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Original Research

Clinical outcomes in patients with COPD hospitalized with SARS-CoV-2 versus non- SARS-CoV-2 community-acquired pneumonia

Daniya Sheikh^{a,*}, Nishita Tripathi^a, Thomas R. Chandler^a, Stephen Furmanek^a, Jose Bordon^b, Julio A. Ramirez^a, Rodrigo Cavallazzi^c

^a Division of Infectious Diseases, University of Louisville, Louisville, KY, USA

^b Washington Health Institute, George Washington University, Washington, DC, USA

^c Division of Pulmonary, Critical Care Medicine and Sleep Disorders, University of Louisville, Louisville, KY, USA



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ABSTRACT

Background: Patients with chronic obstructive pulmonary disease (COPD) have poor outcomes in the setting of community-acquired pneumonia (CAP) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The primary objective is to compare outcomes of SARS-CoV-2 CAP and non-SARS-CoV-2 CAP in patients with COPD. The secondary objective is to compare outcomes of SARS-CoV-2 CAP with and without COPD.

Methods: In this analysis of two observational studies, three cohorts were analyzed: (1) patients with COPD and SARS-CoV-2 CAP; (2) patients with COPD and non-SARS-CoV-2 CAP; and (3) patients with SARS-CoV-2 CAP without COPD. Outcomes included length of stay, ICU admission, cardiac events, and in-hospital mortality.

Results: Ninety-six patients with COPD and SARS-CoV-2 CAP were compared to 1129 patients with COPD and non-SARS-CoV-2 CAP. 536 patients without COPD and SARS-CoV-2 CAP were analyzed for the secondary objective. Patients with COPD and SARS-CoV-2 CAP had longer hospital stay (15 vs 5 days, $p < 0.001$), 4.98 higher odds of cardiac events (95% CI: 3.74–6.69), and 7.31 higher odds of death (95% CI: 5.36–10.12) in comparison to patients with COPD and non-SARS-CoV-2 CAP. In patients with SARS-CoV-2 CAP, presence of COPD was associated with 1.74 (95% CI: 1.39–2.19) higher odds of ICU admission and 1.47 (95% CI: 1.05–2.05) higher odds of death.

Conclusion: In patients with COPD and CAP, presence of SARS-CoV-2 as an etiologic agent is associated with more cardiovascular events, longer hospital stay, and seven-fold increase in mortality. In patients with SARS-CoV-2 CAP, presence of COPD is associated with 1.5-fold increase in mortality.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common disease with a global prevalence of 2% in women and 3.2% in men [1,2]. In the United States, the prevalence of COPD varies largely among states, some of which have figures higher than 9% [3]. Patients with COPD have an 18 times higher risk of developing Community-acquired Pneumonia (CAP) requiring hospitalization as compared with patients without COPD [4]. In fact, COPD is the strongest risk factor for development of CAP requiring hospitalization [1,4,5]. Overall, a third of patients with CAP requiring hospitalization die within a year, and the mortality is 25% greater among patients with COPD [4,5].

The year of 2020 was distinguished by the emergence of the Coronavirus Disease 2019 (COVID-19) pandemic, caused by the severe acute

respiratory syndrome coronavirus 2 (SARS-CoV-2) [6]. As of February 2021, this unprecedented pandemic has caused over 500,000 deaths only in the United States [7]. The predominant clinical manifestation of COVID-19 is respiratory tract infection. In the severe form, patients develop CAP with consequent respiratory failure [8]. Most reports so far indicate COPD is associated with higher mortality in the setting of SARS-CoV-2 infection. But it is not clear how the outcomes of SARS-CoV-2 CAP compare with those of non-SARS-CoV-2 CAP in patients with COPD. Such a comparison will enable a more complete understanding of the interaction between COPD and SARS-CoV-2 in the setting of CAP.

The primary objective of our study is to compare the clinical outcomes of SARS-CoV-2 CAP and non-SARS-CoV-2 CAP in patients with COPD. The secondary objective is to compare the outcomes of SARS-

* Corresponding author. 501 E. Broadway, MedCenter One, Suite-140B, Louisville, KY, 40202.

E-mail address: d0shei01@louisville.edu (D. Sheikh).

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CoV-2 CAP in patients with and without COPD.

