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Smoking, vaping and hospitalization for COVID-19

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Abstract

The study purpose was to examine the prevalence of current e-cigarette use and current smoking among hospitalized patients with COVID-19 in China, considering the high population smoking prevalence in the country (26.6%, 50.5% in males and 2.1% in females).

A systematic research of the literature (PubMed) was performed on April 1. Out of 432 studies, we identified 13 studies examining the clinical characteristics of a total of 5960 hospitalized COVID-19 patients that presented data on the smoking status. No study reported e-cigarette use among COVID-19 patients. The prevalence of current smoking ranged from 1.4% to 12.6%. The random effect pooled prevalence of current smoking was 6.5% (95%CI: 4.9-8.2%). This preliminary analysis does not support the argument that current smoking is a risk factor for hospitalization for COVID-19. Instead, these consistent observations, which are further emphasized by the low prevalence of current smoking among COVID-19 patients in the US (1.3%), raises the hypothesis that nicotine may have beneficial effects on COVID-19. This could be attributed to its immunomodulatory effects and its interaction with the renin-angiotensin system. However, other confounding factors need to be considered and the accuracy of the recorded smoking status needs to be determined. However, the results were remarkably consistent across all studies and were recently verified in the first case series of COVID-19 cases in the US.

In conclusion, the generalized advice to quit smoking as a measure to improve health risk remains valid, but no recommendation can currently be made concerning the effects of smoking on the risk of hospitalization for COVID-19. No studies recording e-cigarette use status among hospitalized COVID-19 patients were identified. Thus, no recommendation can be made for e-cigarette users. The above-mentioned observations, together with the potential mechanisms through which nicotine interacts with the inflammatory process and the renin-angiotensin-aldosterone axis involved in the development of COVID-19, warrant an urgent investigation of the clinical effects of pharmaceutical nicotine on COVID-19 susceptibility, progression and severity.

Keywords: SARS-CoV-2, COVID-19, nicotine, smoking, hospitalization, electronic cigarette.

Introduction

There is a lot of speculation about the effects of smoking on Corona Virus Disease 2019 (COVID-19). Smoking increases

susceptibility to respiratory infections and media reports suggest that it may increase the risk of being infected with acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for COVID-19.

SARS-CoV-2 is known to use the angiotensin converting enzyme 2 (ACE2) as a receptor for cell entry. There is a complex and unclear interplay between COVID-19 and the renin-angiotensin-aldosterone system.[1] Until recently, smoking and nicotine were found to down-regulate ACE2 expression in the lung and other tissues.[2][3] More recent analyses suggest that up-regulation of ACE-2 caused by smoking could be detrimental for COVID-19.[4][5] However experimental data suggest that infection with SARS-CoV and SARS-CoV-2 leads to down-regulation of ACE2, and this downregulation is detrimental due to uncontrolled ACE and angiotensin II activity.[6][7] It has been observed that decreased ACE2 availability contributes to lung injury and ARDS development.[8][9] Therefore, higher ACE2 expression, while seemingly paradoxical, may protect against acute lung injury caused by COVID-19.[10]

China has a high prevalence of smoking (26.6%), much higher among males (50.5%) than females (2.1%).[11] It was recently suggested that there is no strong evidence on a link between smoking and COVID-19 due to the low smoking prevalence among COVID-19 patients in 2 studies compared to the population smoking prevalence in China.[12] The purpose of this study was to examine the prevalence of current smoking among Chinese hospitalized cases with COVID-19 relative to the population prevalence of current smoking in China.

Methods

A systematic review of the literature was performed by searching for publications on PubMed using the terms "[SARS-CoV-2 OR COVID-19 OR 2019-nCoV] AND [Clinical OR Mortality OR Outcome]" in the title or the abstract on April 1. Out of a total of 432 studies, 13 studies which included data about the smoking status of hospitalized COVID-19 patients were identified.[13][14][15][16][17][18][19][20][21][22][23][24][25] No study reported e-cigarette use among COVID-19 patients. The pooled rate of current smoking was calculated by random effect meta-analysis using JASP Version 0.11.1 (JASP Team 2019, University of Amsterdam, Netherlands).

