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Original Research

Outcomes of Patients with COPD Hospitalized for Coronavirus Disease 2019

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Abstract

Rationale: There is controversy concerning the association of chronic obstructive pulmonary disease (COPD) as an independent risk factor for mortality in patients hospitalized with coronavirus disease 2019 (COVID-19). We hypothesize that patients with COPD hospitalized for COVID-19 have increased mortality risk.

Objective: To assess whether COPD increased the risk of mortality among patients hospitalized for COVID-19.

Methods: We conducted a retrospective cohort analysis of patients with COVID-19 between February 10, 2020, and November 10, 2020, and hospitalized within 14 days of diagnosis. Electronic health records from U.S. facilities (Optum COVID-19 data) were used.

Results: In our cohort of 31,526 patients, 3030 (9.6%) died during hospitalization. Mortality in patients with COPD was higher than that of patients without COPD, 14.02% and 8.8%, respectively. Univariate (odds ratio [OR] 1.68; 95% confidence interval [CI] 1.54 to1.84) and multivariate (OR 1.33; 95% CI 1.18 to1.50) analysis showed that patients with COPD had greater odds of death due to COVID-19 than patients without COPD. We found significant interactions between COPD and sex and COPD and age. Specifically, the increased mortality risk associated with COPD was observed among female (OR 1.62; 95% CI 1.36 to 1.95) but not male patients (OR 1.14; 95% CI 0.97 to 1.34); and in patients aged 40 to 64 (OR 1.42; 95% CI 1.07 to 1.90) and 65 to 79 (OR 1.48; 95% CI 1.23 to 1.78) years.

Conclusions: COPD is an independent risk factor for death in adults aged 40 to 79 years hospitalized with COVID-19 infection.

Abbreviations: chronic obstructive pulmonary disease, **COPD**; coronavirus disease 2019, **COVID-19**; odds ratio, **OR**; confidence interval, **CI**, severe acute respiratory syndrome coronavirus 2, **SARS-CoV-2**; electronic health record, **EHR**; *International Classification for Diseases, 10th revision, Clinical Modification*, **ICD-10-CM**; body mass index, **BMI**; chronic kidney disease, **CKD**; end-stage renal disease, **ESRD**; congestive heart failure, **CHF**; coronary artery disease, **CAD**; inhaled corticosteroid, **ICS**

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This article has an online supplement.

Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has caused, to date, 41 million cases and 667,244 deaths in the United States.[1] Coronavirus disease 2019 (COVID-19), the infectious disease caused by SARS-CoV-2, has become the leading cause of death in the United States.[2]

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the United States and affects 16 million Americans.[3] During the COVID-19 pandemic, the association of COPD with adverse outcomes due to COVID-19 has been controversial. Worldwide, studies of patients with COVID-19 have reported COPD to be a risk factor for greater health care utilization,[4] with increased risk of hospitalization, intensive care unit (ICU) admission, and death,[5–12] while others have not shown this association.[13–16] The association between COPD and adverse outcomes from COVID-19 remains disputed.

The prevalence of COPD among patients with COVID-19 varies[8,9,14,17,18] between 1.5% and 18%. This is likely an underestimation, as a SARS-CoV-2 infection can range in presentation from asymptomatic to severe disease. Severe COVID-19 may lead to hospitalization, ICU admission, non-invasive and invasive mechanical ventilation use, and death.[19–24] Given the propensity for patients with COPD to suffer acute exacerbations induced by viral infections, such patients may be particularly vulnerable to adverse outcomes associated with COVID-19.[25]

The prevalence of COPD varies globally,[26] therefore, the reported potential association of COPD as a risk factor for adverse outcomes in COVID-19 may vary by country or national health care system. Consequently, it is important to explore the characteristics and outcomes of patients hospitalized in the United States with COVID-19 and COPD. To evaluate COPD as an independent risk factor for mortality in patients with COVID-19, we conducted a large, nationally representative retrospective cohort study of U.S. patients hospitalized with COVID-19. We hypothesized that, among hospitalized patients with COVID-19, those with COPD would have an increased risk of inpatient mortality.