2. Methods

2.1. Study design

This comparative analysis involved a combination of two large observational studies: the Burden of COVID-19 study [9] and the University of Louisville Pneumonia Study [5]. Both studies were approved by the University of Louisville Institutional Review Board. The Burden of COVID-19 study (Institutional Review Board #20–0257) was a retrospective observational study in the Louisville metropolitan area, including all hospitalized patients who were diagnosed with COVID-19 infection between March 1, 2020 and June 30, 2020 at eight acute-care hospitals in Louisville, KY. The University of Louisville Pneumonia study (Institutional Review Board #11–0615) was a prospective, population-based observational study, performed in all nine adult acute-care hospitals in Louisville over two years, from June 1, 2014 to May 31, 2016.

2.2. Patient population

We selected patients who were hospitalized with CAP. Patients with COPD were selected based on the diagnosis from the electronic medical record. The diagnosis of CAP required the presence of a new pulmonary infiltrate on imaging (computed tomography scan or chest X-ray) at the time of admission to the hospital with at least one of the following signs or symptoms: new or increased cough (per history), a temperature of >37.8 C or <35.6 C, or abnormality in leukocyte count ($>11,000$ or <4000 cells/mL, or left shift with $>10\%$ band forms/mL). For our analysis, patients with CAP who were admitted prior to the COVID-19 pandemic onset were considered as non-SARS-CoV-2 CAP. A patient was defined as having COVID-19 when the virus SARS-CoV-2 was identified in a clinical specimen using polymerase chain reaction. Additionally, to match the time frame for the Burden of COVID-19 study, only patients from the University of Louisville Pneumonia Study who were hospitalized during the time periods of June 1, 2014–June 30, 2014; March 1, 2015–June 30, 2015; and March 1, 2016–June 30, 2016 were considered in our analysis.

2.3. Study group definition

The patients in our study were divided into 3 groups. The first group consisted of patients who had SARS-CoV-2 CAP and COPD and was derived from the Burden of COVID-19 study. The second group consisted of patients who had COPD and non-SARS-CoV-2 CAP, who were taken from the University of Louisville Pneumonia Study database. The third group consisted of patients with SARS-CoV-2 CAP without COPD and was obtained from the Burden of COVID-19 study.

2.4. Variables

Study variables collected from the medical records included demographics, comorbidities, medications, vital signs, laboratory values and the following severity of disease indicators: invasive or non-invasive ventilator support on the first day of admission, vasopressors (e.g. epinephrine, norepinephrine, and phenylephrine) on the first day of admission, and pneumonia severity index (PSI) risk class [10].

2.5. Outcomes

Study outcomes included intensive care unit (ICU) admission, need for invasive mechanical ventilation, hospital length of stay (LOS), cardiovascular events and all-cause in-hospital mortality. Cardiovascular events were defined as any in-hospital events occurring from the onset of symptoms until discharge. The cardiovascular events considered for the

analysis included acute myocardial infarction, pulmonary edema due to congestive heart failure, occurrence of a new serious arrhythmia, acute worsening of long-term arrhythmia, cerebrovascular accidents (e.g. ischemic/hemorrhagic stroke) and pulmonary emboli. LOS was defined in days and was calculated for each patient as the day of discharge minus the day of admission. LOS was treated as a time-dependent outcome and right truncated at 30 days. A patient who died in hospital was given a censored 30-day LOS as a worst outcome. For the SARS-CoV-2 CAP groups, patients who were discharged to hospice were also censored at 30 days. In-hospital mortality was defined as all-cause mortality occurring during the hospitalization.

2.6. Statistical analysis

Continuous patient characteristics were summarized as median and interquartile range. Categorical patient characteristics were summarized as frequencies and percentages. Baseline patient characteristics were compared using Chi-Squared tests of independence, or Fisher's exact test when expected cell counts were insufficient. Adjusted analysis included inverse-propensity-weighted (IPW) logistic regressions for categorical outcomes adjusted for pneumonia severity index and reported as an IPW odds ratio (IPW-OR). Length of stay was analyzed using IPW survival estimation and an IPW log-rank test from the RISC package in R [11]. Full details for inverse propensity score weighting are provided in the supplemental material. Analysis was performed with R version 3.4.0 [12]. P-values were 2-sided, with statistical significance set at $P < 0.05$.

3. Results

A total of 632 patients were hospitalized with SARS-CoV-2 CAP between March 1 and June 30, 2020. Of these hospitalizations, 96 (15%) patients had COPD and 536 (85%) did not have COPD. A total of 1129 patients with non-SARS-CoV-2 CAP and COPD were hospitalized between March 1 and June 30 in 2014, 2015 and 2016 (see Fig. 1).

