Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

different. This difference may account for difference in prevalence of decompensations seen in both the groups.

In conclusion, we would like to emphasize the possibility of multiple hits that may have a role in predisposition of patients with NAFLD to decompensation at lower HVPG. The simultaneous occurrence of pronounced gut-barrier dysfunction, increased systemic inflammatory flux, and a harder liver (as reflected by increased LSM) may act as catalysts triggering the sequence of events that culminate in development of clinical decompensation even at lower HVPG thresholds in patients with NAFLD.

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Conflicts of interest
The authors disclose no conflicts.

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Reply. We would like to thank Dr Mohta and colleagues for their interest in our study and for their comments. As we showed in our work, our cohort of patients with advanced nonalcoholic fatty liver disease (NAFLD) developed clinical decompensation at lower hepatic venous pressure gradient (HVPG) values as compared with a cohort of patients with hepatitis C virus–related chronic liver disease. We hypothesized that this may be a consequence of an underestimation of the actual portal pressure as assessed by the HVPG measurement,[1] although we agree with the authors that the causes underlying this observation may be multifactorial. However, we politely disagree with the comment about the rarity of ascites development in patients with presinusoidal portal hypertension.[2]

As stated by the authors, there is growing evidence that indicates the pathogenic role of the microbiome and derangements in the gut-liver axis in the development of NAFLD. Unfortunately, our study was not designed to look at this link and future studies are needed to evaluate the impact on HVPG values of bacterial translocation and systemic inflammation in patients with NAFLD.

Liver stiffness measurement has been extensively studied and compared with HVPG as a noninvasive tool to predict clinical decompensation in patients with chronic liver disease even in the NAFLD population.[3,4] Data about liver stiffness were not available in our cohort, and therefore we cannot draw any conclusion in this respect. Whether liver elastography correlates better than HVPG with the presence of decompensation, specifically in those patients with an HVPG <10 mm Hg, needs further investigation.

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No Association Between Nonalcoholic Fatty Liver Disease and Severe COVID-19? Something We Might Ignore

Dear Editor:

I read with interest the article by Li et al,[1] who performed large-scale 2-sample Mendelian randomization analyses to explore the relationship between nonalcoholic fatty liver disease (NAFLD) and severe COVID-19. They concluded that there is no evidence supporting

that NAFLD is a causal risk factor for severe COVID-19. I have the following queries about their study.

Supplementary Table 5 showed 4.31% of patients with NAFLD were diagnosed as severe COVID-19, higher than those diagnosed as nonsevere COVID-19 (1.45%). Besides, the authors performed univariate regression analysis to assess the impact of NAFLD on severe COVID-19 in Figure 2. The odds ratio was 3.06 ($P = 1.07 \times 10^{-6}$). The association was significant. After adjusting for the remaining risk factors, the odds ratio was 1.61 ($P = .08$). P value was close to 0.05 but not significant. Thus, the author concluded that NAFLD is not an independent risk factor for severe COVID-19. However, these results seem to suggest a link between NAFLD and COVID-19. I suggest that the author should perform multiple models to prove the robustness of this result in the multivariate regression analysis.

Some of the upper 95% confidence intervals of odds ratio were wrong in Supplementary Table 9. The data lack decimal points, which may lead to misinterpretation. Please check again.

To further test the hypothesis that other NAFLD-associated comorbid factors may causally confound the associations, I suggest that the authors perform multivariable Mendelian randomization instead of two-sample Mendelian randomization analyses in Figure 3. It could reduce bias as far as possible after adjusting for comorbid factors in multivariable Mendelian randomization.

A lot of previous studies have shown that admission C-reactive protein is associated with disease severity in patients with COVID-19.[2-5] However, it seems that no association was found between C-reactive protein and severe COVID-19 in Figure 3. It would be better if the authors explain.

Given the large impact of NAFLD and COVID-19 on human health, further studies are required to assess whether NAFLD is a risk factor for severe COVID-19 disease and requires active intervention.

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Conflicts of interest
The authors disclose no conflicts.

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Reply. We thank Gao and Xu for their interest in our study.[1] We would like to address each of their comments.

Gao and Xu first propose performing multiple models to prove the robustness of the result in our multivariate regression analysis. We agree that this is an insightful comment for our study. To demonstrate the robustness of our conclusion, we performed the leave-one-out analysis. The association between nonalcoholic fatty liver disease (NAFLD) and severe coronavirus disease 2019 (COVID-19) persisted to be mostly insignificant ($P > .05$). However, the models without body mass index (BMI) or cirrhosis were both significant ($P < .05$). The conclusion drawn from this sensitivity analysis was consistent with that in our article.

We believe that the missing decimal points in Supplementary Table 9 are typos induced during the press production procedure. We will work closely with the production team and editors to correct these errors.

In addition, Gao and Xu recommend multivariable Mendelian randomization (MVMR) analysis. The problem of MVMR is its limited statistical power.[2] Nevertheless, we performed MVMR to assess the causal effect of NAFLD on severe COVID-19 while controlling for BMI and C-reactive protein (CRP). Similar to 2-sample Mendelian randomization, the result showed no evidence of a causal effect of NAFLD (odds ratio, 1.02; 95% confidence interval, 0.93–1.11; $P = .68$). In fact, the F statistics for BMI, CRP, and NAFLD decreased from 293.47, 580.61, and 16572.45 in the single-variate model to 20.71, 89.47, and 9.49 in the multiple-variate model, respectively. Therefore, we disagree that the current study would benefit from an MVMR analysis.

Finally, elevated CRP level could be a result of severe COVID-19, rather than a cause. The provided references observed the association, not the causality. Our article aimed to discover causal factors, rather than sequelae. Of course, it is also possible that our finding is only limited to the sample sets we studied.

Again, we appreciate the authors for pointing out the problems and divergences in our article and giving us this opportunity to make clarifications.

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