

COPD is a Risk Factor for COVID-19, But Does Not Confer Increased Severity of the Disease

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Abstract

Epidemiologic studies suggest that COPD is associated with an increased risk of poor outcome in patients with COVID-19, although they failed to demonstrate COPD as a risk factor for acquiring COVID-19. However, most data have come from a limited global population. In this nationwide cohort study based on the Korean national health insurance claims-based database, COPD is associated with increased risk for COVID-19 and having COPD does not seem to confer substantial risk for severe COVID-19 and mortality. These findings indicate that heterogeneity in the populations across many countries may complicate the net effects of COPD on the COVID-19-related outcomes.

Introduction

In the period up to April 2021, the coronavirus disease (COVID-19) pandemic associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has affected approximately 143,000,000 people globally with over 3,000,000 deaths, and poses a great threat to patients with chronic lung diseases (1). However, evaluating the excess risk of chronic obstructive pulmonary disease (COPD) for COVID-19 and, in particular, for more severe disease, is challenging (2). Initially, the prevalence of COPD among hospitalized patients with COVID-19 has been reported to be lower than in the general population and in those reported with other comorbidities (3), a finding contrary to the common speculation that COPD may be more susceptible to contracting respiratory viruses. Paradoxically, COVID-19 in COPD is increasingly associated with critical illness of COVID-19 (2, 4). A nationwide analysis on the comorbidity of 1590 COVID-19 patients in China showed that COPD was a risk factor for reaching the composite end points related to poorer clinical outcomes (5). These findings indicate the heterogeneity of clinical COVID-19 cohorts across different nations and the clinical severity with diverse comorbidities (2).

The aim of this study is to determine whether COPD influences the occurrence and clinical severity of COVID-19.

Methods

This large-scale cohort covers individuals who underwent SARS-CoV-2 testing in South Korea from January 1, 2020 to May 1, 2020 supported by the Korean Centers for Disease Control and the National health insurance service (NHIS). For each patient who underwent SARS-CoV-2 testing, we combined medical data on COVID-19-related outcomes during the hospitalization with claim-based data from January 1, 2015 to May 1, 2020, including personal data (age, sex, region of residence, and socioeconomic status) and health care records of inpatients and outpatients throughout the past 5 years (including health care visits, prescriptions, diagnoses, and procedures), retrospectively. SARS-CoV-2 infection was defined by a positivity on a real-time RT-PCR assay of nasal or pharyngeal swabs (6). A history of COPD (J43-J44, apart from J430), diabetes mellitus (E10-14), ischemic heart disease (I20-25), cerebrovascular disease (I60-64, I69, and G45), hypertension (I10-13 and I15), or chronic kidney disease (N18-19) was defined by the physician diagnosis reporting of at least two claims within 1 year during this

5-year study period according to the appropriate International Classification of Disease, Tenth Revision (ICD-10) code (7). In this study, “exposure” comprised the development of COPD; the “primary outcome” was test positivity for SARS-CoV-2 among all patients who underwent SARS-CoV-2 testing, and the “secondary outcome” was severe disease or mortality of patients who tested positive for SARS-CoV-2. The definition of severe disease included: 1) requirement for oxygen supplementation, 2) intensive care units (ICU) admission, 3) intubation with mechanical ventilation, or 4) application of extracorporeal membrane oxygenation (ECMO).

We performed two rounds of propensity score matching to balance the baseline characteristics and to reduce potential confounders. We evaluated each propensity score matching in a 1:1 ratio using the ‘greedy nearest-neighbor’ algorithm and calculated the predicted probability of (a) individuals with a history of COPD versus individuals without a history of COPD among all patients who underwent SARS-CoV-2 testing (n = 129,120); (b) individuals with a history of COPD versus individuals without a history of COPD among patients with confirmed COVID-19 (n = 8,070). The adequacy of matching was evaluated by comparing the distributions of propensity score and standardized mean differences (SMDs). After utilizing a multivariate logistic regression model adjusted for history of angina, any type of cancer, hypertension (HTN), congestive heart failure (CHF), chronic kidney disease (CKD), cerebrovascular disease (CVD), diabetes mellitus (DM), hepatitis, and myocardial infarction (MI), estimation of the adjusted odds ratios (aORs) with 95% CIs was performed. Patient-related data were anonymized and the protocol was approved by the Institutional Review Board of Jeonbuk National University Hospital (2020-04-067).