3.1. Clinical characteristics of patients with COPD with SARS-CoV-2 CAP and non-SARS-CoV-2 CAP

Patient characteristics are shown in Table 1. Higher proportions of black race (32%, $n = 31$), nursing home residents (30%, $n = 29$), and a history of obesity (48%, $n = 46$), diabetes mellitus (51%, $n = 49$), renal disease (41%, $n = 39$), essential arterial hypertension (80%, $n = 77$), and substance abuse (14%, $n = 13$) were present in patients with COPD and SARS-CoV-2 CAP as compared with patients with COPD and non-SARS-CoV-2 CAP. Patients with COPD and SARS-CoV-2 CAP presented with higher PSI scores (median = 118, IQR = 86–137) and lower serum glucose (median = 120 mg/dL, IQR = 102–171) as compared with patients with COPD and non-SARS-CoV-2 CAP. The latter were more likely to be current smokers (40%, $n = 451$) and have coronary artery disease (34%, $n = 389$) than patients with COPD and SARS-CoV-2 CAP. Patients with COPD and non-SARS-CoV-2 CAP patients also had increased white blood cell counts (median = $12.4 \times 1000/\mu\text{L}$, IQR = 8.8–16.7).

3.2. Clinical characteristics of patients with SARS-CoV-2 CAP with and without COPD

Patient characteristics are shown in Table E3 in supplemental material. SARS-CoV-2 CAP patients with COPD were older (median = 71 years, IQR = 65–78) than SARS-CoV-2 CAP patients without COPD (median = 60 years, IQR = 45–72). Higher proportions of nursing home residents (30%, $n = 29$), current smokers (19%, $n = 18$), obesity (48%, $n = 46$), and most co-morbidities were present in SARS-CoV-2 CAP patients with COPD as compared with SARS-CoV-2 CAP patients without COPD.

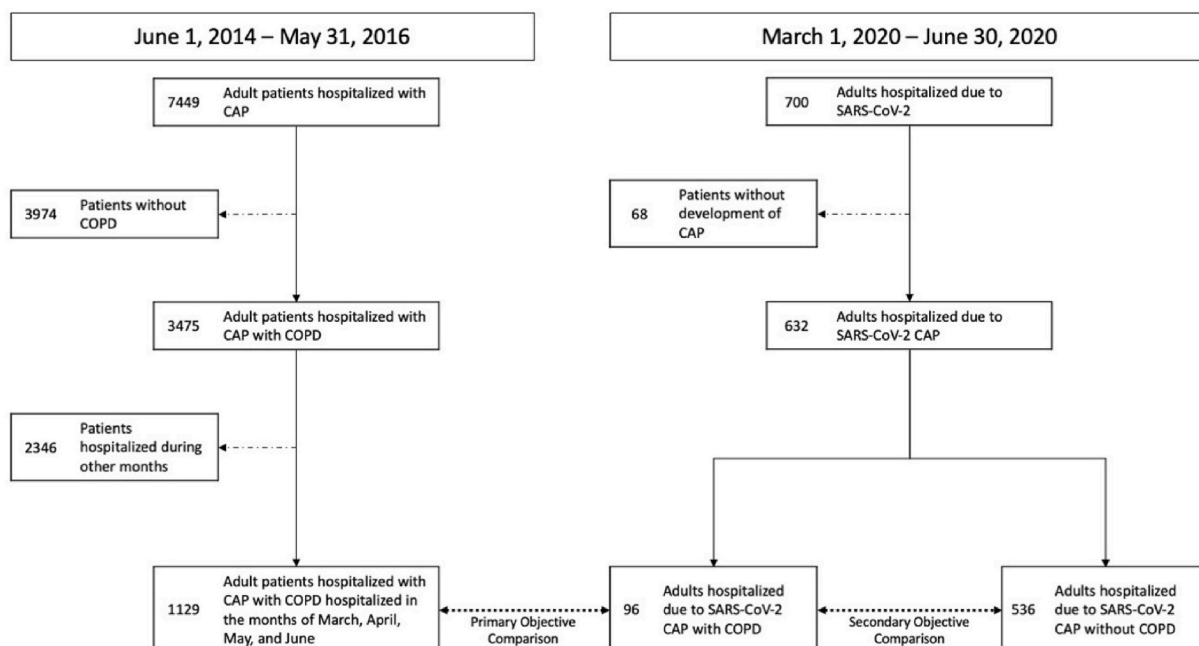


Fig. 1. Flow diagram displaying the number of participants in each study group. CAP: Community-acquired pneumonia; COPD: Chronic obstructive pulmonary disease; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2. This analysis was a combination of two large observational studies. The left arm of the flow diagram represents the University of Louisville Pneumonia Study, which ran from June 1, 2014 to May 31, 2016. The right arm of the flow diagram represents the Burden of COVID-19 study, running from March 1, 2020 to June 30, 2020.

