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RESEARCH LETTER

Mortality from COVID-19 in Patients with COPD: A US Study in the N3C Data Enclave

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Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), emerged in late 2019 leading to a global pandemic. COVID-19, a cause of severe viral pneumonia, has resulted in over 2.6 million deaths worldwide and over 500,000 deaths in the United States as of February 2021.[1,2] Observational research suggests that the risk of mortality increases with the presence of comorbidities: obesity, hypertension (HTN), diabetes mellitus type 2 (DM), and chronic lung disease.[3] Over the last 40 years in the United States, chronic obstructive pulmonary disease (COPD) has become the fourth leading cause of death.[4] Pneumonia is associated with an increased risk of hospitalization, intubation, and mortality in people with COPD.[5] Patients with COPD may be susceptible to worse outcomes from COVID-19 pneumonia than patients without COPD.[6,7]

Given the increased vulnerability of this population, it is important to understand the risk of COVID-19 related mortality in people with COPD. The National Center for Advancing Translational Sciences (NCATS) established the National COVID Cohort Collaboration (N3C), a partnership among 81 academic hubs to share COVID-19 clinical data from electronic health records as part of a platform for answering critical research questions.[8,9] The N3C compiles data from patients who were tested for COVID-19, or who were symptomatic and highly suspected to have COVID-19. The data obtained from electronic health records include demographics, symptoms, lab test results, procedures, medications, medical conditions, and physical measurements. The data are placed in a cloud-based research environment maintained by NCATS. We used this novel tool to assess the risk of mortality following COVID-19 diagnosis in patients with COPD compared with patients without COPD.

Methods and Analysis

We performed a query of the N3C limited data set. Patients were selected for inclusion if they were over the age of 35 and had a positive COVID-19 PCR test. We collected data on demographics, hospitalization, and prior ICD-9/10 diagnoses of COPD, chronic kidney disease (CKD), obesity, DM, and HTN. We used the chi-square test to assess differences in characteristics between patients with and without COPD. We performed multivariable logistic regression, adjusting for age, male sex, DM, HTN, CKD, and obesity to assess the odds of mortality following COVID-19 diagnosis in patients with and without COPD. Statistical analysis was done using the secure NCATS Data Enclave, which utilizes the Palantir platform and resides in Amazon

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Web Services GovCloud. Through Palantir we performed analyses using R (version 3.5.1). This study was reviewed by the Northwestern University Institutional Review Board (IRB) and received an exemption determination. The requirement for informed consent was waived, as confirmation that the data was anonymized and maintained with confidentiality, and the investigators agreed to make no attempt to identify patients based on the variables in the limited dataset.

Results

As of February 16, 2021 a total of 3,453,825 patients were part of the N3C database. Of those, 387,008 patients tested positive for COVID-19 by PCR and 7549 had a diagnosis of COPD (Table 1). The mean age of patients with COPD was 70.5 years versus 57.9 years for patients without COPD. The majority of patients with COPD were white (71%) followed by African American (19%). Patients with COPD had higher rates of HTN (74% vs 39%), DM (38% vs 22%), obesity (34% vs 24%), and CKD (31% vs 10%). Patients with COPD had higher rates of hospital admissions (62% vs 28%). The mortality rate of patients with COPD was 15% compared to 4% in patients without COPD. Our unadjusted odds ratio of mortality of patients with COPD and COVID-19 diagnosis was 6.19 (95% CI 5.79–6.62, p-value <0.001). In a multivariable logistic regression analysis the adjusted odds ratio for mortality [95% CI] in patients with versus without COPD was 2.1 [1.96, 2.26, p-value <0.001] (Figure 1).

Discussion

Among patients in the N3C, the odds of mortality from COVID-19 were higher in patients who had COPD compared with those who did not, even after adjusting for other known risk factors. The major strength of this study is the large number of patients included in the analysis. We found that even after adjusting for other comorbidities, the presence of COPD was associated with a higher mortality from COVID-19. Limitations of this retrospective observational study include the potential presence of residual confounders or misclassification of patients with COPD or other comorbidities. We were not able to assess smoking status, a critical potential confounder, because this information was not documented in the majority of patients. Possible mechanisms underlying an increased risk of death from COVID-19 in patients with COPD include a heightened bronchial epithelial cell expression of angiotensin-converting enzyme- 2 (ACE-2) expression, known to be needed for infection.[10] Other potential factors include worse baseline lung function and lower oxygen levels in patients with COPD. Our findings are consistent with prior work demonstrating worse outcomes from bacterial pneumonia in patients with COPD.[5] Further prospective research is needed to confirm and elucidate the cause of this association.

Table 1 Characteristics of Patients with COVID-19 (PCR Positive) in the N3C Data Enclave

	COPD (n = 7449)	NO COPD (n = 273,963)	p-value
Age, mean (years)	70.5	57.9	
Gender			
Female, No. (%)	3500 (47%)	147,639 (54%)	< 0.001
Race			< 0.001
Black, No. (%)	1412 (19%)	47,046 (17%)	
White, No. (%)	5310 (71%)	174,487 (64%)	
Asian, No. (%)	93 (1%)	6765 (2%)	
Hispanic, No. (%)	294 (4%)	32,331 (12%)	< 0.001
Comorbidities			
Diabetes, No. (%)	2849 (38%)	59,459 (22%)	< 0.001
Obesity, No. (%)	2539 (34%)	64,591 (24%)	< 0.001
CKD, No. (%)	2328 (31%)	28,195 (10%)	< 0.001
HTN, No. (%)	5541 (74%)	108,105 (39%)	< 0.001
Hospitalizations, n (%)	4631 (62%)	76,875 (28%)	< 0.001
Deaths, n (%)	1107 (15%)	10,126 (4%)	< 0.001

Variable	OR (95% CI)
Age (1 Year Increase)	1.07 (1.07 - 1.07)
Gender (Male)	1.59 (1.53 - 1.66)
COPD	2.07 (1.93 - 2.22)
Obesity	1.35 (1.29 - 1.42)
Chronic Kidney Disease	2.09 (2.00 - 2.19)
Hypertension	1.03 (0.98 - 1.08)
Diabetes	1.58 (1.51 - 1.65)

* denotes p-value < 0.001

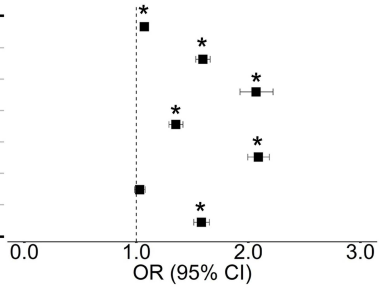

Figure 1 Multivariable logistic regression analysis of risk factors for death from COVID-19 in the N3C data set. Multivariable logistic regression analysis demonstrated that age, male gender and presence of COPD, obesity, chronic kidney disease, and diabetes were all associated with increased odds of death from COVID-19 in the N3C data set.

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Disclosure

Dr Ravi Kalhan reports personal fees from AstraZeneca, personal fees from GlaxoSmithKline, personal fees from CVS Caremark, outside the submitted work.

Dr Paul A Reyfman reports personal fees from Medscape, personal fees from Guidepoint, and salary from MSD, outside the submitted work. The authors report no other conflicts of interest in this work.

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