Results

The studies examined are presented in **Table 1**. One study presented the combined current and former smoking prevalence, and all were considered current smokers in this analysis.[13] Two other studies reported the smoking status as "history of smoking" or "smoking".[22][24] While it was unclear if these definitions included both current and former smokers, we analyzed the data assuming they were all current smokers.

Table 1. Studies reporting the smoking status of hospitalized COVID-19 patients in China.

	Hospitalized cases with data on smoking status	Age	Males	Females	Hospitalized Current smokers	Hospitalized Current smokers
	N	median (IQR) or mean (SD)	n	n	n	% (95%CI)
Guan, Liang et al.	1590	49 (16)	904	674	111	7.0 (5.7-8.2)
Guan, Ni et al.	1085	47 (35-58)	637	459	137	12.6 (10.6-14.6)
Lian et al.	788	41 (11) 68 (7)	407	381	54	6.9 (5.1-8.6)
Jin et al.	651	46 (14)	331	320	41	6.3 (4.4-8.2)
Chen et al.	274	56 (46-67)	171	103	12	4.4 (2.0-6.8)
Zhou et al.	191	54 (42-66)	119	72	11	5.8 (2.4-9.1)
Mo et al.	155	57 (25-87)	86	69	6	3.9 (0.8-6.9)
Zhang et al.	140	38 (33.57)	71	69	2	1.4 (0.0-3.4)
Wan et al.	135	49 (41-58)	72	63	9	6.7 (2.5-10.9)
Liu et al.	78	38 (33.57)	39	39	5	6.4 (1.0-11.8)
Huang et al.	41	49 (41-58)	30	11	3	7.3 (0.0-15.3)
Guo et al.	187	59 (15)	91	96	18	9.6 (5.4-13.9)
Zhang, Cai et al.	645	35 (14) 47 (14)	328	317	41	6.4 (4.5-8.2)

Note: In Guan, Ling et al., data on sex was presented for 1578 patients. In Guan, Ni et al., data on sex was presented for 1096 patients.

Figure

A total of 5960 patients with data on smoking status were presented, with 55.1% being males. Current smoking was reported by a total of 450 patients, with the prevalence ranging from 1.4% (95%CI: 0.0-3.4%) to 12.6% (95%CI: 10.6-14.6%) across all studies. The pooled prevalence of current smoking was 6.5% (95%CI: 4.9-8.2%). The random effect meta-analysis is presented in **Figure 1**.

