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Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19)

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To the Editor,

Coronavirus disease 2019 (COVID-19) is a respiratory and systemic illness that may progress to severe hypoxemia needing some form of ventilatory support in as many as 15–20% of suspected and confirmed cases [1]. In outbreak regions, the surge in critically ill patients has placed significant strain on intensive care units (ICUs), with volume demands that overwhelm current capacity [1]. There is a compelling need to identify clinical predictors of severe COVID-19 to enable risk stratification and optimize resource allocation.

Chronic Obstructive Pulmonary Disease (COPD) is associated with increased risk of morbidity and mortality in community-acquired pneumonia (CAP) [2]. Alterations in local/systemic inflammatory response, impaired host immunity, microbiome imbalance, persistent mucus production, structural damage, and use of inhaled corticosteroids have been hypothesized to contribute to such risk [3]. With respect to COVID-19, levels of angiotensin converting enzyme 2 (ACE2), the reported host receptor of the virus responsible of COVID-19 (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2), have been observed to be increased in patients with COPD [4,5]. However, early individual COVID-19 studies have not consistently reported a significantly higher rate of severe disease in COPD patients [6,7]. In this article, we analyze if COPD may be associated with increased odds of severe COVID-19 infection.

An electronic search was performed in Medline (PubMed interface), Scopus and Web of Science, using the keywords "chronic obstructive pulmonary disease" OR "COPD" OR "clinical characteristics" AND "coronavirus 2019" OR "COVID-19" OR "2019-nCoV" OR "SARS-CoV-2", between 2019 and present time (i.e., March 9, 2020). No language restrictions were applied. The title, abstract and full text of all articles captured with the search criteria were evaluated, and those reporting the rate of COPD in COVID-19 patients with a clinically validated definition of severe disease were included in this meta-analysis. The reference list of all identified studies was also analyzed (forward and backward citation tracking) to detect additional articles.

The obtained data was pooled into a meta-analysis, with estimation of the odds ratio (OR) and its 95% confidence interval (95% CI) in patients with or without severe forms of COVID-19. The statistical analysis was performed using MetaXL, software Version 5.3 (EpiGear International Pty Ltd., Sunrise Beach, Australia). The study was carried out in accordance with the declaration of Helsinki and with the term of local legislation.

Overall, 87 articles were initially identified based on our electronic and reference search, which after screening by tile, abstract, and full text, 80 were excluded as not related to COVID-19 (n = 27), were review articles (n = 7), did not provide relevant data (n = 28), were editorials (n = 10), did not provide data on severity or comorbidities (n = 5), compared patients by mortality not severity (n = 2) or compared mild cases to critical cases (n = 1). Thus, a total number of 7 studies were finally included in our meta-analysis, totaling 1592 COVID-19 patients, 314 of which (19.7%) had severe disease [6–12].

The essential characteristics of the included studies are shown in Table 1, whilst the individual and pooled OR of COPD for predicting severe COVID-19 is presented in Fig. 1. Only in a single study was the individual OR found to be a significant predictor of COPD [8]. However, when the data of the individual studies was pooled, COPD was found to be significantly associated with severe COVID-19 (OR: 5.69 [95:CI: 2.49–13.00], $I^2 = 0.0\%$, Cochran's Q, p = 0.95). A leave-one-out sensitivity analysis, excluding the largest study by Guan et al. [8] which accounted for 52.3% of pooled weight, found no significant differences (OR: 5.88 [95%CI: 1.78–19.50]).

In conclusion, the results of this concise meta-analysis demonstrate COPD is associated with a significant, over five-fold increased risk of severe CODID-19 infection. Patients with a history of COPD should be encouraged adopt more restrictive measures for minimizing potential exposure to SARS-CoV-2 and contact with suspected or confirmed cases of COVID-19. Clinicians should also carefully monitor all COPD patients with suspected infection and, finally, it may be advisable to consider COPD as a variable in future risk stratification models.

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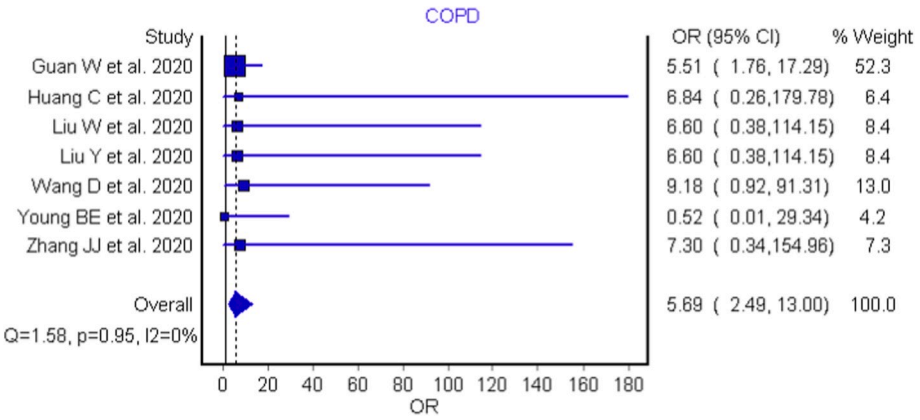

Fig. 1. Forest plot demonstrating association of Chronic Obstructive Pulmonary Disease with severe COVID-19 disease.

Table 1
Characteristics of included studies.

Study	Setting	Sample Size	Outcomes	Severe patients			Non-severe patients		
				n (%)	Age (yrs)[a]	Women (%)	n (%)	Age (yrs)[a]	Women (%)
Guan W et al., 2020	China	1099	Admission to ICU, MV, death	173 (15.7%)	52 (40–65)	42%	926 (84.3%)	45 (34–57)	42%
Huang C et al., 2020	China	41	ICU Care	13 (31.7%)	49 (41–61)	15%	28 (68.3%)	49 (41–58)	32%
Liu W et al., 2020	China	78	Admission to ICU, MV, Death	11 (14.1%)	66 (51–70)	36%	67 (85.9%)	37 (32–41)	52%
Liu Y et al., 2020	China	12	Respiratory Failure, MV	6 (50%)	64 (63–65)	50%	6 (50.0%)	44 (35–55)	17%
Wang D et al., 2020	China	138	Clinical Variables, MV, Death	36 (26.1%)	66 (57–78)	39%	102 (73.9%)	51 (37–62)	48%
Young BE et al., 2020	Singapore	18	Treatment, ICU Care, Death	6 (33.3%)	56 (47–73)	67%	12 (66.6%)	37 (31–56)	42%
Zhang JJ et al., 2020	China	140	Respiratory Distress/ Insufficiency	58 (41.4%)	64 (25–87)	43%	82 (58.6%)	52 (26–78)	54%

[a] Age data presented as median (IQR). MV – Mechanical Ventilation, ICU – Intensive Care Unit.

Declaration of competing interest

None declared.

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