Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Letter to the Editor

Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19)

In the ongoing coronavirus disease 2019 (COVID-19) pandemic, some unique clinical features have been described [1]. In a report of 44,672 cases from China, a case fatality rate of 2.8% for males versus only 1.7% for females was observed [2]. It has been hypothesized that this may be due a higher prevalence of comorbidities among males, in particular the rate of smoking, which is reported to be 52.1% in men and 2.7% among women in China [3]. However, decreased 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), are observed in smokers [4,5]. In this article, we aimed to investigate the association between active smoking and severity of COVID-19 illness.

An electronic search was conducted in Medline (PubMed interface), Scopus and Web of Science, using the keywords "smoking" OR "cigarette" AND "coronavirus 2019" OR "COVID-19" OR "2019-nCoV" OR "SARS-CoV-2", between 2019 and present time (i.e., March 9, 2020), without language restriction. The title, abstract and full text of all documents captured with these search criteria were scrutinized, and those reporting the rate of active smokers in COVID-19 patients with clinically validated definition of severe disease were included in this meta-analysis. The reference list of the identified studies was also analyzed (forward and backward citation tracking) for detecting other potentially eligible articles.

A meta-analysis was then performed, 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 carried out 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, 27 documents could be initially identified based on our search criteria and from the reference lists, 22 of which were excluded after title, abstract or full text reading, since they were review articles ($n = 4$), commentaries or other editorial materials ($n = 2$), they did not deal with COVID-19 disease ($n = 11$), or did not provided the rate of active smokers in patients with or without severe disease ($n = 5$). Therefore, 5 studies could finally be included in our meta-analysis,

Table 1
Characteristics of the studies included.

Authors	Setting	Sample size	Outcome	Severe patients n (%)	Age (yrs)*	Women (%)	Non-severe patients n (%)	Age (yrs)*	Women (%)
Guan W et al., 2020 to ICU, mechanical ventilation, death.	China	1085 52	Admission 42%	172 (16%) 913 (84%)	45 (34–57)	42%			
Huang C et al., 2020	China	44	ICU Care	13 (30%)	49 (41–61)	15%	31 (70%)	49 (41–58)	32%
Liu W et al., 2020 to ICU, mechanical ventilation, death.	China	78 66	Admission 36%	11 (14%) 67 (86%)	37 (32–41)	52%			
Yang X et al., 2020	China	50	Death	32 (64%)	65 (45–87)	34%	18 (36%)	52 (26–77)	30%
Zhang JJ et al., 2020	China	142	Respiratory distress/ insufficiency	60 (42%)	64 (25–87)	43%	82 (58%)	52 (26–78)	54%

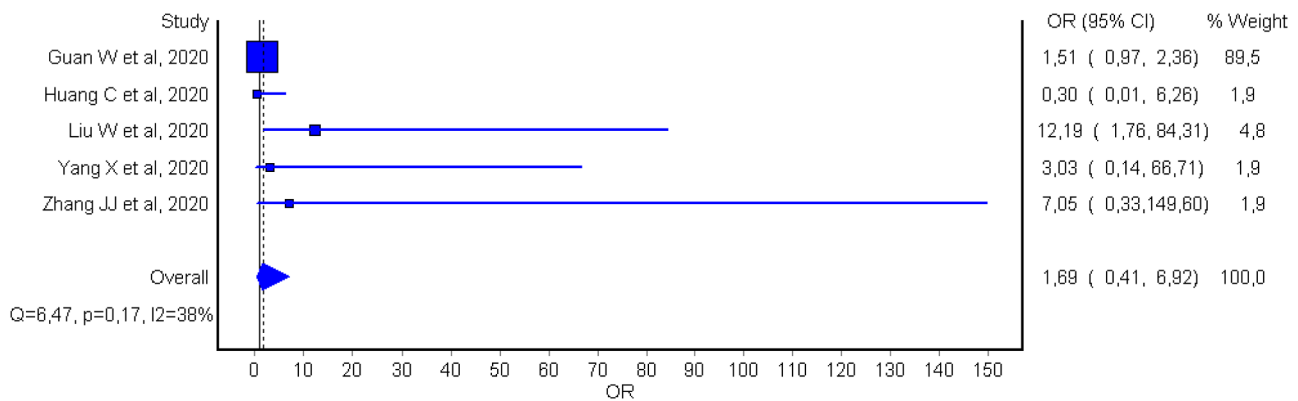* Median and interquartile range.