Methods

Data Source

In this retrospective cohort study, we used Optum's longitudinal COVID-19 electronic health record (EHR) database of more than 90 million patients across multiple hospital networks from all regions in the United States. The database contains de-identified inpatient and ambulatory encounter-level information, as well as procedure, prescription, and medication administration data. The University of Texas Medical Branch Institutional Review Board approved this study (IRB# is 20-0180). Written informed consent was not required due to the de-identified nature of the patient data.

Cohort

The study cohort included patients diagnosed with COVID-19 between February 10, 2020, and November 10, 2020, who were hospitalized within 14 days of diagnosis. COVID-19 was identified by a positive laboratory test for SARS-CoV-2 or by the *International Classification for Diseases, 10th revision, Clinical Modification* (ICD-10-CM) diagnosis code U07.1 (See Table S1 in the online data supplement). Patients younger than 40 years at the time of diagnosis were excluded due to the low prevalence of COPD in this population[27] (Figure S1 in the online data supplement).

Variables

The primary outcome was inpatient mortality among patients with COVID-19-associated hospitalization. The main independent variable of interest was COPD and was defined as having experienced ≥1 inpatient or ≥2 outpatient visits for COPD in the 1 year before the COVID-19 diagnosis (See Table S2 in the online data supplement).

We collected information on patient demographics

as well as clinical and medication history. Comorbidities present before the COVID-19 diagnosis were identified using ICD-10-CM diagnosis codes. Convalescent plasma and medications administered during hospitalization (remdesivir, systemic corticosteroids) were identified from National Drug Codes or procedure codes. Inhaled corticosteroid use was defined as having at least 1 prescription in the 12 months preceding the COVID-19 diagnosis. For body mass index (BMI) and insurance status, when multiple observations were available, we recorded the value at the date closest to the COVID-19 diagnosis.

Statistical Analysis

Patient and clinical characteristics were summarized as frequencies and percentages or means±standard deviations and compared with chi-square statistics or *t*-tests as appropriate. To determine the effect of COPD on inpatient mortality, we fit a logistic regression model with COPD as the primary predictor, adjusted for covariates. We tested a priori interactions between COPD and sex, COPD and age, COPD and race, and COPD and inhaled corticosteroids. For significant interaction terms, we stratified our cohort in subgroups and examined the effect of COPD on inpatient mortality within each stratum with separate multivariate models. All analyses were performed with SAS 9.4 (SAS, Inc., Cary, North Carolina).

Results

Demographics and Patient Characteristics

During the study period, 31,526 patients hospitalized with COVID-19 were identified and baseline characteristics of the cohort are presented in Table 1. Patients with COPD comprised 15.09% of the cohort (4758 patients), which consisted of mostly White (68.6%) males (52.1%) with a BMI<30 kg/m^2 (46%) and mean age of 72±11.2 years. A greater percentage of patients with COPD were admitted to the ICU (COPD 28.8% versus non-COPD 22.2%, p<0.0001) and received mechanical ventilation (COPD 20.2% versus non-COPD 13.8%, p<0.0001), systemic steroids (COPD 56.3% versus non-COPD 43.7%, p<0.0001), convalescent plasma (COPD 4.5% versus non-COPD 3.7%, p=0.0053), and remdesivir (COPD 12.9% versus non-COPD 11.5%, p=0.0051). Similarly, a greater percentage of patients with COPD received a palliative care consultation (COPD 20.3% versus non-COPD 14.3%, p<0.0001) (Table 2). In addition, more patients with COPD were discharged to a non-home setting compared to patients without COPD. In patients with COPD, the most common non-home setting discharge destination was a skilled nursing facility (18.2%), followed by hospice (4.6%) (Table S3 in the online data supplement).