3.3. Primary objective (comparison of SARS-CoV-2 CAP and non-SARS-CoV-2 CAP in patients with COPD)

Fig. 2 illustrates the results for the primary and secondary objectives. Patients hospitalized with SARS-CoV-2 CAP more frequently required admission to the ICU during hospital stay (48%, $n = 46$; vs 25%, $n = 278$). After IPW and PSI adjustment, patients with SARS-CoV-2 CAP had 2.41 times increased odds of ICU admission during hospitalization (IPW-OR = 2.41, 95% CI: 2.01–2.91, $p < 0.001$).

A total of 29 (30%) patients hospitalized with SARS-CoV-2 CAP required invasive mechanical ventilation, compared to 158 (14%) patients in the non-SARS-CoV-2 CAP group. After IPW and PSI adjustment, patients in the SARS-CoV-2 CAP group had 2.23 times higher odds of requiring IMV (IPW-OR = 2.23, 95% CI: 1.80–2.77, $p < 0.001$).

Cardiovascular events were also more numerous in the SARS-CoV-2 CAP patient group. A total of 28 (29%) of patients in that group experienced cardiovascular events, compared to 81 (7%) patients in the non-SARS-CoV-2 CAP group. Table 2 details individual cardiovascular events by study group. After IPW and PSI adjustment, patients in the SARS-CoV-2 CAP group had 4.98 times higher odds of experiencing a cardiovascular event (IPW-OR = 4.98, 95% CI: 3.74–6.69, $p < 0.001$).

Patients hospitalized with SARS-CoV-2 CAP had a median length of stay of 15.5 days (IQR = 6.8–30.0). Patients hospitalized with non-SARS-CoV-2 CAP had a median length of stay of 5.0 days (IQR = 3.0–9.0). Fig. 3 displays the IPW Kaplan-Meier curves for length of stay. After IPW adjustment, this difference in length of stay remained significant ($p < 0.001$, see Fig. 3). A total of 28% ($n = 27$) patients in the SARS-CoV-2 CAP group died during hospitalization, compared to 5% ($n = 52$) in the non-SARS-CoV-2 CAP group. After IPW and PSI adjustment, patients in the SARS-CoV-2 CAP group had 7.31 times higher odds of expiring in the hospital (IPW-OR = 7.31, 95% CI: 5.36–10.12, $p < 0.001$).

3.4. Secondary objective (comparison of SARS-CoV-2 CAP patients with and without COPD)

After IPW and PSI adjustment, there were no significant differences in cardiovascular events and need for invasive mechanical ventilation between the two groups (see Fig. 2). Patients with SARS-CoV-2 CAP and COPD were more likely to be admitted to the ICU (IPW-OR = 1.74, 95% CI: 1.39–2.19, $p < 0.001$) and die in the hospital (IPW-OR = 1.47, 95% CI: 1.05–2.05, $p = 0.024$).

Patients hospitalized with SARS-CoV-2 CAP and COPD had a median length of stay of 15.5 days (IQR = 6.8–30.0). Patients hospitalized with SARS-CoV-2 CAP without COPD had a median length of stay of 7.8 days (IQR = 3.7–21.9). Figure E3 in supplemental material displays the IPW Kaplan-Meier curves for length of stay. After IPW adjustment, this difference in length of stay was not statistically significant ($p = 0.200$, see Figure E3).

4. Discussion

Our analysis showed that patients with COPD and SARS-CoV-2 CAP had seven times higher risk of in-hospital mortality compared to patients with COPD and non-SARS-CoV-2 CAP in previous years. We found that patients with COPD and SARS-CoV-2 CAP had nearly twice the risk of requiring invasive mechanical ventilation, 2.5 times the risk of admission to the ICU, 5 times the risk of experiencing cardiovascular events and three times the median length of stay compared to patients with COPD and non-SARS-CoV-2 CAP. Additionally, we demonstrated that in patients with SARS-CoV-2 CAP, the presence of COPD is associated with a 74% increase in need for ICU admission and a 47% increase in in-hospital mortality.

