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#### CORRESPONDENCE



# Letter to the editor: Complications following SARS-CoV-2 infection in patients with chronic liver disease

#### To the editor,

Recently, Hartl et al. reported a study on liver-related complications after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.<sup>[1]</sup> This single-center retrospective study includes 65 patients with NAFLD/NASH-predominant chronic liver disease (CLD). They described the pattern of progression of cholestatic liver injury following SARS-CoV-2 infection. Hartl et al. noted that the patients were more likely to develop secondary sclerosing cholangitis (SSC) than control patients infected with non-COVID-19 pneumonia. This study provided essential data for our understanding of clinical outcomes following SARS-CoV-2 infection in patients with CLD. In addition to the results already shown in the study, we believe that some issues deserve further discussion.

First, this study selected patients hospitalized for COVID-19 at the Vienna General Hospital from March 2020 to July 2021. The significant variants have changed many times, such as alpha, beta, gamma, delta, and omicron. Different variants could exhibit different replicative capacities and pathogenicity.<sup>[2]</sup> We hope the authors provide the main types of variants infected by the enrolled patients, which would help avoid overinterpretation of the study results.

Second, this study used a case-control study design to assess the potential impact of SARS-CoV-2 infection on patients with CLD. However, the authors did not provide the screening process and matching method of patients in the control group. In addition, the patients in the control group were all from the intensive care unit ward, and their intubation rate and mortality were significantly higher than those in the COVID-19 group. If the population characteristics of the control group and the study group were different, the case-control design of the study was not reasonable. Furthermore, the analysis did not include important factors that could lead to SSC, such as whether the patients had a history of biliary tract surgery, cholelithiasis, drug-resistant bacterial infection, and immune dysfunction.<sup>[3]</sup> We believe that the authors should try to perform a logistic regression analysis with the occurrence of SSC as the outcome in order to further quantify the impact of SARS-CoV-2 infection on patients with CLD.

Finally, we suggest that the authors use a directed acyclic graph to select covariates to exclude mediators'

influence on the regression model.<sup>[4]</sup> For example, the authors included both bilirubin and the model of endstage liver disease (MELD) score in a univariate Cox regression analysis. However, the MELD score already included the assessment of bilirubin, which may affect the accuracy of the regression model to some extent.

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# CONFLICT OF INTEREST

Nothing to report.

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#### REFERENCES

- Hartl L, Haslinger K, Angerer M, Semmler G, Schneeweiss-Gleixner M, Jachs M, et al. Progressive cholestasis and associated sclerosing cholangitis are frequent complications of COVID-19 in chronic liver disease patients. Hepatology. 2022 May 21. https://doi.org/10.1002/hep.32582. [Epub ahead of print]
- Pérez-Then E, Lucas C, Monteiro VS, Miric M, Brache V, Cochon L, et al. Neutralizing antibodies against the SARS-CoV-2 Delta and Omicron variants following heterologous CoronaVac plus BNT162b2 booster vaccination. Nat Med. 2022;28:481–5.
- Ruemmele P, Hofstaedter F, Gelbmann CM. Secondary sclerosing cholangitis. Nat Rev Gastroenterol Hepatol. 2009;6:287–95.
- Shrier I, Platt RW. Reducing bias through directed acyclic graphs. BMC Med Res Methodol. 2008;8:70.

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