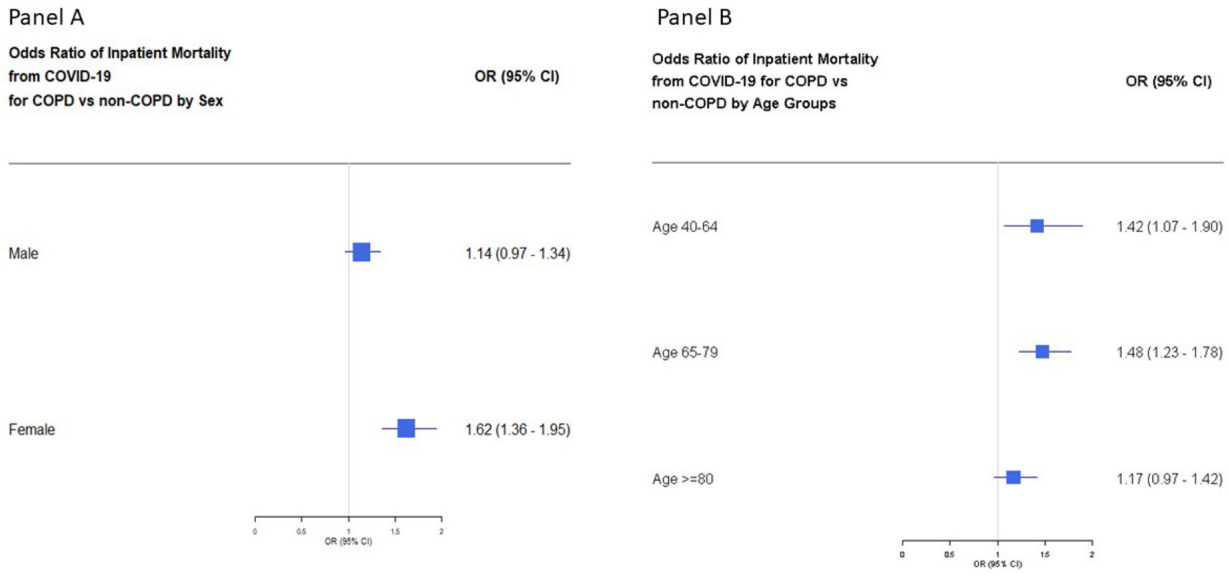
Effect of COPD on COVID-19 Inpatient Mortality

Overall hospital mortality was 9.61% for hospitalized patients with COVID-19. Mortality was significantly higher in patients with COPD than in patients without COPD, 14.02% and 8.83%, respectively, p<0.0001 (Table 2). In univariate analysis, patients with COPD had 68% greater odds of death due to COVID-19 than patients without COPD (odds ratio [OR] 1.68; 95% confidence interval [CI] 1.54 to 1.84). After adjusting for clinical and demographic factors, we observed a modest reduction in the odds of mortality in patents with COVID-19 and COPD (OR 1.33; 95% CI 1.18 to1.50) (See Table 3). We found significant interactions between COPD and sex and COPD and age, but not between COPD and race or COPD and inhaled corticosteroid (ICS) use. Specifically, the increased mortality risk associated with COPD was observed among female (OR 1.62; 95% CI 1.36 to 1.95) but not male patients (OR 1.14; 95% CI 0.97 -to 1.34); and in patients aged 40 to 64 (OR 1.42; 95% CI 1.07 to 1.90) and 65 to 79 (OR 1.48; 95% CI 1.23 to 1.78) years, but not in patients aged 80 years or older (OR 1.17; 95% CI 0.97 to 1.42) (Figure 1).

Discussion

In this large, nationally representative U.S. cohort study, we found that COPD was an independent risk factor for inpatient mortality in patients hospitalized with COVID-19. This association was primarily driven by the effect in women and in adults between 40 and 79 years of age. This association persisted after adjustment for a wide range of potentially confounding variables, including age, race, medications received during hospitalization (remdesivir, systemic steroids), BMI, comorbidities, and use of mechanical ventilation.

Figure 1. Interaction Effects Examined in the Multivariate Model Showing the Association Between COPD and Mortality by Sex[a] and Mortality by Age[b] and Adjusted for All Other Covariates in Patients Hospitalized with COVID-19[c]



[a]Panel A
[b]Panel B
[c]in the United States

The results of the interaction effects showed that the association between COPD and mortality varied significantly by sex (p<0.0001) and age (p=0.014), but not race (p=0.323) or ICS use (p=0.725) (data not shown).

