# Smoking and Angiotensin-converting Enzyme Inhibitor/Angiotensin Receptor Blocker Cessation to Limit Coronavirus Disease 2019

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Coronavirus disease 2019, COVID-19, SARS-CoV-2, cigarette smoking, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers

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We read with interest the paper by Komiyama and Hasegawa on the need for smoking cessation as a public health measure to limit the coronavirus disease 2019 (COVID-19) pandemic.[1] It seems obvious to reiterate that smoking cessation is advisable to reduce many other severe conditions, such as chronic lung and cardiovascular diseases and some types of cancer, which are leading causes of morbidity and mortality. Cigarette smoking kills more than 8 million people each year worldwide, with more than 7 million of those deaths being the result of direct tobacco use and around 1 million occurring in non-smokers exposed to second-hand smoke.[2]

Aside from this, regarding the COVID-19 pandemic, the authors state that published data appear to indicate an increased risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, morbidity and mortality in smokers due to the possible effect of smoking in overexpressing angiotensin-converting enzyme 2 (ACE2). This protein is found in various tissues, mainly in the lungs, gastrointestinal tract and testes, which SARS-CoV-2 uses to enter the host cell, so this possibly increases the risk of infection.[3]

However, published data at the time the authors' paper was submitted to *European Cardiology Review* (7 April 2020), coming mainly from China, indicated the opposite, noting that current smokers are strongly under-represented among patients hospitalised for COVID-19.[4,5] A recent analysis covering 8,910 patients hospitalised for COVID-19 in Asia, Europe and the US showed that only 5.5% were current smokers and 94.5% were former or non-smokers and, among non-survivors, the percentage of current smokers was lower than that of former smokers.[6]

In a recent published paper, we reported that among 132 patients hospitalised at the University Hospital of Padova for COVID-19 pneumonia, none were current smokers, 84.8% were former smokers and 15.2% had never smoked.[7] Nonetheless, we are far from hypothesising that cigarette smoking has a 'protective' role regarding susceptibility to SARS-CoV-2 infection or COVID-19 complications.

We are also aware that any public health policy perspective cannot be left only to science. If scientific evidence shows that smoking is protective against COVID-19, we absolutely cannot suggest people smoke to avoid SARS-CoV-2 infection.

Researchers have to gain more insight into the pathogenesis of SARS-CoV-2 to discover any possible biological mechanism related to the low prevalence of smokers among COVID-19 patients, considering for example the role of ACE2 expression that has been shown to be downregulated by cigarette smoking at least in experimental animals.[8]

Furthermore, Komiyama and Hasegawa state that ACE inhibitors (ACEis) and angiotensin receptor blockers (ARBs) increase the expression of ACE2, the putative receptor that SARS-CoV-2 uses to enter the host cell.[1] To this regard, they report that many scientific societies, including the European Society of Cardiology (ESC), have issued alerts suggesting patients discontinue ACEis and ARBs and switch to calcium antagonists. This is not correct. In its recent position statement, the ESC Council on Hypertension has expressed concern over any speculation about the safety of ACEi or ARB treatment in relation to COVID-19, since this does not have any scientific basis or evidence to be supported at yet. In that statement, patients are recommended to continue their usual antihypertensive therapy because of a lack of any clinical or scientific evidence to suggest that treatment with ACEis or ARBs should be discontinued to prevent SARS-CoV-2 infection or reduce COVID-19 severity.[9] Many other highly reputable scientific societies, including the American Heart Association, the American College of Cardiology and the Heart Failure Society of America, have issued similar recommendations.[10]

Recent data published after the Komiyama and Hasegawa paper did not provide evidence that patients treated with ACEis and ARBs were at a higher risk for COVID-19.[1,6] Those treated with ACEis had a better chance of survival to hospital discharge and there was no

such association for ARBs. However, these results should be considered with caution since they were not derived from a randomised controlled study.[6]

In conclusion, Komiyama and Hasegawa's suggestions do not seem to fit adequately with what is currently known from the literature.[1] Nonetheless, the advice to stop smoking must be followed anyway. ■


1. Komiyama M, Hasegawa K. Smoking cessation as a public health measure to limit the coronavirus disease 2019 pandemic. *Eur Cardiol* 2020;15:e16. https://doi.org/10.15420/ecr.2020.11; PMID: 32373189.
2. WHO. Tobacco. Key facts. 2019. https://www.who.int/news-room/fact-sheets/detail/tobacco (accessed 27 May 2020).
3. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 2020;181:271–80.e8. https://doi.org/10.1016/j.cell.2020.02.052; PMID: 32142651.
4. Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). *Eur J Intern Med* 2020;75:107–8. https://doi.org/10.1016/j.ejim.2020.03.014; PMID: 32192856.
5. Miyara M, Tubach F, Pourcher V, et al. Low rate of daily active tobacco smoking in patients with symptomatic COVID-19. *Qeios* 2020. https://doi.org/10.32388/WPP19W.4; preprint.
6. Mancia G, Rea F, Ludergnani M, et al. Renin–angiotensin–aldosterone system blockers and the risk of Covid-19. *N Engl J Med* 2020;382:2431–40. https://doi.org/10.1056/NEJMoa2006923; PMID: 32356627.
7. Rossato M, Russo L, Mazzocut S, et al. Current smoking is not associated with COVID-19. *Eur Respir J* 2020;55:2001290. https://doi.org/10.1183/13993003.01290-2020; PMID: 32350106.
8. Oakes JM, Fuchs RM, Gardner JD, et al. Nicotine and the renin-angiotensin system. *Am J Physiol Regul Integr Comp Physiol* 2018;315:R895–906. https://doi.org/10.1152/ajpregu.00099.2018. PMID: 30088946.
9. European Society of Cardiology. Position statement of the ESC Council on Hypertension on ACE-inhibitors and angiotensin receptor blockers. 2020. https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang (accessed 27 May 2020).
10. American College of Cardiology. HFSA/ACC/AHA statement addresses concerns re: using RAAS antagonists in COVID-19. 2020. https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-RAAS-antagonists-in-COVID-19 (accessed 27 May 2020).