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Letter to the Editor

Inpatient use of glucocorticoids may mediate the detrimental effect of new-onset hyperglycemia on COVID-19 severity



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We read with great interest the original investigation by Fadini et al. which indicated that newly-diagnosed diabetes and admission hyperglycemia can predict COVID-19 severity due to rapid respiratory deterioration [1]. The study question is urgent and important, given the high proportion of new-onset hyperglycemia observed in patients with COVID-19, as clearly shown in a recent commentary [2]. We appreciate that the authors noted several limitations in their manuscript and accordingly appropriately tempered their interpretation of the data. Nonetheless, we are concerned that the existence of residual confounding may lead to an overestimation of the effect size, hence many readers may still overinterpret the impressive relative risks.

For instance, the use of glucocorticoids during hospitalization may serve as one of the important confounders that were not properly adjusted or matched in this study. Although the use of glucocorticoids in the setting of COVID-19 has been intensely debated, recent clinical trials have provided supportive evidence for their use in severe cases [3,4]. Steroid-induced hyperglycemia is a common metabolic side effect of glucocorticoid treatment in hospitalized patients with and without pre-existing diabetes [5,6]. It is reported that 20%–50% of patients without a previous history of diabetes show hyperglycemia after steroid administration [7–9]. In addition, Xiao et al. [7] have reported that 33 of the 95 (34.7%) patients with severe acute respiratory syndrome (SARS) who received glucocorticoid treatment were diagnosed as steroid-induced diabetes according to the fasting plasma glucose. After adjusting age and gender, the daily maximal dose of methylprednisolone was the only predictor for the new-onset diabetes.

In the study by Fadini et al, the newly-diagnosed diabetes group had a larger proportion of patients receiving in-hospital

glucocorticoids (61.9%) compared to patients with no diabetes (38.8%) and pre-existing diabetes (45.3%), although the difference between pre-existing diabetes vs newly-diagnosed diabetes was not statistically significant ($p = 0.174$). As glucocorticoids are mainly used in severe cases of COVID-19, and steroid-induced hyperglycemia is common in hospitalized patients with and without diabetes, glucocorticoid treatment can therefore conceivably mediate the detrimental effect of hyperglycemia on COVID-19 severity. This mediating effect should be taken when interpreting the results. Further evidence from randomized controlled trials or large-scale prospective studies are urgently needed to definitely establish a cause-effect relationship between new-onset hyperglycemia and COVID-19 severity.

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Declaration of Competing Interest

None.

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