COPD=chronic obstructive pulmonary disease; COVID-19=coronavirus disease 2019; ICS= inhaled corticosteroid; OR=odds ratio; CI=confidence interval

Interestingly, all patients with COVID-19 and COPD had higher rates of ICU admission, mechanical ventilation, and palliative care consultation than those without COPD. Our results of worse outcomes amongst COVID-19 patients with COPD are consistent with previous research.[5–12]

Our finding of worse mortality risk in women with COPD who were hospitalized due to COVID-19 is contrary to the overall outcomes of women with COVID-19 without COPD.[9,12,13,28] Why do women with COVID-19 who have COPD have increased risk of mortality? Prior to the COVID-19 pandemic, we knew that women with COPD have worse symptoms and airflow limitation compared to men, despite lower pack years of smoking.[29] Also, women's COPD-related hospitalizations and deaths in the United States are worse compared to those of men.[30,31] In addition, women's smaller lung size and other sex-specific factors may explain the observed association of worse mortality in women with COPD and COVID-19 compared to men.[32] For example, estrogen has been reported to have an anti-inflammatory effect in pre-menopausal women[33,34] as well as against coronaviruses.[35] It is likely that the protective effect observed among women with COVID-19 has been driven primarily by pre-menopausal women.[33] Most women with COPD are post-menopausal[27] and likely have lost the protective effect of estrogen.[30–32]

In addition to the interaction between sex and COPD, we found that patients with COPD who are 40 to 79 years old are at increased risk of death due to COVID-19, but those 80 years and older are not. Patients who are ≥80 years old have likely accumulated several comorbidities that may impair their health at baseline and ours (see Table 3) and other's studies have consistently shown that older age and comorbidities are associated with worse outcomes from COVID-19.[11,15,23,28,36] Very likely, these 2 variables have concealed any association between COPD and mortality from COVID-19 in this age group (≥80 years old). On the other hand,

Table 1. Characteristics of Patients With and Without COPD and Hospitalized Due to COVID-19[a]

Characteristics	Category	Total[b]	Patients with COPD[c] N=4758 N (%)	Patients without COPD N=26,768 N (%)	*p*-value
Age, mean (SD)		31,526	72.0 (±11.2)	65.2 (±13.7)	<0.0001
Age	40-64	14,562	1243 (26.1)	13,319 (49.8)	<0.0001
	65-79	10,775	2171 (45.6)	8604 (32.1)	
	≥80	6189	1344 (28.3)	4845 (18.1)	
Gender	Female	14,703	2277 (47.9)	12,426 (46.4)	0.0675
	Male	16,823	2481 (52.1)	14,342 (53.6)	
Race/Ethnicity[d]	White	17,037	3265 (68.6)	13,772 (51.5)	
	Black	6168	895 (18.8)	5273 (19.7)	<.0001
	Asian	774	51 (1.1)	723 (2.7)	
	Hispanic[e]	4139	250 (5.3)	3889 (14.5)	
	Other/Unknown	3408	297 (6.2)	3111 (11.6)	
BMI, mean Kg/m^2 (SD)		23,450	30.5 (8.9)	31.3 (8.0)	<0.0001
BMI	<30Kg/m^2	11,808	2190 (46.0)	9618 (35.9)	<0.0001
	≥30Kg/m^2	11,642	1840 (38.7)	9802 (36.6)	
	Unknown	8076	728 (15.3)	7348 (27.5)	
Census Bureau Region	Midwest	12,275	2043 (42.9)	10,232 (38.2)	<0.0001
	Northeast	9102	1095 (23.0)	8007 (29.9)	
	South	6872	1134 (23.8)	5738 (21.4)	
	West	2349	319 (6.7)	2030 (7.6)	
	Other/Unknown	928	167 (3.5)	761 (2.8)	
Insurance Status	Commercial	9663	756 (15.9)	8907 (33.3)	<0.0001
	Medicaid	3325	461 (9.7)	2864 (10.7)	
	Medicare	15,876	3429 (72.1)	12,447 (46.5)	
	Unknown/Other	2662	112 (2.4)	2550 (9.5)	
Diabetes Mellitus	Yes	9725	1829 (38.44)	7896 (29.5)	<0.0001
	No	21,801	2929 (61.56)	18,872 (70.5)	
Hypertension	Yes	19,155	3718 (78.14)	15,437 (57.67)	<0.0001
	No	12,371	1040 (21.86)	11,331 (42.33)	
Asthma	Yes	3651	1084 (22.78)	2567 (9.59)	<0.0001
	No	27,875	3674 (77.22)	24,201 (90.41)	
CKD	Yes	3908	1010 (21.23)	2898 (10.83)	<0.0001
	No	27,618	3748 (78.77)	23870 (89.17)	
ESRD	Yes	1043	205 (4.31)	838 (3.13)	<0.0001
	No	30,483	4553 (95.69)	25930 (96.87)	
Stroke	Yes	9308	1507 (31.67)	7801 (29.14)	0.0004
	No	22,218	3251 (68.33)	18967 (70.86)	
CHF	Yes	5496	1833 (38.52)	3663 (13.68)	<0.0001
	No	26,030	2925 (61.48)	23,105 (86.32)	
Cancer	Yes	777	202 (4.25)	575 (2.15)	<0.0001
	No	30,749	4556 (95.75)	26,193 (97.85)	
CAD	Yes	6453	1951 (41)	4502 (16.82)	<0.0001
	No	25,073	2807 (59)	22266 (83.18)	
Liver Disease	Yes	2787	608 (12.78)	2179 (8.14)	<0.0001
	No	28,739	4150 (87.22)	24589 (91.86)	