The increase in mortality in patients with COPD and SARS-CoV-2 CAP in our study may be explained by several biological mechanisms. The use of receptor angiotensin-converting enzyme-2 for SARS-CoV-2 cell entry [13] and the upregulated ACE-2 expression in patients with COPD may be factors predisposing these patients to poor outcomes. The ACE-2 expression in patients with COPD can be upregulated by two

Table 1
Clinical characteristics of patients with COPD with SARS-CoV-2 CAP and non-SARS CoV-2 CAP.

	SARS-CoV-2 CAP n = 96	Non-SARS-CoV-2 CAP n = 1129	P-value
Demographics and Medical History			
Age*	71 [65, 78]	69 [60, 78]	0.087
Sex: Male (%)	39 (41)	499 (44)	0.569
Black (%)	31 (32)	189 (17)	<0.001
Nursing home residents (%)	29 (30)	128 (11)	<0.001
Current smoker (%)	18 (19)	451 (40)	<0.001
Former smoker (%)	47 (49)	508 (45)	0.521
Obesity (%)	46 (48)	412 (36)	0.056
Diabetes mellitus (%)	49 (51)	388 (34)	0.001
Renal disease (%)	39 (41)	317 (28)	0.007
Heart failure (%)	24 (25)	392 (35)	0.662
Coronary artery disease (%)	24 (25)	389 (34)	0.077
Cerebrovascular disease (%)	20 (21)	152 (13)	0.065
Neoplastic disease (active/ within last year) (%)	15 (16)	149 (13)	0.607
Liver disease (non-cirrhotic) (%)	5 (5)	87 (8)	0.490
Essential Arterial Hypertension (%)	77 (80)	814 (72)	0.111
Hyperlipidemia (%)	47 (49)	519 (46)	0.648
Prior Myocardial Infarction (%)	17 (18)	165 (15)	0.504
Atrial Fibrillation (%)	18 (19)	225 (20)	0.885
History of substance abuse (%)	13 (14)	76 (7)	0.024
Management of Comorbid Disease			
Oral corticosteroid use prior to admission (%)	24 (25)	198 (18)	0.092
Home oxygen therapy (%)	21 (22)	257 (23)	0.942
Aspirin (%)	39 (41)	421 (37)	0.591
Beta-blocker (%)	43 (45)	469 (42)	0.609
ACE inhibitor (%)	21 (22)	308 (27)	0.304
Antiplatelet (%)	22 (23)	79 (7)	<0.001
Statins (%)	48 (50)	446 (40)	0.058
Physical Examination and Laboratory findings			
Pneumonia Severity Index*	118 [86, 137]	105 [78, 134]	0.099
Heart Rate (beats/min)*	94 [83, 109]	106 [91, 129]	<0.001
Respiratory Rate (breaths/ min)*	22 [20,28]	23 [20,28]	0.321
Systolic Blood Pressure (mmHg)*	119 [103, 147]	115 [99, 134]	0.041
Diastolic Blood Pressure (mmHg)*	63 [53, 76]	56 [48, 65]	<0.001
Temperature (degrees C)*	37.3 [36.8, 38.2]	37.1 [36.8, 37.7]	0.352
WBC x 1000/ μ L*	6.5 [5.0, 8.7]	12.4 [8.8, 16.7]	<0.001
Hematocrit (%)*	37 [33, 42]	36 [32, 40]	0.089
Glucose (mg/dL)*	120 [102, 171]	151 [117, 208]	<0.001
Blood urea nitrogen (mg/ dL)*	25 [16, 43]	19 [13,28]	<0.001
Creatinine (mg/dL)*	1.20 [0.93, 2.20]	0.97 [0.70, 1.31]	<0.001
Procalcitonin (ug/L)*	0.17 [0.07, 0.74]	0.30 [0.06, 2.79]	0.128
Lactate (mmol/L)*	1.45 [1.20, 1.90]	1.50 [1.10, 2.30]	0.306
C-Reactive Protein (mg/L)*	17.7 [6.8, 54.1]	20.2 [3.7, 60.3]	0.753
Oxygen and Respiratory Support on First Day of Admission			
Need for invasive mechanical ventilation (%)	14 (15)	68 (6)	0.003
Need for non-invasive ventilation (%)	6 (6)	124 (11)	0.203
SpO ₂ (percentage)*	93 [90–96]	93 [91–96]	0.385
PaO ₂ /FiO ₂ (ratio) *	187 [143–298]	200 [138–279]	0.839

CAP: community-acquired pneumonia; COPD: chronic obstructive pulmonary disease; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; ACE inhibitors: angiotensin-converting enzyme inhibitors; WBC: white blood cells; SpO₂: oxygen saturation; PaO₂/FiO₂: pressure of arterial oxygen to fractional inspired oxygen concentration.