Results

Among 129,120 patients who underwent SARS-CoV-2 testing (mean age \pm SD, 41.7 \pm 19.6 years), we identified 8,070 (6.25%) patients who tested positive (all SMDs < 0.1). There were 4,800 patients with a history of COPD in the entire cohort (n = 129,120). Then, we performed 1:1 propensity score matching in the full-unmatched cohort and identified 4,800 patients without a history of COPD (**Table 1**, all SMDs < 0.05). Among all patients tested, the positivity rate of SARS-CoV-2 testing in patients with COPD was 7.3% (350/4800), compared with 4.8% (230/4800) in those without COPD (aOR, 1.54; 95% CI, 1.3–1.83) (**Table 1 and Fig. 1**). Furthermore, we identified 350 patients with COPD among the patients who tested positive for SARS-CoV-2 (n = 8,070). We also performed 1:1 propensity score matching in the full-unmatched cohort and identified 350 patients with no history of COPD (Table 2, all SMDs < 0.1). The rate of severe disease in patients with COPD was 28.9% (101/350) among patients who tested positive for SARS-CoV-2, compared with 25.1% (88/350) in those without COPD (aOR, 1.23; 95% CI, 0.85–1.76). In particular, among patients confirmed to have COVID-19, the rate of mortality in patients with COPD was 17.7% (62/350), compared with 13.7% (48/350) in those without COPD (aOR, 1.39; 95% CI, 0.87–2.23) (Table 2 **and Fig. 1**).

Discussion

Herein, we have identified that COPD is associated with an increased risk for COVID-19. Moreover, having COPD does not seem to confer a substantial risk for severe disease and mortality. These are interesting in that the results from numerous epidemiologic studies have suggested that COPD is associated with an increased risk of poor outcome in patients with COVID-19, although they failed to clearly demonstrate COPD as a risk factor for acquiring COVID-19 (2, 4). Since most data so far that can potentially explain the relationship between COPD and SARS-CoV-2 in the emergence of COVID-19 has come from a limited global population, the data will inevitably involve heterogeneous patients having different proportions of medical comorbidities under the variability in testing and admission strategies (2), and this may obscure the effect of COPD on contracting COVID-19. Indeed, increased angiotensin-converting enzyme-2, an entry protein for SARS-CoV-2, was observed in the airways of COPD patients who smoke, a similar finding that favors the potential implication of COPD as a risk factor for COVID-19 (8).

Furthermore, once a host has become infected with SARS-CoV-2 in the airways, a unique phenotype of systemic immune/inflammatory responses has been reported to be associated with COVID-19 acute respiratory distress syndrome (ARDS) compared to their non-COVID-19 counterparts, although patients with COVID-19 had less severe ARDS initially (9). In the same context, excluding respiratory diseases, most comorbidities were associated with an increased risk of COVID-19-related death (10). These findings suggest that systemic general medical conditions shaping overall immune/inflammatory responses are critically implicated in the regulation of the clinical course of COVID-19, even to a greater extent than the medical conditions involving the respiratory tract itself.

Although we could not define the various phenotypes of COPD (2) and obtain information on smoking status and treatment modalities for COPD (11, 12, 13) because data were claim-based, our findings suggest that COPD may be associated with an increased risk for COVID-19 and having COPD does not seem to confer a substantial risk for severe COVID-19 and mortality.

Declarations

Author Contributions:

J.S.J. conceived and designed the research, interpreted the data, and wrote the manuscript. J.S.K. conceived and designed the research, collected the data and performed the analysis. Y.C.L. conceived and designed the research, interpreted the data, and edited the manuscript. Y.S.Y. and S.W.Y. data curation, formal analysis.

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Tables

Table 1. Baseline demographics for all severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) tested patients in South Korea (N=129,120).