[a]Between February 10, 2020, and November 10, 2020, in the United States
[b]Our cohort was obtained from Optum's COVID-19 database, which includes EHR data for more than 90 million patients across multiple hospital networks from all regions in the United States. Cohort included patients who were diagnosed with COVID-19 between February 10,

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2020, and November 10, 2020, and were hospitalized within 14 days from diagnosis. COVID-19 was identified by a positive laboratory test for SARS-CoV-2 or by ICD-10-CM diagnosis code U07.1 Prior to enrollment patients needed to have had received care in Optum's healthcare network at least once in the 12 months before COVID-19 diagnosis.
[c]Presence of COPD was defined as having at least 1 inpatient or 2 outpatient diagnoses in the 1 year before COVID-19 diagnosis (See Table S2 in the online data supplement).
[d]Persons self-identifying as non-Hispanic ethnicity, where categorized based on race (White, Black, Asian, Other/Unknown).
[e]Patients self-identifying as Hispanic ethnicity, were included in the "Hispanic" group, regardless of race.

COPD=chronic obstructive pulmonary disease; COVID-19=coronavirus disease 2019; SD=standard deviation; BMI=body mass index; CKD=chronic kidney disease; ESRD=end stage renal disease; CHF=congestive heart failure; CAD=coronary artery disease; EHR= electronic health record; SARS-CoV-2=severe acute respiratory syndrome coronavirus-2; ICD-10-CM=*International Classification of Diseases, 10th revision, Clinical Modification.*

Table 2. Process of Care and Outcomes of Patients With and Without COPD Hospitalized Due to COVID-19[a]

Characteristics	Category	Total[b]	Patients with COPD N=4758[c] N (%)	Patients without COPD N=26,768 N (%)	*p*-value
Mechanical Ventilation	Yes	4659	959 (20.2)	3700 (13.8)	<0.0001
	No	26,867	3799 (79.8)	23,068 (86.2)	
ICS[d]	Yes	4794	2596 (54.6)	2198 (8.2)	<0.0001
	No	26,732	2162 (45.4)	24,570 (91.8)	
Systemic Steroids[e]	Yes	14,360	2677 (56.3)	11,683 (43.7)	<0.0001
	No	17,166	2081 (43.7)	15,085 (56.4)	
Remdesivir[f]	Yes	3702	616 (12.9)	3086 (11.5)	0.0051
	No	27,824	4142 (87.1)	23,682 (88.5)	
Convalescent Plasma Therapy[e]	Yes	1206	216 (4.5)	990 (3.7)	0.0053
	No	30,320	4542 (95.5)	25,778 (96.3)	
Palliative Care Consultation	Yes	4779	964 (20.3)	3815 (14.3)	<0.0001
	No	26,747	3794 (79.7)	22,953 (85.8)	
Length of Stay[f] Mean (SD)			9.8 (9.9)	8.5 (10.1)	<0.0001
Inpatient Death	Yes	3030	667 (14.0)	2363 (8.8)	<0.0001
	No	28,496	4091 (86.0)	24,405 (91.2)	

[a]Between February 10, 2020, and November 10, 2020, in the United States
[b]COVID-19 was identified by a positive laboratory test for SARS-CoV-2 or by ICD-10-CM diagnosis code U07.1
[c]Presence of COPD was defined as having at least 1 inpatient or 2 outpatient diagnoses in the 1 year before COVID-19 diagnosis (See Table S2 in the online data supplement).
[d]ICS prescription obtained within a year of COVID-19 diagnosis.
[e]Convalescent plasma and medications administered during hospitalization (remdesivir, systemic steroids) were identified from National Drug Codes or procedure codes.
[f]Length of stay as measured in days.

