

Response to the Comment 'Smoking and Angiotensin-converting Enzyme Inhibitor/Angiotensin Receptor Blocker Cessation to Limit Coronavirus Disease 2019

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Thank you very much for your interesting and important comments on our review that discussed smoking cessation to limit the coronavirus disease 2019 (COVID-19) pandemic.^{1,2} As you pointed out, the reported number of hospitalised COVID-19 patients who are current or former smokers is small.^{3,4} One reason for this small number of smokers is that an unknown history of smoking may be treated as a non-smoking history. Most emergency or sub-emergency COVID-19 patients are admitted to hospital as new patients. Because medical workers face difficulty in managing these patients, smoking history is often insufficiently assessed in the real-world clinical setting. Another reason for the small number of hospitalised COVID-19 patients who are current smokers is that older age is associated with a reduced prevalence of current smoking and an increased prevalence of former smoking. As you reported, former smokers constitute a major category of hospitalised COVID-19 patients.⁵

Furthermore, former smokers, as a result of a long history of smoking, have comorbidities, such as cardiovascular disease, chronic obstructive pulmonary disease, diabetes and cancer. In fact, the report cited in our

review states that the proportion of patients with progression to severe COVID-19 status was the highest in former smokers, followed by current smokers, whereas the proportion was low in non-smokers.³ However, a systematic literature review and meta-analysis has demonstrated that current smoking is associated with a greater risk of critical or mortal COVID-19 status.⁶ Therefore, smoking cessation is an important measure to limit the severity of COVID-19.

There may be multiple mechanisms underlying the association of smoking with disease progression. Angiotensin-converting enzyme (ACE) 2 appears to play a protective role against pneumonia. At the beginning of the pandemic, concerns were raised that ACE inhibitors could predispose individuals to severe COVID-19. However, recent evidence has shown that ACE inhibitors and angiotensin receptor blockers do not increase the risk of severe COVID-19.⁷ This is in agreement with international guideline recommendations that these medications should not be withdrawn in patients currently taking them and that there is no contraindication at present for the use of ACE inhibitors/angiotensin receptor blockers in patients with COVID-19.⁸ ■

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