* Data expressed as median and interquartile range.

mechanisms. First, chronic exposure to smoke causes expansion of ACE-2 secretory cells [14]. Second, cigarette smoke, by virtue of its pro-inflammatory nature, promotes the production of inflammatory mediators, which trigger an upregulation of ACE-2 receptors [15]. Additionally, patients with COPD have low basal lung function, damaged airways and dysfunctional immunity caused by smoking [16], all of which are conducive to SARS-CoV-2 infection and poor outcomes from it [17,18].

Other studies have assessed the impact of COPD on mortality in hospitalized patients with SARS-CoV-2 infection. Taken together, these studies, like ours, indicate that the presence of COPD is associated with a 1.3–2.7 fold increased risk of in-hospital mortality [17–23]. But our own data shows that COPD is not associated with increased mortality in non-SARS-CoV-2 CAP in the short-term [4]. These findings suggest that SARS-CoV-2 modifies the short-term deleterious effects of COPD in patients with CAP. It is important to note that during pandemic surges, resource limitations likely had an impact on the outcomes of patients with COVID-19 in some areas of the country. However, the healthcare system in the city Louisville remained in good shape during that time.

The high frequency of cardiovascular events in patients with COPD and SARS-CoV-2 CAP found in our study could be attributed to a variety of mechanisms. Earlier in the pandemic, increased cytokine levels described in patients with COVID-19 were proposed as a mechanism of COVID-19 induced organ dysfunction. However, it was more recently demonstrated that even though cytokine levels are increased in patients with COVID-19, they are not necessarily higher than those of other critically ill patients with acute respiratory failure [24]. Thrombotic microangiopathy seems to play a more important role. As an example, a post-mortem study showed a distinctive feature of lung injury caused by SARS-CoV-2 is the presence of disseminated thrombosis with microangiopathy in the pulmonary vessels, and angiogenesis [25]. Clinically, patients with COVID-19 often have elevated levels of D-dimer, and their levels are on aggregate higher than those of patients with sepsis from other etiologies [24]. Chronic hypoxia, augmented inflammation, and right ventricular dysfunction [26] are commonly present features in patients with COPD and can compound the increased predisposition to cardiovascular events imparted by SARS-CoV-2 infection.

One of the most contrasting results between SARS-CoV-2 CAP and non-SARS-CoV-2 CAP in patients with COPD in our study was length of stay. The prolonged length of stay in patients with SARS-CoV-2 infection is driven by respiratory failure, which in the early phase is characterized by perfusion impairment causing ventilation-perfusion mismatch and increased dead space. Other features in the early phase include high minute-ventilation and relative high lung compliance. Later in the course of the disease, the acute respiratory failure may evolve into a pattern that resembles traditional acute respiratory distress syndrome with low lung compliance and positive end-expiratory pressure (PEEP) responsiveness [27]. The prolonged hospital stay in patients with SARS-CoV-2 infection is not unique to patients with COPD. For instance, in a clinical trial that included hospitalized patients with SARS-CoV-2 infection, the experimental arm had a median length of hospital stay of 12 days. In those requiring mechanical ventilation or extracorporeal membrane oxygenation, the median length of hospital stay was 17 days [28].

The impact that the COVID-19 pandemic has had in residents of assisted living facilities cannot be overstated. In our study, approximately one third of the patients with COPD and SARS-CoV-2 infection came from nursing homes. According to a report from Centers for Disease Control and Prevention (CDC), 1 out of 5 assisted living facility residents with COVID-19 have died whereas there has been 1 death out of 40 in persons with COVID-19 in the general population [29].