Patient who underwent SARS-CoV-2 test (total n = 129120)					
COPD					
characteristic	No		Yes		SMD
Total, n (%)	4800		4800		
Age, mean SD	62.7	15.6	62.4	15.6	0.018
Sex, n (%)					0.024
Male	2427	(50.6)	2484	(51.7)	
Female	2373	(49.4)	2316	(48.3)	
Social economic status, n (%)					0.006
Low	3048	(63.5)	3061	(63.8)	
High	1752	(36.5)	1739	(36.2)	
History of Angina, n (%)	1307	(27.2)	1290	(26.9)	0.008
History of Cancer, n (%)	1145	(23.9)	1188	(24.8)	0.021
History of HTN, n (%)	1065	(22.2)	1064	(22.2)	0.001
History of CHF, n (%)	482	(10.0)	518	(10.8)	0.001
History of CKD, n (%)	993	(20.7)	999	(20.8)	0.025
History of CVD, n (%)	1010	(21.0)	994	(20.7)	0.003
History of diabetes mellitus, n (%)	652	(13.6)	674	(14.0)	0.008
History of hepatitis, n (%)	1402	(29.2)	1401	(29.2)	0.013
History of MI, n (%)	371	(7.7)	406	(8.5)	0.001
COVID-19, n (%)	230	(4.79)	350	(7.29)	
Minimally adjusted OR (95% CI)	Reference		1.55	(1.3-1.83)***	
Fully adjusted OR (95% CI)	Reference		1.54	(1.3-1.83)***	

Abbreviations: CHF, congestive heart failure; CKD, chronic kidney disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HTN, hypertension; MI, myocardial infarction; SMD, standardized mean difference. ***: Statistically significant

Table 2. Baseline characteristics of propensity score-matching group (no previous COPD versus COPD groups) with laboratory confirmed COVID-19 in a Korean nationwide cohort.

	Patient who tested positive for SARS-CoV-2 test (total n = 8070)				
	Influenza				
characteristic	No		Yes		SMD
Total, n (%)	350		350		
Age, mean SD	62.5	15.5	62.3	15.9	0.011
Sex, n (%)					0.040
Male	166	(47.4)	173	(49.4)	
Female	184	(52.6)	177	(50.6)	
Social economic status, n (%)					0.050
Low	252	(72.0)	244	(69.7)	
High	98	(28.0)	106	(30.3)	
History of Angina, n (%)	98	(28.0)	104	(29.7)	0.038
History of Cancer, n (%)	86	(24.6)	81	(23.1)	0.034
History of HTN, n (%)	92	(26.3)	95	(27.1)	0.019
History of CHF, n (%)	39	(11.1)	43	(12.3)	0.036
History of CKD, n (%)	79	(22.6)	84	(24.0)	0.034
History of CVD, n (%)	79	(22.6)	82	(23.4)	0.020
History of diabetes mellitus, n (%)	46	(13.1)	46	(13.1)	0.001
History of hepatitis, n (%)	82	(23.4)	93	(26.6)	0.073
History of MI, n (%)	36	(10.3)	44	(12.6)	0.072
Severe clinical outcomes of COVID-19	88	(25.1)	101	(28.9)	
Minimally adjusted OR (95% CI)	Reference		1.22 (0.85-1.74)		
Fully adjusted OR (95% CI)	Reference		1.23 (0.85-1.76)		
Death	48	(13.7)	62	(17.7)	
Minimally adjusted OR (95% CI)	Reference		1.35 (0.87-2.11)		
Fully adjusted OR (95% CI)	Reference		1.39 (0.87-2.23)		

Abbreviations: CHF, congestive heart failure; CKD, chronic kidney disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HTN, hypertension; MI, myocardial infarction; SMD, standardized mean difference. ***: statistically significant

