

# Comment on Shao et al.'s "risk factors associated with COVID-19 pneumonia in Chinese patients with pre-existing interstitial lung disease during the SARS-CoV-2 pandemic"

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## **Comment on Shao et al.'s "risk factors associated with COVID-19 pneumonia in Chinese patients with pre-existing interstitial lung disease during the SARS-CoV-2 pandemic"**

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Dear Editor,

We read the article with great interest by Shao et al, where a retrospective study analyzed the risk factors for pneumonia related to the 2019 coronavirus disease (COVID-19) in patients with various types of interstitial lung disease (ILD) caused by SARS-CoV-2 infection. According to Cox's multivariate analysis, only male

gender and the use of corticosteroids emerged as risk factors for developing new coronavirus pneumonia following illness. On the other hand, receiving two to three doses of vaccination proved protective for individuals with preexisting ILD who contracted COVID-19 pneumonia.[1] As a result, it is recommended that patients with preexisting ILD, especially those who are male and using corticosteroids, receive more than two doses of the vaccine for enhanced protection. Since 2019, WHO has reported 770 million confirmed COVID-19 cases and 6.9 million deaths globally.[2] Studies have linked interstitial lung disease to worse COVID-19 outcomes, showing a four-fold mortality increase.[3] Interstitial lung disease includes inflammatory and fibrotic conditions, with incidence rates of 7 to 1,650 per 100,000.[4, 5] In contrast, COVID-19 can also trigger interstitial lung disease.[6] As COVID-19 spreads, global lung disease rates will increase. Identifying risk factors for interstitial lung disease after a COVID-19 diagnosis is crucial for early prevention, resource allocation, and effective management. However, some details in the article still need to be further clarified.

First, this paper analyzed several variables in developing pneumonia during COVID-19 infection, including age, sex, vaccination history, common immunosuppressants, antifibrotic agents, and corticosteroids. However, it should be noted that certain risk factors, such as smoking, diabetes mellitus, autoimmune diseases, and recurrent COVID-19 infections, still exhibit a high association with pneumonia and were not included in the analysis.[7-9] Therefore, we recommend that the authors consider incorporating these factors into future similar studies. The paper analyzed corticosteroid use as a potential risk factor but without mentioning the timing of administration. The Centers for Disease Control and Prevention (CDC) recommends steroids for COVID-19 cases beyond a sure severity threshold. Failing to differentiate when they were given may overestimate the proportion of pneumonia cases using steroids, affecting p-values. Some ILD patients use multiple immunosuppressants, impacting immune function and COVID-19 pneumonia risk. While the article lists common medications, it doesn't analyze the number of patients receiving combined therapy. Therefore, we recommend that future studies assess the risk associated with concurrently using immunosuppressants to understand the implications of combination therapy better.

Second, this paper reveals an intriguing shift, as sarcoidosis appears to become a protective factor against pneumonia following a COVID-19 diagnosis. It could be a groundbreaking revelation since the articles consistently state that sarcoidosis is an excessively high-risk factor for severe COVID-19 pneumonia.[10] No literature has delved into this phenomenon, its mechanisms, or potential implications. Given the substantial representation of sarcoidosis patients in this study, we recommended that authors separately analyze its subgroup, examining their disease site, activity, severity, and medication use differences. Furthermore, future research should focus on investigating the interaction mechanisms and conducting comprehensive comparative studies to unlock the full potential of this discovery.

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