
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.

example, previous studies have shown that obesity and diabetes were associated with chronic liver disease.[5] Tjur's $R^2$ varies between 0 and 1, with 1 indicating perfect predictive power.[6] In this study, Tjur's $R^2$ of the multivariate model for mechanical ventilation after COVID-19 was 0.067, and Tjur's $R^2$ of the multivariate model for day-30 mortality after COVID-19 was 0.137. The explanatory power of these 2 models is weak. Therefore, collinearity analyses should be performed to improve the goodness of fit of the 2 models for mechanical ventilation and for day-30 mortality. Then, the odds ratio based on non-collinearity variables in the new models can be estimated.

In summary, we agree with the authors and appreciate this important study, which indicated that chronic liver disease increased the risk of COVID-19-related death. However, baseline differences must be excluded to obtain a more reliable conclusion.

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## Conflict of interest
The authors declare no conflict of interest pertaining to this work.

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## Authors' contributions
All authors were involved in the writing of this commentary and reviewed it prior to submission.

## Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2021.07.011.

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# Reply to: "Association of chronic liver disease with the prognosis of COVID-19 patients"

**Prognosis of COVID-19 patients with chronic liver disease in France in 2020**

*To the Editor*:

We thank Dr. Zhao and colleagues [1] for their interest in our study evaluating the outcome of inpatients with chronic liver disease (CLD) and COVID-19 in a nationwide study conducted over 2020 in France. However, we believe that they might have been caught up in some statistical details and missed the general health policy implications of our study. Compared with other inpatients with COVID-19, we found that patients with CLD were at higher risk of mechanical ventilation (adjusted odds ratio [aOR] 1.54; 95% CI 1.44–1.64; $p$ <0.001) and 30-day mortality (aOR 1.79; 95% CI 1.71–1.87; $p$ <0.001). The term 'chronic liver disease' comprises a spectrum of conditions and liver disease stages, and this heterogeneity may affect COVID-19 outcomes. In particular, we found that inpatients with a liver-related complication recorded before COVID-19 had less chance of receiving mechanical ventilation (aOR 0.69; 95% CI 0.57–0.84; $p$ <0.001), although they were at higher risk of COVID-19-related death (aOR 2.98; 95% CI 2.69–3.30; $p$ <0.001). These findings suggest that a limitation of therapeutic efforts in patients with CLD and liver-related complications contributed to the COVID-19 death toll in France, in 2020. To our knowledge, the role of the limitation of therapeutic efforts on COVID-19 prognosis in selected groups of patients, independently of age, was not uncovered in previous prognostic studies, including in patients with CLD.[2,3] Regarding statistical analyses, Dr. Zhao and colleagues claim that a propensity-matched analysis should have been performed rather

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than conventional multivariate regression analysis. Propensity-matched analysis is generally preferred to a multivariate regression analysis when sample size is small, otherwise results are basically similar.[4] In our nationwide study, sample size was obviously large with 259,110 inpatients with COVID-19, including 15,476 (6.0%) patients with CLD. We relied conservatively on a propensity-matched analysis to study COVID-19 outcomes in 1,182 patients recorded with primary liver cancer, and the reduced access to mechanical ventilation was clear. By contrast, the correspondents cited 2 US studies relying on a propensity-matched analysis as sample sizes were much smaller: 363 inpatients with COVID-19 including 69 (19.0%) with CLD[5]; and 10,859 inpatients with COVID-19 including 192 (1.8%) with CLD.[6] More importantly, the correspondents may have noticed that the proportion of CLD inpatients with COVID-19 was quite different between the 2 US studies, suggesting selection bias. By contrast, our nationwide study was conducted in France, a country with universal access to hospitals, with records from all public and private hospitals. No selection procedure was applied among covariates in the multivariate regression analysis given the large sample size. In addition, issues of multicollinearity, a concern for our correspondents, were unlikely given the large sample size: the median variance inflation factor was 1.15 (range 1.00-1.44) and 1.18 (range 1.00-1.46) in the regression models regarding mechanical ventilation and 30-day mortality, respectively. As a rule of thumb, collinearity becomes an issue for values of the variance inflation factor above 5.[7] We agree with the correspondents that the predictive power of the 2 regression models was low, but this is expected in epidemiology and even more so with large sample sizes, although coefficients of determination are generally not reported, including in the studies cited by Dr. Zhao and colleagues. Future studies on the risks of severe COVID-19 should include measures of the therapeutic effort to adapt health policies to future pandemics. Similar studies in other geographical areas would be very interesting.

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## Authors' contributions
VM, MS: conception of the study, analysis and interpretation of the data, draft of the manuscript. All other members of the Demosthenes group facilitated the study or took care of the reported patients.

## Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2021.09.022.

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# Plasma and ascites pharmacokinetics of meropenem in patients with decompensated cirrhosis and spontaneous bacterial peritonitis☆

*To the Editor:*

With great interest, we read the study of Wong *et al.* who investigated risk factors for an acute-on-chronic liver failure (ACLF) in patients with decompensated cirrhosis and bacterial infections. Spontaneous bacterial peritonitis (SBP) was the most frequent site of infection and an independent risk factor for ACLF development. Moreover, ACLF was more common in patients

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