Fig. 1. Odds ratio (OR) and 95% confidence interval (95% CI) of active smoking between coronavirus disease 2019 (COVID-19) patients with or without severe disease. .

totaling 1399 COVID-19 patients, 288 of whom (20.6%) with severe disease [6–10]. The essential characteristics of the five included studies are shown in Table 1, whilst the individual and pooled OR of smoking for predicting severe COVID-19 is shown in Fig. 1. Overall, in only one study [8] active smoking was found to be a significant predictor of COVID-19 severity, whilst in the other four studies the association was not statistically significant. Despite a trend towards higher risk was appreciable, no significant association could neither be found between active smoking and severity of COVID-19 when data of individual studies were pooled (OR, 1.69; 95% CI, 0.41–6.92; $p = 0.254$). No significant association could also be found when the large study by Guan et al. (89.5% of all samples size) [6] was excluded from statistical analysis (OR, 4.35; 95% 0.86–21.86; $p = 0.129$; I^2 29%, $p = 0.24$).

In conclusion, the results of this preliminary meta-analysis based on Chinese patients suggest that active smoking does not apparently seem to be signicantly associated with enhanced risk of progressing towards severe disease in COVID-19.

Declaration of Competing Interest

None

References

[1] Mattiuzzi C, Lippi G. Which lessons shall we learn from the 2019 novel coronavirus outbreak? Ann Transl Med 2020;8:48.
[2] The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) — China. 2020. China CDC Wkly 2020;2:113–22.
[3] Parascandola M, Xiao L. Tobacco and the lung cancer epidemic in China. Transl Lung Cancer Res 2019;8(Suppl 1):S21–30. https://doi.org/10.21037/tlcr.2019.03.12.
[4] Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from wuhan: an analysis based on decade-long structural studies of sars. J Virol 2020 Jan 29. https://doi.org/10.1128/JVI.00127-20. pii: JVI.00127-20[Epub ahead of print].
[5] Oakes JM, Fuchs RM, Gardner JD, Lazartigues E, Yue X. Nicotine and the renin-angiotensin system. Am J Physiol Regul Integr Comp Physiol 2018;315(5):R895–906.
[6] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in china. N Engl J Med 2020 Feb 28. https://doi.org/10.1056/NEJMoa2002032. [Epub ahead of print].
[7] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in wuhan. China. Lancet 2020;395:497–506.
[8] Liu W, Tao Z-W, Lei W, Ming-Li Y, Kui L, Ling Z, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J February 2020. https://doi.org/10.1097/CM9.0000000000000775.
[9] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine 2020;0(0). https://doi.org/10.1016/S2213-2600(20)30079-5.
[10] Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected by SARS-CoV-2 in wuhan, China. Allergy 2020 Feb 19. https://doi.org/10.1111/all.14238. [Epub ahead of print].

Giuseppe Lippi[a,*], Brandon Michael Henry[b]

[a] *Section of Clinical Biochemistry Department of Neuroscience Biomedicine and Movement, University of Verona, Verona, Italy*
[b] *Cardiac Intensive Care Unit The Heart Institute Cincinnati Children's Hospital Medical Center, Ohio, United States*
E-mail address: giuseppe.lippi@univr.it (G. Lippi).

* Corresponding author. Section of Clinical Biochemistry, University Hospital of Verona, Piazzale LA Scuro, 37134 Verona, Italy