Another important epidemiological feature from our study is that there was a substantially higher proportion of blacks in the group of patients with COPD and SARS-CoV-2 CAP as compared to the group of COPD and non-SARS-CoV-2. This in line with population-based data from the CDC. Compared with white, non-Hispanic persons, the rate of

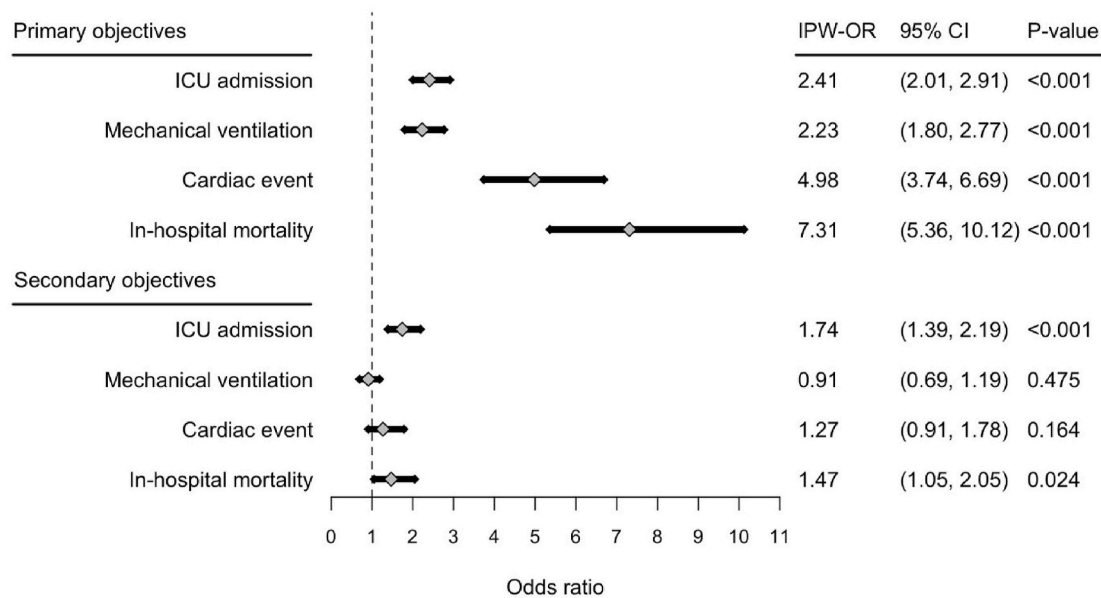


Fig. 2. Adjusted effect estimates for the primary and secondary objectives. IPW-OR: inverse propensity scores weighted odds ratio; 95% CI: 95% confidence interval for the IPW-OR. The primary objective compared patients with COPD hospitalized for SARS-CoV-2 CAP and non-SARS-CoV-2 CAP. The secondary objective compared patients with SARS-CoV-2 CAP with and without COPD.

Table 2
Cardiovascular events reported in patients with COPD hospitalized with CAP.

	SARS-CoV-2 CAP n = 96	Non-SARS-CoV-2 CAP n = 1129
Any cardiovascular event (%)	28 (29)	81 (7)
New arrhythmia (%)	15 (16)	30 (3)
Acute worsening of long-term arrhythmia (%)	6 (6)	33 (3)
Acute myocardial infarction (%)	6 (6)	15 (1)
Pulmonary Edema (%)	7 (7)	7 (1)
Cerebrovascular accident (%)	3 (3)	1 (<1)
Pulmonary embolism	0 (0)	1 (0)

CAP: community-acquired pneumonia; COPD: chronic obstructive pulmonary disease; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

hospitalization by COVID-19 was 3.2 times higher in Hispanic persons, 2.9 times higher in black persons, and 3.7 times higher in American Indian or Alaska Native persons [30]. These numbers lay bare the health disparities experienced by these groups, which largely reflect their lower social economic status, higher proportions in service occupations [31], lower access to health care [32], and residential segregation [33]. The latter is particularly pervasive in Louisville where there are minority populated neighborhoods without access to healthy food [34].

Our study has limitations. The main limitation of our study is the lack of data regarding COPD severity from our study cohorts. While we were able to capture chronic steroid use and need for home oxygen therapy prior to hospitalization, we were unable to collect data on FEV1, FVC, and other common markers of severity among patients with COPD. The diagnosis of COPD was not confirmed by spirometry, which could lead to misclassification bias. The latter would be non-differential as both groups were susceptible to it. However, it has been previously shown that a self-reported history of COPD highly increases the likelihood that COPD will be confirmed if a spirometry is performed [35]. There was an approximate 4 years difference between the two studies that provided the cohorts for the current analysis, a time frame in which treatment and outcomes could have evolved. Additionally, our study highlights the initial management of COVID-19 in hospitalized patients, which is constantly evolving. Strengths of the study include its comprehensive datasets with a wealth of clinical data not generally found in studies

relying on administrative datasets. The study was multicenter and encompassed all adult hospitals in the city. Furthermore, the epidemiology of the city of Louisville resembles that of the United States [36].

