The association between immunosuppressants and outcomes of COVID-19

Received: 19 April 2022
Accepted: 18 June 2022

To the Editor:

We read with great interest the study investigating the association between immunosuppressant and the outcome of patients with severe acute respiratory syndrome coronavirus 2 (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 (aRR) 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 neurological 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 coronavirus disease 2019 (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 hospitalised patients with COVID-19 and can be associated with severe COVID-19, increased acute respiratory distress syndrome rate, mortality, and need for mechanical ventilation [2]. Although the authors described the use of diabetes drugs, 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 COPD and asthma were classified together 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 hospitalisation, 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 outcomes in COVID-19 [4]. In contrast, another meta-analysis of 59 studies demonstrated that COPD could be associated with increased odds of hospitalisation (OR 4.23, 95% CI 3.65–4.90), intensive care unit 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 the single term “pulmonary disease” cannot fit all.

Third, many 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.

Shareable abstract (@ERSpublications)
Immunosuppressants and underlying diseases could affect the outcome of patients of COVID-19, and this requires further analysis https://bit.ly/3A6rSeJ

Cite this article as: Hsu C-K, Lai C-C. The association between immunosuppressants and outcomes of COVID-19. *Eur Respir J* 2022; 60: 2200816 [DOI: 10.1183/13993003.00816-2022].

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

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