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Is chronic obstructive pulmonary disease an independent predictor for adverse outcomes in coronavirus disease 2019 patients?

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Abstract. – OBJECTIVE: This study aimed to investigate whether pre-existing chronic obstructive pulmonary disease (COPD) was an independent predictor for adverse outcomes in coronavirus disease 2019 (COVID-19) patients.

MATERIALS AND METHODS: We searched electronic databases, including PubMed, Web of Science, EMBASE, and Chinese National Knowledge Infrastructure (CNKI) to screen for eligible articles. A quantitative meta-analysis was performed on the basis of adjusted effect estimates.

RESULTS: We observed that COPD was significantly associated with an increased risk of adverse outcomes in COVID-19 patients, which is based on 18 studies with 26,075 cases reporting adjusted effect estimates (pooled effect = 1.53, 95% confidence interval (CI): 1.29-1.8; I^2 = 35.4%, random-effects model).

CONCLUSIONS: We found that pre-existing COPD was an independent risk factor for predicting the adverse outcomes in COVID-19 patients.

Key Words:
Coronavirus disease 2019, Chronic obstructive pulmonary disease, Adverse outcomes, Adjusted effect estimates.

Introduction

Recently, Lippi et al[1] reported that pre-existing chronic obstructive pulmonary disease (COPD) was significantly associated with an increased risk of severe coronavirus disease 2019 (COVID-19) (odds ratio (OR) = 5.69, 95% confidence interval (CI): 2.49-13.00) by using a quantitative meta-analysis. However, the findings of Lippi et al[1] were based on unadjusted effect estimates. To the best of our knowledge, several papers have reported a significant association between COPD and severe COVID-19 using univariate analysis. However, this significant association did not exist in multivariate analysis[2-4], suggesting that factors such as age, gender and pre-existing disorders may have significant effects on the association between COPD and adverse outcomes in COVID-19 patients. Therefore, the aim of this study was to clarify the association between pre-existing COPD and adverse outcomes in COVID-19 patients by performing a quantitative meta-analysis based on adjusted effect estimates.

Materials and Methods

We searched electronic databases, including PubMed, Web of Science, EMBASE, and Chinese National Knowledge Infrastructure (CNKI) to screen for eligible articles. The following keywords were used: "coronavirus disease 2019" OR "SARS-CoV-2" OR "2019 novel coronavirus" OR "2019-nCoV" OR "COVID-19" AND "chronic obstructive pulmonary disease" OR "COPD" (up to July 31, 2020). The articles were included if they reported adjusted effect estimates on the association of pre-existing COPD with adverse outcomes (severe, critical, and mortal) in COVID-19 patients. In addition, we screened the references of all articles to find potentially eligible papers. STATA 11.2 was used for all analyses. I^2 was used to assess heterogeneity between articles[5]. A fixed-effects model was used if there was no heterogeneity; otherwise, a random-effects model was selected. The sensitivity analysis was used to check the robustness of the results. Publication bias was assessed by Begg's test and Egger's test.

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Table I. Characteristics of the included studies.