COPD=chronic obstructive pulmonary disease; COVID-19=coronavirus disease 2019; ICS=inhaled corticosteroid; SD=standard deviation; SARS-CoV-2=severe acute respiratory syndrome coronavirus-2; ICD-10-CM=*International Classification of Diseases, 10th revision, Clinical Modification*

of particular concern is our finding of a 42% higher likelihood of death from COVID-19 in younger patients with COPD, those aged 40 to 64 years. These patients may have developed "early COPD" and possibly were exposed to significant smoking and other risk factors earlier in life that led to the development of likely anatomical, immunologic, and physiologic abnormalities[37] that may have made them more susceptible to die from COVID-19.

Although the interaction between COPD and ICS use on COVID-19 mortality in our cohort was non-significant, we did find that a history of an ICS prescription was associated with a lower risk of death in all hospitalized patients due to COVID-19. Despite this provocative finding, we do not know whether the ICS prescription had been filled. Use of an ICS was assumed if patients had a history of an ICS prescription 1 year prior to the COVID diagnosis or if the patient reported use. Furthermore, a recent United Kingdom-based observational study did not provide definitive answers to explain this association[38] and more studies would be necessary to further characterize this finding.

It is unclear what mechanisms drive the worse outcomes seen in patients with COPD hospitalized with COVID-19, but several biological factors have

Table 3. Multivariate Logistic Regression Model of the Effect of COPD on COVID-19-related Mortality in Patients Hospitalized Due to COVID-19[a]

Variables		Odds Ratio (95% CI)	*P* value
COPD[b]	Yes vs No	1.33 (1.18–1.50)	<0.0001
Age	65-79 vs 40-64	2.44 (2.19–2.71)	<0.0001
	≥80 vs 40-64	5.74 (5.09–6.49)	<0.0001
Gender	Male vs Female	1.22 (1.12–1.33)	<0.0001
Race/Ethnicity[c]	Black vs White	1.11 (0.99–1.25)	0.0813
	Asian vs White	1.31(1.03–1.68)	0.0293
	Hispanic vs White	1.29 (1.13–1.48)	0.0002
	Other/Unknown vs White	1.35 (1.18–1.54)	<0.0001
BMI[d]	≥30Kg/m^2 vs <30Kg/m^2	0.96 (0.86–1.06)	0.3956
	Unknown vs <30Kg/m^2	1.41 (1.27–1.57)	<0.0001
Diabetes	Yes vs No	1.02 (0.92–1.121)	0.7463
Hypertension	Yes vs No	0.94 (0.84–1.04)	0.2394
Asthma	Yes vs No	1.01 (0.88–1.17)	0.8503
CKD	Yes vs No	1.27 (1.11–1.45)	0.0004
ESRD	Yes vs No	1.24 (0.99–1.56)	0.0603
STROKE	Yes vs No	1.12 (1.01–1.21)	0.0286
CHF	Yes vs No	1.09 (0.97–1.23)	0.1342
Cancer	Yes vs No	1.12 (0.87–1.44)	0.3811
CAD	Yes vs No	1.15 (1.03–1.28)	0.0142
Liver Disease	Yes vs No	1.10 (0.95–1.28)	0.1885
Systemic Steroids[e]	Yes vs No	1.07 (0.98–1.17)	0.1394
Remdesivir[e]	Yes vs No	1.54 (1.35–1.75)	<0.0001
Convalescent Plasma[e]	Yes vs No	1.02 (0.83–1.24)	0.8873
ICS[f]	Yes vs No	0.73 (0.64–0.84)	<0.0001
Mechanical Ventilation	Yes vs No	9.27 (8.42–10.20)	<0.0001
Length of Stay[g]	-	1.01(1.00–1.01)	0.0074

