge (n=169)				
Readmission at 3 months n (%)	9 (5,3%)	3 (13%)	6 (4,1%)	0,760
Death at 3 months n (%)	3 (1,8%)	1 (4,3%)	2 (1,4%)	0,315

COPD: chronic obstructive lung disease

Discussion

With 14% of admitted patients having a previous diagnosis of COPD, this case series reports a higher prevalence of this condition than previous works **(**3,5–7**)**. Furthermore, our population is representative of the prevalence of COPD in the Lisbon region, which is set at 14,2% **(**8**)** and, consequently, these patients do not seem to be at higher risk for hospital admission due to COVID-19. These results are a reflection of a time when stricter isolation policies were in place and patients belonging to risk groups were advised to self-isolate. Therefore, it is unclear whether we will see a future increase in the number of COPD patients admitted to hospitals by COVID-19. Even though this group of patients may appear to have a slightly higher fatality rate and also to be at increased risk for hospital readmission at 3 months, these findings had no statistical significance. This tendency may also be explained by the older age of the patients with COPD in our series and, possibly, by the small sample size.

This study took place at a time when, to be classified as cured, the patient had to have two negative nasopharyngeal swabs which caused a delay in hospital discharges for patients who could not isolate themselves from co-habitants. As the criteria for cure shifts to 10 days after the onset of symptoms given that the patient is asymptomatic for at least 3 days, we will observe for sure a decrease in the length of stay.

We were surprised to find that there was no difference in corticotherapy prescription between groups given that corticoids are a cornerstone of the treatment of acute exacerbation of COPD **(**9**)**. This could partially be explained by the initial cautious approach in corticoid use given the reports of negative outcomes in Severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) **(**10**)**. Contrary to our findings, one could also expect an increased tendency for antibiotic prescription in the COPD group given the lower threshold for its use in these patients **(**9**)**. One explanation could be that initial protocols favored early antibiotic therapy for all severe patients, whereas currently this prescription is reserved for cases highly suspicious of bacterial superinfection.

Of course, we have to consider the limitations of the single-center retrospective study design and, even though we report a higher COPD prevalence than previous studies, this is still a small sample size. In conclusion, contrary to previous publications, **(**3,5**)** we didn't find an association between COPD and the severity of SARS-CoV-2 infection.

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