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that in the healthy control subjects and not related to ongoing treatments.8 Therefore, we suggested that the patients with autoimmune disease should be analyzed separately.

Finally, a total of 3 participants reported grade 3 alanine aminotransferase elevation and 1 of them was hospitalized. We noticed that these 3 patients had elevated alanine aminotransferase level before vaccination. So, whether patients with abnormal alanine aminotransferase should postpone the COVID-19 vaccination needs further investigation.

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Conflicts of interest

The authors disclose no conflicts.



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Reply. We would like to thank Cao et al¹ for their constructive comments on our recent publication.2 We would like to provide some

clarifications and explanations on their comments.

First, Cao et al¹ highlight the time interval from the second dose of SARS-CoV-2 vaccine to serum collection may affect antibody titers. We agree that it is important to accurately assess the time interval between completed vaccination and serum collection, because antibody titers decline over time.³ We limited this time interval within 14-90 days when conducting the multicenter study, but the data regarding the time interval were partially missing in our study because some patients were unable to determine their exact vaccination date. However, among

patients who have these data available, we further analyzed the time interval from the second dose of vaccination to serum collection. The overall time interval from the second dose to serum collection was 29.0 (range, 19.0-39.0) days, and there was no significant difference between subgroups (P = .78). We will continue our followup of patients and hope to provide more valuable information for this question in the future. At the same time, we are initiating another study that will examine the effect of the third homologous booster vaccination using inactivated vaccines (ClinicalTrials.gov ID: NCT05204602) to answer the questions regarding dynamic changes of antibodies after vaccination in patients with chronic liver disease (CLD) and the efficacy and safety of booster vaccination in this special population.

Second, our study showed that the absolute titer of neutralizing antibodies in the decompensated cirrhosis group was slightly higher than that in the healthy control group, but there was no statistical difference. However, we were limited by relatively small sample size of the decompensated cirrhosis subgroup. More importantly, the proportion of neutralizing antibody positive (defined as absolute titer value >10 AU/mL) in patients with decompensated cirrhosis was significantly lower than that in healthy control subjects (76.7% vs 90.3%; P < .05).

Third, our study enrolled a subset of patients with CLD with autoimmune liver disease but excluded patients receiving systemic immunosuppressive therapy, to reduce the effect of immunosuppressive drugs on final antibody outcomes.^{3,4} When comparing immunogenic outcomes, we adjusted for different etiologies. In the future, we will continue to expand the large-scale autoimmune liver disease cohort, especially patients with autoimmune liver disease under immunosuppressive treatment for further analysis.

Finally, our study concluded that inactivated vaccines were safe for patients with CLD. In our study, only 3 patients had grade 3 abnormal liver function after vaccination, and they had different degrees of elevated transaminases before vaccination, and 1 patient with later hospitalization had a history of discontinuing anti-hepatitis B virus agents before SARS-CoV-2 vaccination. The long-term follow-up of these patients showed that they had no persistent deterioration of liver function. Because of the limited number of patients with abnormal liver function postvaccination in our study, we think the topic of whether patients with abnormal transaminases need to postpone SARS-CoV-2 vaccination should be more cautiously evaluated using larger real-world cohorts.

Importantly, recent studies have confirmed that preexisting liver diseases are associated with disease progression, intensive care, and high mortality in patients with COVID-19.⁵⁻⁷ Our studies seem to be the first to evaluate the safety and immunogenicity of inactivated whole-virion SARS-CoV-2 vaccines in patients with CLD.^{2,8} Nonetheless, because of that the population of patients with CLD mainly had chronic hepatitis B in our study, further large-scale studies are warranted to validate our findings in populations with other causes of liver disease.

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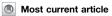
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