



## Early View

### Correspondence

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# **The association between immunosuppressant and the outcome of COVID-19**

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*To the Editor,*

We read with great interest the study investigating the association between immunosuppressant and the outcome of patients with SARS-CoV-2 infection [1].

They found that the prior use of immunosuppressant would be associated with a significantly increased risk of death (adjusted relative risk [RR], 1.56; 95% CI, 1.10-2.22) which was mainly driven by exposure to systemic glucocorticoids (aRR, 2.38; 95% CI 1.72-3.30). Overall, it is a well-designed study; however, we have three concerns about the findings of this study.

First, the study group with immunosuppressant exposure had more underlying comorbidity than those without exposure. The results could be due to bias by indication where patients with more severe disease receive immunosuppressive drugs.

Compared with the unexposed group, the exposed group were older, and had more neurologic and musculoskeletal disease, and skin disease (all standard mean difference > 0.1)(table 1). Therefore, the baseline characteristics of the study and the control group were not perfectly balanced. In addition, because the patients may have multiple comorbidities and more comorbidities would be associated with the worse outcome of patients with COVID-19, we wondered whether the number of comorbidities using Charlson comorbidity index were matched or not between these two groups. Finally, diabetes mellitus (DM) is a common underlying disease of

hospital patients with COVID-19 and can be associated with severe COVID-19, increased ARDS rate, mortality, and need for mechanical ventilation [2]. Although the authors described the use of diabetes drug, they did not show the prevalence of DM among the study subjects. Because all the above could affect the outcome of COVID-19, further analysis to clarify these issues is warranted.

Second, although chronic obstructive pulmonary disease (COPD) and asthma, which were supposed to be classified as pulmonary disease in this study, the impacts of COPD and asthma on COVID-19 were different [3, 4]. For patients with asthma, a meta-analysis of 51 studies showed the risk ratios for COVID-19 associated hospitalization, intensive care unit admission, ventilator use and mortality were 1.18 (95% CI 0.98-1.42), 1.21 (95% CI 0.97-1.51,  $p=0.09$ ), 1.06 (95% CI 0.82-1.36,  $p=0.65$ ) and 0.94 (95% CI 0.76-1.17,  $p=0.58$ ) and suggest that asthma was not associated with adverse outcome of COVID-19 [4]. In contrast, another meta-analysis of 59 studies demonstrated that COPD could be associated with increased odds of hospitalization (odds ratio [OR], 4.23; 95% CI, 3.65-4.90), ICU admission (OR, 1.35; 95% CI, 1.02-1.78), and mortality (OR, 2.47; 95% CI, 2.18-2.79) [3]. Therefore, we think using a single term – pulmonary disease cannot fit all.

Third, many anti-COVID-19 medications, such as remdesivir, JAK inhibitor, corticosteroid and interleukin-6 blockade could help improve the clinical outcomes of

patients with COVID-19 [5-8], however, none of these important agents were mentioned in the present study.

Although we raised some concerns regarding the study reported by Ward et al.[1], this study still provided useful information.

Conflict of interest: C-K. Hsu has nothing to disclose. C-C. Lai has nothing to disclose.

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