Fixed and Random Effects

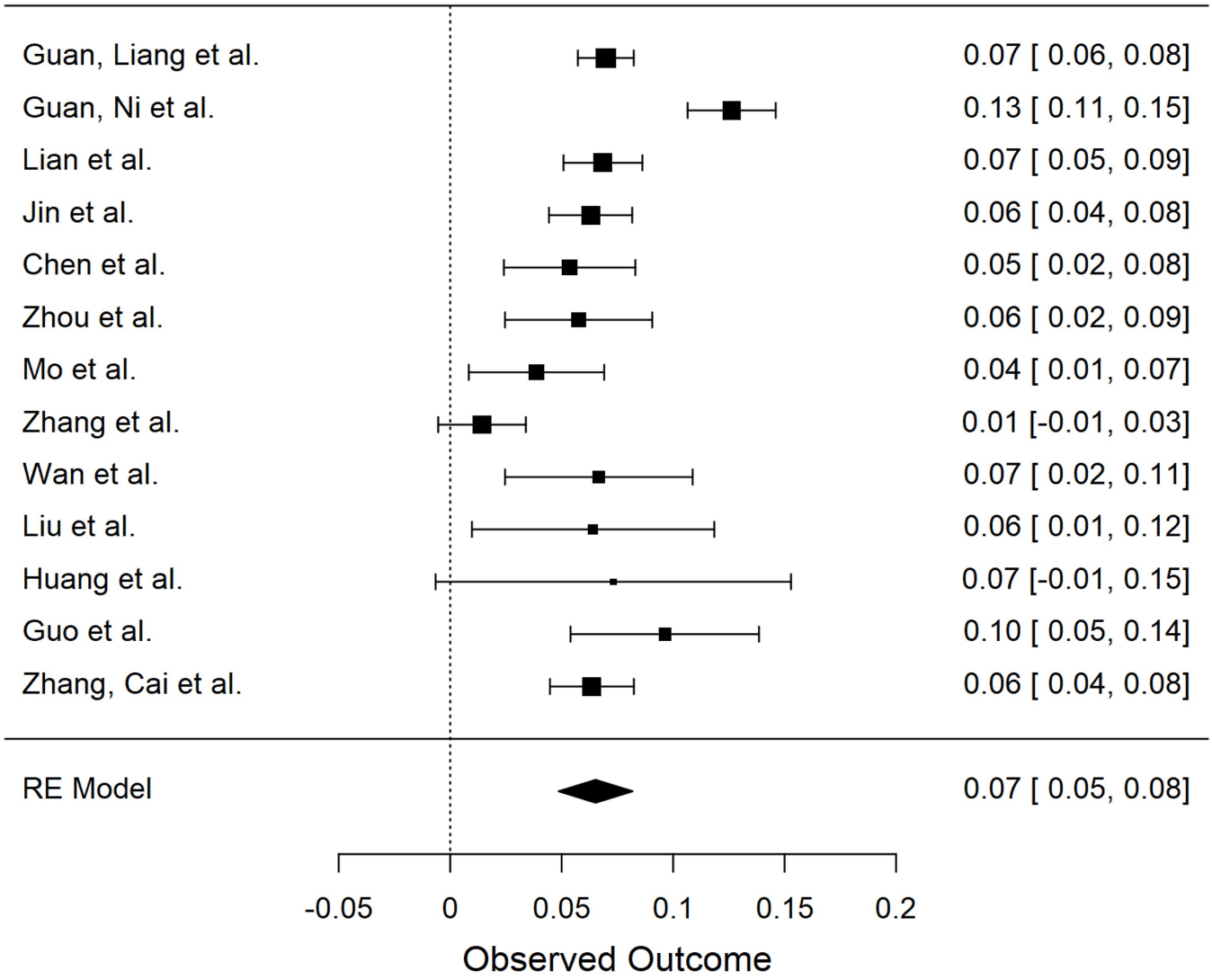
	Q	df	p
Omnibus test of Model Coefficients	59.3438	1	1.3240e -14
Test of Residual Heterogeneity	69.0069	12	4.9108e -10

Note. *p* -values are approximate.

Coefficients

	Estimate	Standard Error	z	p	Lower Bound	Upper Bound
intrcpt	0.0652	0.0085	7.7035	1.3240e -14	0.0486	0.0818

Note. Wald test.



Figure

Discussion

The current study examined for the first time the prevalence of current smoking among hospitalized patients with COVID-19 in China. An unusually low prevalence of current smoking among hospitalized COVID-19 cases in China was observed

when considering the population smoking prevalence. The pooled prevalence observed in the 13 studies analyzed was approximately 1/4th the population prevalence. Consistently low prevalence of current smoking was observed in all studies.

