



Hypertension and severe COVID-19

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Keywords COVID-19 · Hypertension · Severity

Received: 5 January 2023 / Accepted: 13 January 2023 / Published online: 27 February 2023
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We read with appreciation the recently published report [1] from the Japanese Society of Hypertension project team on COVID-19 which presents the updated information on the impact of the COVID-19 pandemic on blood pressure control, the association between hypertension and severe COVID-19, the use of the renin-angiotensin system inhibitors in patients with COVID-19, the blood pressure changes as one of the possible post-acute sequelae of COVID-19, the evidence of telemedicine, as well as COVID-19 vaccination in hypertensive subjects. The report elegantly summarizes the various aspects related to hypertension during the COVID-19 pandemic.

We are particularly interested in the discussion pertaining to the association between hypertension and severe COVID-19, where the authors concluded that there is currently mixed evidence on the risk of severe COVID-19 in patients with hypertension, upon reviewing the published findings about the association. We agree with the authors in which the association between hypertension and severe COVID-19 may not be straightforward, and this is indeed exemplified in a recently published systematic review and meta-analysis [2]. In the systematic review and meta-analysis [2], pre-existing hypertension was significantly associated with mortality due to COVID-19, both in unadjusted (hazard ratio = 2.58; 95% confidence interval 1.66 to 4.02)

and adjusted models (hazard ratio = 1.55; 95% confidence interval 1.22 to 1.97), but with significant heterogeneity in both models ($I^2 = 97$ and 89%). In addition, the association disappeared when the results adjusted for crucial and strong predictors of mortality in patients with COVID-19 (e.g., body weight).

Concurring with the opinion of the authors, we believe the quality of blood pressure control can influence the association between hypertension and severe COVID-19. Of late, we understand that the immune system can be affected by hypertension, where patients with hypertension can have higher proportion of neutrophils and lower proportions of lymphocytes, including CD4(+) T-cells, natural killer cells, and B cells, compared to those without hypertension [3]. In fact, the neutrophil-to-lymphocyte ratio shows a positive correlation with blood pressure in patients with hypertension and is higher in patients without adequate blood pressure control relative to those with adequate blood pressure control [4].

Being a simple and reliable indicator of inflammation, neutrophil-to-lymphocyte ratio is also a marker of the severity of COVID-19, where elevated neutrophil-to-lymphocyte ratio on admission in hospitalized patients with COVID-19 has been associated with poor prognosis [5]. The observation comes as no surprise since emerging evidence implicates neutrophils in the pathogenesis of severe COVID-19. Patients with hypertension, especially those with poor control of blood pressure and have elevated baseline neutrophil-to-lymphocyte ratio, could fare worse upon development of COVID-19, compared to those without poor control of blood pressure.

Therefore, future studies investigating the association between hypertension and severe COVID-19 should also take into consideration how the quality of blood pressure control can interact with the association. In the meantime, clinicians should also emphasize on adequate blood pressure control in the management of hypertensive patients during the COVID-19 pandemic.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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