

# Use of corticosteroids in SARS-CoV-2 infection: foe, or can they become a friend?

**To the editor** We read with interest the recently published systematic review and meta-analysis authored by Pei et al,<sup>1</sup> which provides top level evidence regarding the impact of drug therapy on odds for death in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Notably, Pei et al<sup>1</sup> demonstrated that the use of glucocorticoids is associated with an increase in the odds for death in the context of the disease, bringing into question the use of this drug class in SARS-CoV-2 infection.

In another recent systematic review and meta-analysis, it was shown that corticosteroid use in patients infected with coronaviruses (severe acute respiratory syndrome coronavirus [SARS], Middle East respiratory syndrome coronavirus [MERS], or SARS-CoV-2) did not increase the odds for death, while, in a time-adjusted analysis according to risk factors such as age or comorbidities, corticosteroids were associated with a decrease in the risk of death.<sup>2</sup>

Of note, in the randomized, open-label RECOVERY study enrolling hospitalized patients with SARS-CoV-2 infection, dexamethasone was shown to decrease the rate of death by 36% in patients receiving mechanical ventilation and by 18% in those receiving oxygen supplementation without mechanical ventilation, compared with placebo.<sup>3</sup> In a real world study conducted in France enrolling hospitalized patients with SARS-CoV-2 infection, it was demonstrated that initiation of corticosteroids in the treatment protocol of SARS-CoV-2 pneumonia was associated with a 53% decrease in the risk of death and a 63% decrease in the risk of intensive care unit admission or death before intensive care unit admission.<sup>4</sup>

Thus, despite the fact that in other cases of viral pneumonia such as influenza pneumonia corticosteroid use is not recommended and might increase mortality indeed,<sup>5</sup> it seems that we have a long journey to go in the COVID-19 pandemic era. More data are required in order to elucidate the role of corticosteroid treatment in the context of SARS-CoV-2 infection.

## ARTICLE INFORMATION

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- 3 RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in Hospitalized Patients with Covid-19 - Preliminary Report. *N Engl J Med.* 2020 Jul 17. [Epub ahead of print].
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- 5 Ni YN, Chen G, Sun J, Liang BM, Liang ZA. The effect of corticosteroids on mortality of patients with influenza pneumonia: a systematic review and meta-analysis. *Crit Care.* 2019; 23: 99. [↗](#)

**Authors' reply** In our meta-analysis,<sup>1</sup> the pooled estimate from retrospective studies suggested that the use of glucocorticoids was associated with an increased risk of death. However, this result should be interpreted with caution because the inherent limitations of retrospective studies make it difficult to infer a causal relationship between the use of glucocorticoids and mortality in patients with coronavirus disease 2019 (COVID-19).

Our other study,<sup>2</sup> which has been accepted by *The Journal of Clinical Investigation* recently, also suggested that glucocorticoids use was associated with increased rate of 28-day all-cause mortality and delayed SARS-CoV-2 RNA clearance in patients with severe COVID-19 and acute respiratory distress syndrome. This finding was consistent even after we used propensity score

matching analyses, which allowed us to compare the outcomes between the 2 cohorts (the glucocorticoid treatment group vs the nonglucocorticoid treatment group) with similar distributions for baseline variables.

However, the RECOVERY trial<sup>3</sup> revealed that the 28-day mortality was significantly lower in the dexamethasone group than in the usual care group. The underlying mechanisms which led to the inconsistent findings between our studies and the RECOVERY trial are largely unknown. But a number of factors (including participants, dosage, and regimen of glucocorticoids, timing of initiation, and duration of administration) which may affect the response to glucocorticoid therapy should be taken into account. For example, in the RECOVERY trial, dexamethasone use did not show benefit (and possibly harmful effects) in patients who did not receive oxygen therapy. In addition, the overwhelming majority of glucocorticoid regimens used in China involved methylprednisolone rather than dexamethasone. Although the RECOVERY trial suggested that glucocorticoids may be a promising drug for patients with COVID-19, further research is still needed to fill current evidence gaps, including answers to the following questions: who will benefit from glucocorticoids therapy, which glucocorticoid regimen and dosage is preferred, when should glucocorticoids therapy be initiated and stopped.

## ARTICLE INFORMATION

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