This preliminary analysis, assuming that the reported data are accurate, does not support the argument that current smoking is a risk factor for hospitalization for COVID-19. However, other confounding factors, such as socioeconomic status, should be considered in examining if access of Chinese smokers with COVID-19 to hospital care may be different compared to the non-smoking population. At this time, it is impossible to perform a multivariate analysis or examine the prevalence of COVID-19 infection and hospitalization according to the smoking status of the whole population. The accuracy of the recorded smoking status also needs to be determined. It is possible that some patients may have quit smoking shortly after disease initiation and before admission to hospital, and thus would be registered as former smokers. Only 3 of the studies reported the proportion of former smokers among patients, which was particularly low (1.9%, 3.0% and 5.0%).[14][17][20] Another limitation is that differences in smoking prevalence exist between age groups, particularly considering that hospitalization for COVID-19 may be more likely for older people. A study by Liu et al. reported that the highest smoking prevalence in China was observed in males aged 40-59 years.[26] The median age in all the studies analyzed herein was < 59 years, with the exception of one subgroup of patients in a study comparing elderly with young cases.[15] Additionally, high smoking prevalence was observed among older Chinese males by Liu et al. Specifically, the prevalence of current smoking in males was: 46.5% in 18-29 years, 57.6% in 30-39 years, 60.3% in 40-49 years, 59.5% in 50-59 years, 52.2% in 60-69 years and 41.5% in 70+ years. In females, the highest smoking rates were observed in those aged 50 years or higher (4.7-8.7%) compared to younger age groups (1.7-2.6%).[26] Thus, it is unlikely that age was a factor that substantially affected the present analysis. Finally, the present analysis examined only hospitalized cases. Thus, no conclusion can be drawn on the susceptibility of smokers to less severe COVID-19 that would not require hospitalization.

The study also has implications when examining the effect of smoking status on disease progression, complications and death among hospitalized COVID-19 patients. One study reported that current smoking is associated with higher odds of severe COVID-19.[27] However, it is well-established that smokers are more likely than non-smokers to suffer from comorbidities, such as cardiovascular disease, which are risk factors for adverse COVID-19 outcomes. It remains unclear whether smoking *per se* or other factors related to comorbidities may be responsible for an adverse outcome.

Considering the above-mentioned uncertainties, the generalized advice to quit smoking as a measure to improve health risk remains valid, but no recommendation can be currently made concerning the effects of smoking on the risk of hospitalization for COVID-19. In fact, the consistently low prevalence of current smoking among Chinese patients with COVID-19 was further supported by the recent data recently released from the US CDC.[28] From a total of 7162 patients in the US, only 1.3% were current smokers. low smoking prevalence was also observed among hospitalized non-ICU (2.1%) and ICU cases (1.1%), while the population smoking prevalence in the US is 13.8%. These observations raise a possible hypothesis that nicotine might reduce the risk for severe COVID-19. Hospitalization for COVID-19 will inevitably result in abrupt withdrawal of nicotine and its beneficial effect linked to this hypothesis in smokers or users of other nicotine products. This could, at least partly, explain the association between smoking and COVID-19 severity among

hospitalized patients.[27] Nicotine has been found to prevent acute lung injury in an animal ARDS model and has immunomodulatory effects.[29][30] There is also evidence for an interaction between nicotine and the renin-angiotensin-aldosterone axis, although such interactions remain unclear.[2][3][4][5] In any case, the observations of a consistently low prevalence of smoking among COVID-19 cases in China and the US, together with the potential mechanisms through which nicotine interacts with the inflammatory process and the renin-angiotensin-aldosterone axis involved in the development of COVID-19, warrant an urgent investigation of the clinical effects of pharmaceutical nicotine on COVID-19 susceptibility, progression and severity. The potential need to provide pharmaceutical nicotine products to smokers who experience an abrupt withdrawal of nicotine when hospitalized for COVID-19 or aim to follow medical advice to quit smoking to relieve underlying conditions that may increase vulnerability to serious or fatal symptoms should also be examined.

Finally, an important issue that also needs to be addressed is the effect of e-cigarette use on COVID-19 risk, particularly for Europe and the US where prevalence of use is higher compared to China. No studies recording e-cigarette use status among hospitalized COVID-19 patients in China were identified. Thus, no recommendation can be made for e-cigarette users, but all the above-mentioned issues relevant to the hypothesis about the effects of nicotine and nicotine withdrawal on COVID-19 progression and severity are equally applicable to e-cigarette users.

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