5. Conclusion

In summary, our analysis showed that inpatients with COPD and CAP, the presence of SARS-CoV-2 infection is associated with more cardiovascular events, higher ICU admission rates, higher need for mechanical ventilation, longer hospital length of stay, and a staggering 7-fold increase in hospital mortality. Furthermore, in patients with SARS-CoV-2 CAP, the presence of COPD is associated with a 1.5-fold increase in hospital mortality. Our data clarifies the interaction between SARS-CoV-2 and COPD in the setting of CAP and highlights the need for vaccination and other prevention efforts to avoid CAP in patients with COPD.

Source of support

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CRedit authorship contribution statement

Daniya Sheikh: Conceptualization, Visualization, Investigation, Writing – original draft, Writing – review & editing. **Nishita Tripathi:** Writing – original draft, Visualization, Investigation. **Thomas R. Chandler:** Methodology, Software, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Stephen Furmanek:** Methodology, Software, Formal analysis, Data curation, Visualization, Writing – original draft, Writing – review & editing. **Jose Bordon:** Writing – original draft, Writing – review & editing, Visualization. **Julio A. Ramirez:** Conceptualization, Methodology, Visualization, Investigation, Project administration, Supervision, Writing – original draft, Writing – review & editing, Resources, Validation. **Rodrigo Cavallazzi:** Conceptualization, Methodology, Visualization, Project administration, Supervision, Writing – original draft, Writing – review & editing, Validation.

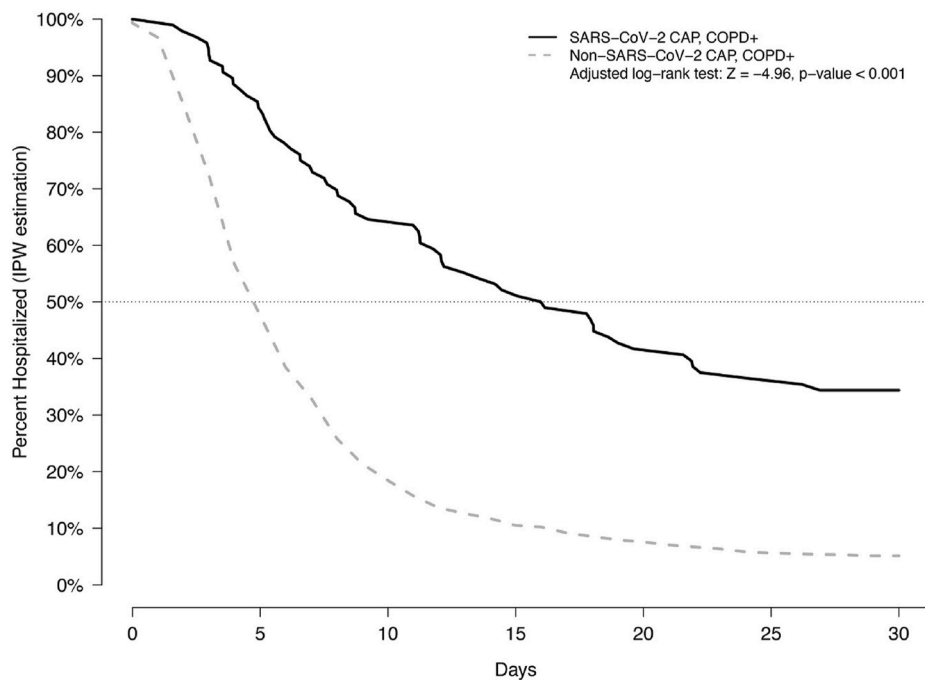


Fig. 3. Kaplan-Meier estimates for length of stay. CAP: Community-acquired pneumonia; COPD: Chronic obstructive pulmonary disease; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2. The black line depicts time to discharge for patients with SARS-CoV-2 CAP. The dashed gray line depicts time to discharge for patients with non-SARS-CoV-2 CAP. The horizontal dotted line represents the time at which 50% of the patients have been discharged from the hospital per group. The test statistic comes from inverse-propensity score weighted log-rank tests comparing the two curves.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmed.2021.106714>.

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