# Smoking Cessation as a Public Health Measure to Limit the Coronavirus Disease 2019 Pandemic

Maki Komiyama and Koji Hasegawa

*National Hospital Organization Kyoto Medical Center, Kyoto, Japan*

## Abstract

The novel coronavirus disease 2019 (COVID-19) has already evolved into a rapidly expanding pandemic. Risk factors for COVID-19, such as cardiovascular disease, chronic obstructive pulmonary disease and diabetes, are all strongly associated with smoking habits. The effects of cigarette smoking on the transmission of the virus and worsening of COVID-19 have been less addressed. Emerging data indicate that smoking history is the major determinant of worsening COVID-19 outcomes. Smoking cessation recovers airway ciliary clearance and immune function. Thus, smoking cessation awareness is strongly encouraged as a public health measure to limit the global impact of COVID-19.

## Keywords

Smoking, COVID-19, SARS-CoV-2, coronavirus, pandemic

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**Correspondence:** Koji Hasegawa, Division of Translational Research, National Hospital Organization Kyoto Medical Center, 612-8555, Kyoto, Japan.
E: koj@kuhp.kyoto-u.ac.jp



The novel coronavirus disease 2019 (COVID-19) first occurred in December 2019 in Wuhan, Hubei Province, China, and has already evolved into a rapidly expanding pandemic. The WHO has declared COVID-19, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), to be a public health emergency of international concern.[1] Until effective therapeutics and vaccines become available, minimising the spread of COVID-19 is a pressing global challenge. Approximately 80% of infected individuals remain asymptomatic or present only with minor symptoms, whereas 15% become moderately to severely ill with cough and shortness of breath, and 5% require intensive care. Elderly people with underlying diseases, such as cardiovascular disease, diabetes, hypertension, chronic respiratory disease and malignancies, are at greater risk of developing severe COVID-19. Behavioural measures, such as coughing etiquette, hand washing, social distancing and reducing physical contact, are recommended to prevent the spread of SARS-CoV-2. However, the effects of cigarette smoking on the transmission of the virus and worsening of COVID-19 have been less addressed.

Smoking is a major risk factor for many respiratory infections, and could also accelerate disease progression in those infected.[2] Previous studies have shown that smokers are more likely to contract influenza and exhibit more severe symptoms than nonsmokers.[3] Additionally, with the previous Middle East respiratory syndrome coronavirus (MERS-CoV) outbreaks, smoking was reported to be a risk factor for MERS-CoV infection and associated with high mortality.[4] The mechanisms by which smoking increases the risk of worsening pneumonia include altered airway architecture, inhibition of airway ciliary clearance and reduced immune function.[3]

There are several reasons why smoking adversely affects the immune system. First, smoking reduces $CD4^+$ T-cells (helper T-cells), which promote antibody production in B-cells and activate killer T-cells to attack pathogens. Second, nicotine, a major component in tobacco products, which promotes the secretion of catecholamines and corticosteroids, could impair immune function and suppress the body's ability to combat infections.[5,6] Third, nicotine also reportedly inhibits the production of interleukin-22, which helps suppress lung inflammation and repair damaged cells.[7] Thus, in COVID-19, as well as in other infectious diseases, the risk of infection and increased disease severity could be higher in smokers. However, although there are reports of age, sex and underlying diseases being factors driving SARS-CoV-2 transmission and disease deterioration, few studies have focused on the association with cigarette smoking.

Unfortunately, the COVID-19 pandemic is still ongoing, and limited data on the clinical characteristics and prognostic factors of COVID-19 patients are available. However, emerging data appear to indicate an increased risk of infection, morbidity and mortality of SARS-CoV-2 in individuals with a history of smoking. According to the WHO, the mortality rate due to SARS-CoV-2 in China is higher among men (4.7%) than women (2.8%), which might reflect the large sex difference in smoking habits in China (52.1% in men and 2.7% in women).[8,9] In Western countries, where infection transmission has recently soared, smoking tends to be higher among men, although the sex difference is not as great as in China. The European Centre for Disease Prevention and Control (ECDC) reported that COVID-19 deaths were more frequent among men; a higher smoking rate in men might be attributable to the higher mortality.[10]

In a report on 1,099 infected individuals from China, 12.4% of current smokers and 23.8% of past smokers developed critical outcomes, including being admitted into an intensive care unit or fitted with a ventilator, or mortality. In comparison, only 4.7% of those who had never smoked developed critical outcomes.[11] Additionally, the proportion of patients with severe symptoms was 21.2% among current smokers and 42.9% among past smokers, which was higher compared with those who had never smoked (14.5%).[11] In this report, the analysis was just a simple comparison. Usually, past smokers were older than current smokers. Therefore, a high age in past smokers may contribute to their worsening outcomes.

A small study from China using multivariate analysis identified the following four factors as being associated with COVID-19 deterioration: smoking history, body temperature of >37.3°C at the time of admission, respiratory failure and age ≥60 years.[12] Among these, the OR for smoking history was highest at 14 (CI [1.6–45]; p=0.018), which was higher than the ORs for other factors associated with disease deterioration (8.5–9.0). As noted earlier, COVID-19 is considered to be severe and associated with a higher mortality rate in elderly patients with underlying diseases; it is worth noting that underlying diseases related to the severity of COVID-19, such as cardiovascular disease, chronic obstructive pulmonary disease and diabetes, are all strongly associated with smoking.[13,14]

COVID-19 is primarily a disease of the respiratory tract, and virus entry into cells, viral replication and virion release occur within the respiratory tract.[15] Angiotensin-converting enzyme (ACE) 2 converts the vasoconstrictor angiotensin II to vasoprotective angiotensin.[1–7] Multiple studies have shown that ACE-2 is a host receptor for SARS-CoV-2.[16] SARS-CoV-2 enters cells through ACE-2 receptors present in mucosal epithelial cells and alveolar tissues in a clathrin-dependent process. Cigarette smoking increases the expression of ACE-2 in pulmonary tissues, which could in part account for the increased risk of infection.[17,18] Additionally, the WHO has noted that smokers perform repeated hand to face reciprocal movements, which contribute to increased opportunity for virus entry.[19]

ACE inhibitors and angiotensin-receptor blockers also increase the expression of ACE-2 receptors, which could increase the risk of COVID-19 infection. In fact, the ECDC reported that 74% of COVID-19 fatalities in Italy had concomitant hypertension, suggesting an association with these drugs.[10] Many societies, including the European Society of Cardiology, have issued alerts that patients with cardiovascular diseases discontinue ACE inhibitors and angiotensin-receptor blockers.[20] Switching to calcium antagonists has been suggested; however, further evidence for this is needed.[21]

Although only a few reports on smoking have been published to date and further accrual of evidence is warranted, smoking is likely to be an important and significant factor associated with COVID-19 severity. Cigarette smoking decreases lung function, and evidently poses a general risk factor for severe respiratory infections, thus there is an apparent association between cigarette smoking and COVID-19 severity. The detailed mechanism by which COVID-19 becomes more severe in patients with a history of cigarette smoking warrants further investigation. There is also a need for more evidence on the effect of second-hand smoke on the spread of SARS-CoV-2. However, according to published COVID-19 research reports, even at this stage, it might be well assumed that smokers are likely to be at serious risk for contracting SARS-CoV-2 infection. Smoking cessation recovers airway ciliary clearance and immune function as early as 1 month. Thus, smoking cessation awareness is strongly encouraged as part of public health measures to limit the global impact of COVID-19. ■


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