Author	Country	Cases (n)	Age (years)	Male (%)	Study design	COPD (%)	Adjusted effect estimates (95% CI)	Confounders
Barman et al[2]	Turkey	607	62.5 ± 14.3	334 (55)	R	73 (12)	OR 2.99 (0.34-25.96)	Age, hypertension, CAD, creatinine, uric acid, Glu, CRP, presence of cardiac injury, d-dimer
Chen et al[3]	China	3309	62 (49-69)	1642 (49.6)	R	42 (1.3)	OR 1.72 (0.80-3.71)	Gender, age, comorbidity, days from onset to admission
Zhang et al[4]	China	788	NA	407 (51.6)	R	3 (0.4)	OR 7.7 (0.8-75.6)	Age, gender, family cluster, time from illness onset to first hospital admission, symptoms, coexisting disorder
Wang et al[6]	China	339	71 ± 8	166 (49)	R	21 (6.2)	HR 2.24 (1.115-4.497)	Age, CVD, cerebrovascular disease
Zhao et al[7]	China	1000	61 (46-70)	466 (46.6)	R	23 (2.3)	HR 1.47 (0.627-3.481)	Age
Del Valle et al[8]	USA	1268	63 (53-72)	787 (60.1)	P	44 (3.5)	HR 0.84 (0.33-2.16)	Cytokines, demographics, comorbidities, laboratory measurements
Cen et al[9]	China	1007	61 (49-68)	493 (49.0)	P	46 (4.6)	HR 2.01 (1.38-2.926)	Age, gender, smoking, hypertension, DM, CAD, duration of anti-viral therapy
Guan et al[10]	China	1590	48.9 ± 16.3	904 (57.3)	R	24 (1.5)	OR 2.681 (1.424-5.058)	Age, smoking status
Bravi et al[11]	Italy	1603	58.0 ± 20.9	758 (47.3)	R	69 (6)	OR 1.88 (1.32-2.7)	Gender, age, DM, hypertension, major CVD, cancer, renal disease
Magleby et al[12]	USA	678	NA	514 (61.1)	R	41 (6)	OR 0.65 (0.23-1.28)	Age, race, CAD, CHF cerebrovascular disease, hypertension, days of symptoms prior to admission, symptoms upon presentation, initial chest x-ray findings, level of oxygen support within three hours of arrival to the ED
Shah et al[13]	USA	552	63 (50-72)	218 (58.2)	R	47 (9)	OR 1.48 (0.65-3.34)	Age, BMI, gender, race, comorbidities, tobacco smoking
Arshad et al[14]	USA	2541	64 (53-76)	1243 (48.9)	R	325 (12.8)	HR 1.202 (0.924-1.563)	HCQ alone, AZM alone, HCQ+AZM, age, gender, race, BMI, lung comorbidity, immunodeficiency comorbidity, cardiovascular comorbidity, CKD, hypertension, asthma, DM, percent O_2 saturation, admitted to ICU, ventilator, given steroid, given tocilizumab

Table Continued

Table I. Characteristics of the included studies.

Author	Country	Cases (n)	Age (years)	Male (%)	Study design	COPD (%)	Adjusted effect estimates (95% CI)	Confounders
Gupta et al[15]	USA	2215	62 (51-71)	1436 (64.8)	P	173 (7.8)	OR 1.39 (0.95-2.04)	Age, gender, race, hypertension, diabetes, BMI, CAD, CHF, current smoker, active cancer, ≤3 d from symptom onset to ICU day 1, lymphocyte count <1000/μL on ICU day 1, PaO_2:FiO_2 on ICU day 1, IMV support, shock on ICU day 1, coagulation component of SOFA score, liver component of SOFA score, renal component of SOFA score, No. of ICU beds
Grasselli et al[16]	USA	3988	NA	3188 (79.9)	R	93 (2.3)	HR 1.68 (1.28-2.19)	Age, gender, respiratory support, hypertension, hypercholesterolemia, heart disease, type 2 diabetes, malignancy, ACE inhibitor therapy, ARB therapy, statin, diuretic, PEEP at admission, FiO_2 at admission, PaO_2/FiO_2 at admission
Atkins et al[17]	UK	507	73.3 ± 4.4	311 (61.3)	R	36 (11.6)	OR 1.91 (1.10-3.32)	Age, gender, ethnicity, education, baseline assessment centre, prevalent disease, prevalent conditions
Yao et al[18]	USA	242	65 (53-77)	138 (57)	R	22 (9.1)	HR 0.86 (0.30-2.46)	Clinical characteristic, therapies received with significant between-group differences
van Gerwen et al[19]	USA	3703	56.8 ± 18.2	2049 (55.3)	R	172 (4.6)	OR 1.20 (0.82-1.75)	Age, gender, race, BMI, smoking status, hypertension, CAD, atrial fibrillation, CHF, PVD, CVA/TIA, dementia, diabetes, hypothyroidism, CKD, malignancy, asthma, prior VTE
Pinto et al[20]	Italy	138	NA	85 (61.6)	P	18 (13)	OR 0.38 (0.11-1.28)	Age, gender, metastatic disease, time since cancer diagnosis, at 40 days since hospital admission