Figures

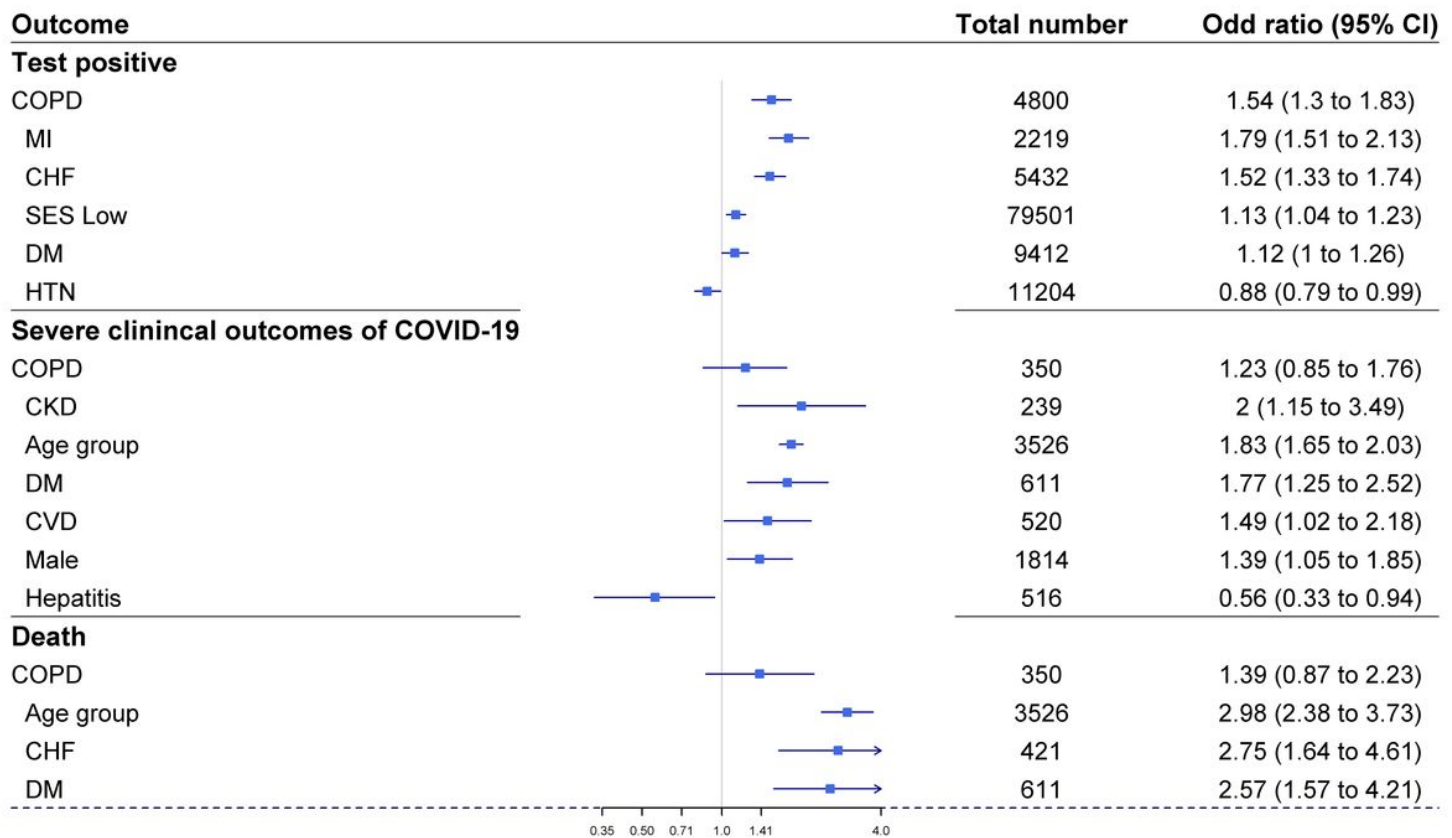


Figure 1

Propensity score-matched association of chronic obstructive pulmonary disease (COPD) with test positivity for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (primary outcome) among all patients who underwent SARS-CoV-2 testing (n = 129,120) and the association of COPD with severe disease and mortality (secondary outcome) among patients with confirmed coronavirus disease (COVID-19) (n = 8,070). CHF, congestive heart failure; CKD, chronic kidney disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HTN, hypertension; MI, myocardial infarction ; SES, socioeconomic status.