Comments on COVID-19 Vaccination and Exacerbation of Idiopathic Pulmonary Fibrosis

To the Editor:

We read with great interest the research article by Sgalla and colleagues (1) regarding the coronavirus disease (COVID-19) vaccine and acute exacerbation of idiopathic pulmonary fibrosis (AE-IPF). We appreciate the authors' valuable contribution to understanding that COVID-19 vaccination may act as a potential trigger of AE-IPF. However, there are still concerns worth further discussion.

First, this study involved a total of 26 patients diagnosed with IPF. However, the small number of cases in this study may lead to a series of biases and not be able to reveal the influence of the COVID-19 vaccine on patients with IPF. Hence, more patients are suggested to be involved to have a solid research result.

Second, this study categorized the patients into two groups: "triggered" and "idiopathic" AE-IPF. However, according to the protocol, the two groups of cases were not well matched. For example, patients with idiopathic AE-IPF had a higher CRP (C-reactive protein). The higher use of long-term oxygen therapy rate may be associated with an increased mortality rate. Therefore, the two groups of cases should be matched to reduce bias.

Third, previous studies showed that patients with interstitial lung disease had a higher prevalence of other autoimmune diseases, such as rheumatoid arthritis and progressive systemic sclerosis (2–4). However, they also had similar phenotypes of usual interstitial pneumonia. Glucocorticoids are best suited for the initial management or treatment of acute exacerbations while transitioning to other therapies with more favorable long-term safety profiles. It is possible that vaccine-associated acute exacerbation is characterized by better steroid responsiveness, and some patients might have both IPF and subclinical autoimmune diseases. Before we generalize the results of this trial to all patients with IPF, we recommend a *post hoc* analysis of baseline immune profiles, such as RF (rheumatoid factor), ACPA (anti-cyclic citrullinated peptide antibodies), ANA (antinuclear antibody), and ENA (extractable nuclear antigen antibody).

Above all, this study contributes to understanding that COVID-19 vaccination may act as a potential trigger of AE-IPF. Further studies are suggested to involve more patients in the study, match the study groups, and conduct a *post hoc* analysis. ■

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