All values are n (%), mean ± SD (standard deviation) or median (interquartile range, IQR); NA, not available; P, prospective; R, retrospective; HR, hazard ratio; OR, odds ratio; CVD, cardiovascular disease; CKD, chronic kidney disease; DM, diabetes mellitus; CAD, coronary artery disease; CHF, congestive heart failure; CRP, C-reactive protein; Glu, glucose; BMI, body mass index; HCQ, hydroxychloroquine; AZM, azithromycin; ED, emergency department; ICU, intensive care unit; PaO_2:FiO_2, ratio of the PaO_2 over the fraction of inspired oxygen; IMV, invasive mechanical ventilation; SOFA, sequential organ failure assessment; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; PEEP, positive end-expiratory pressure; FiO_2, fraction of inspired oxygen; PaO_2, arterial partial pressure of oxygen; PVD, peripheral vascular disease; CVA/TIA, cerebrovascular accident/transient ischemic attack; VTE, venous thromboembolism.

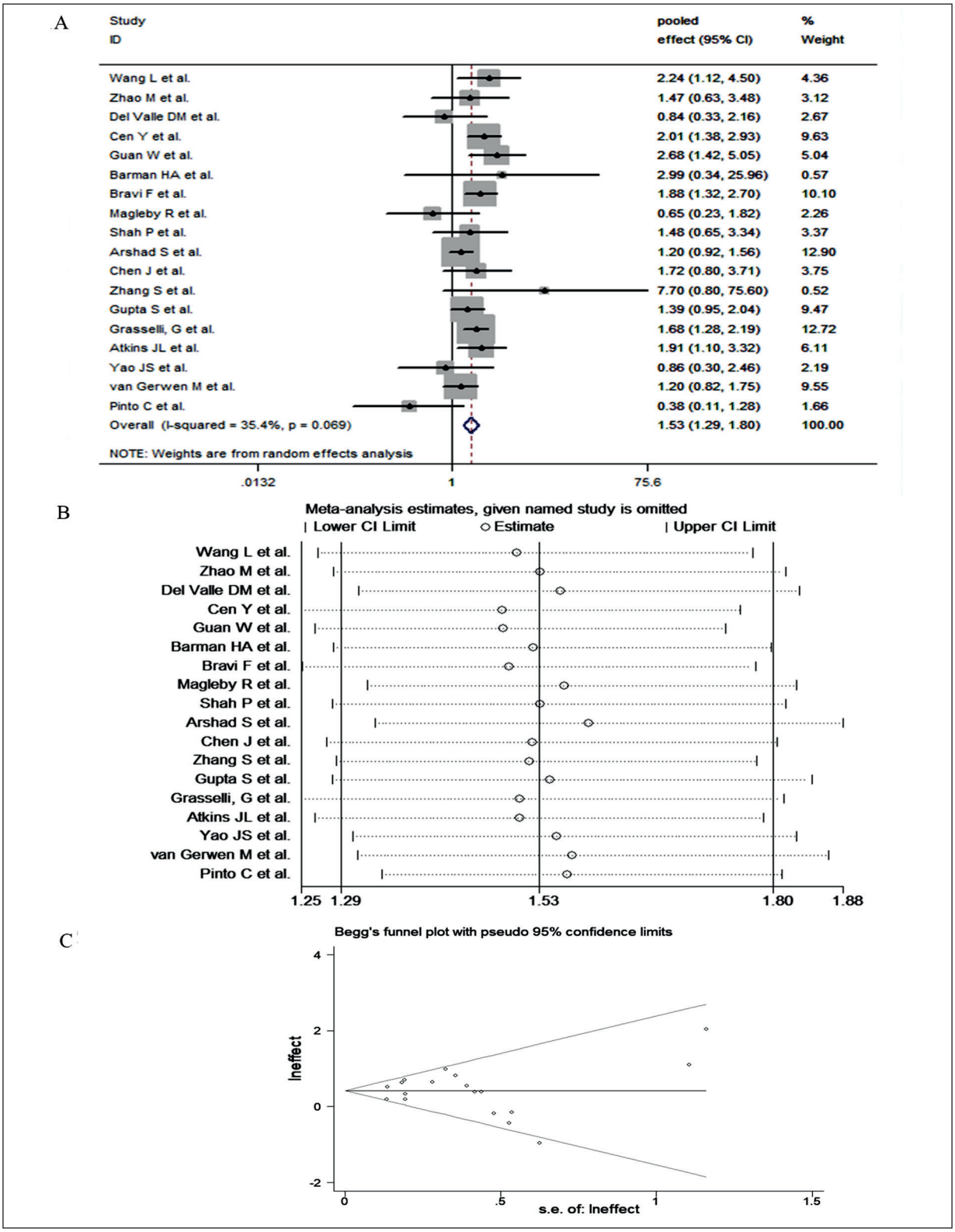

Figure 1. The pooled effects and 95% confidence interval (CI) of the relationship between COPD and adverse outcomes in COVID-19 patients (**A**); Sensitivity analysis of the relationship between COPD and adverse outcomes in COVID-19 patients (**B**); Publication bias was assessed by funnel plot (**C**).

Results

A total of 163 articles were reviewed. After carefully screening, 18 articles with 26,075 patients were enrolled in the study[2-4,6-20]. 6 studies were from China, 8 were from the United States, 2 were from Italy, and one study was from UK and Turkey. The characteristics of the included studies are shown in Table I.

The results of our meta-analysis revealed that pre-existing COPD was significantly associated with an increased risk of adverse outcomes in COVID-19 patients based on 18 studies reporting adjusted effect estimates (pooled effect = 1.53, 95% CI: 1.29-1.8; $I^2 = 35.4\%$, random-effects model) (Figure 1A). As shown by the sensitivity analysis, none of the studies had a significant impact on the overall results, which means that the results were steady (Figure 1B). Also, there was no publication bias in our study (Begg's test, $p = 0.449$ and Egger's test, $p = 0.893$) (Figure 1C).

Discussion

Our findings indicated that pre-existing COPD was significantly associated with poor clinical outcomes among COVID-19 patients. Some studies[21-23] have reported that viral infections, especially respiratory virus infections, could lead to deterioration of the disease. Although COPD prevalence was low in COVID-19 cases, pre-existing COPD was associated with severity and mortality rates in COVID-19 patients[24]. Also, older people with COPD had a higher risk of death[25]. This suggests that COVID-19 patients with pre-existing COPD need more clinical attention to prevent the progression of the disease.

Some limitations in our study are: firstly, although this meta-analysis was based on adjusted effect estimates, the adjusted factors were not uniform among the included studies. Secondly, the judgment criteria of adverse outcomes in the included studies were not consistent in all the studies. Adverse outcomes included severe, critical and mortal outcomes in different studies. Thirdly, the primary treatment data for COVID-19 patients with pre-existing COPD are unknown. Thus, we could not evaluate the effects of clinical treatment on the association between COPD and COVID-19 patients with adverse outcomes. Considering these limitations, well-designed studies with larger sample sizes are needed to confirm our findings in the future.

Conclusions

For the first time, the results of our meta-analysis demonstrated that pre-existing COPD was an independent risk factor for predicting the adverse outcomes in COVID-19 patients.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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