[a]Between February 10, 2020, and November 10, 2020, in the United States.
[b]Presence of COPD was defined as having at least 1 inpatient or 2 outpatient diagnoses in the 1 year before COVID diagnosis (Table S2 in the online supplement).
[c]Persons self-identifying as non-Hispanic ethnicity, were categorized based on race (White, Black, Asian, Other/Unknown). Patients self-identifying as Hispanic ethnicity, were included in the "Hispanic" group, regardless of race.
[d]For BMI and insurance, when multiple observations were available, we recorded the value at the date closest to COVID-19 diagnosis.
[e]Convalescent plasma and medications administered during hospitalization (remdesivir, systemic steroids) were identified from National Drug Codes or procedure codes.
[f]ICS use was evaluated by having at least one prescription in the 12 months preceding COVID-19 diagnosis.
[g]For each day of inpatient stay, the odds of dying increase by 0.5%.

COPD=chronic obstructive pulmonary disease; COVID-19=coronavirus disease 2019; CI=confidence interval; BMI=body mass index; CKD=chronic kidney disease; ESRD=end stage renal disease; CHF=congestive heart failure; CAD=coronary artery disease; ICS=inhaled corticosteroids

been proposed, including chronic lung inflammation, oxidative stress, protease-antiprotease imbalance, and increased airway mediators.[6,39,40] Additionally, patients with COPD have increased levels of angiotensin-converting enzyme 2, the receptor used by SARS-CoV-2 to enter host cells, that may enhance viral pathogenicity.[41–44] Moreover, viral infections can contribute to COPD exacerbations, leading to hospitalization, and acute exacerbations of COPD has been associated with poor outcomes[45]

It is unknown whether patients with COPD have a higher risk of acquiring the SARS-CoV-2 infection. Studies based in the United Kingdom, Europe, and Asia report a varied prevalence of patients with COPD amongst hospitalized patients with COVID-19,[9,18,40] and COPD has been shown to be a risk factor for hospitalization due to COVID-19.[15] The association between COPD, severe COVID-19, and mortality related to COVID-19 varies.[9–13,15,46] The current study represents the largest cohort

studied to date of patients with COPD who have been hospitalized due to COVID-19 in the United States. Similarly, our findings of increased mortality associated with COPD support previous reports of poor outcomes in COVID-19 patients with chronic respiratory conditions. For example, patients with interstitial lung disease and COVID-19 were more likely to be hospitalized, require ICU care, and die compared to patients with COVID-19 without interstitial lung disease.[47,48]

We acknowledge that this study has limitations, including its retrospective nature. The results merely show an association between COPD and mortality in hospitalized patients with COVID-19. Since we used ICD-10-CM codes to identify COPD, it is possible that our population may over- or under-represent the true prevalence of COPD in the general population.[49] In addition, we were not able to assess when remdesivir and systemic steroids were administered in relation to a patient's hospitalization, the selection criteria used for drug prescription, or the duration of COVID-19 illness prior to the hospital admission. These unmeasured variables may have influenced whether the use of remdesivir and systemic corticosteroids affected clinical outcomes in hospitalized patients with COVID-19. Finally, patients with COPD have significant comorbid conditions,[50] and these may have mediated the association between COPD and increased hospital mortality. Yet, after adjustment for demographic and clinical factors, our findings indicated that COPD was an independent factor for mortality in patients hospitalized with COVID-19.

In conclusion, COPD is an independent risk factor for death in adults aged 40 to 79 years hospitalized due to COVID-19.

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Author contributions:

All authors have contributed to the current manuscript in the following manner:

- Substantial contribution to the conception, design, data acquisition, analysis and interpretation of the manuscript.
- Drafted and/or revised the manuscript for important intellectual content.
- Approved the final version to be submitted for publication.
- Agreed to be accountable for all aspects of the work and have ensured that questions related to the accuracy and integrity of any part of the manuscript are appropriately investigated and resolved.

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Declaration of interest

Drs. Puebla Neira, Watts, Seashore, Duarte, Nishi, Baillargeon and Sharma, along with Ms. Polychronopoulou, have nothing to disclose. Dr. Kuo reports grants from the UTMB Claude D. Pepper Older Americans Independence Center and from the Agency of Healthcare Research and Quality during the conduct of the study.

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