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Correspondence

Liver fibrosis and adverse outcomes in COVID-19



Dear Editor,

Recently, an interesting study entitled “**Liver fibrosis in patients with metabolic associated fatty liver disease is a risk factor for adverse outcomes in COVID-19**” was published in *Digestive and Liver Disease* [1]. In this retrospective cohort study, the authors explored the relationship between liver fibrosis and poor prognosis in patients with coronavirus disease (COVID-19). After controlling for potential confounding factors, the authors found that the presence of liver fibrosis was associated with higher mechanical ventilation, acute kidney injury (AKI), and mortality. It is undeniable that the author's great efforts provide new evidence for predicting the poor prognosis of COVID-19 patients. However, some potential concerns need to be carefully explained.

First of all, although described in statistical analysis that “**The normality of the data was evaluated using Shapiro-Wilk test**”, there were still some continuous variables that do not conform to the normal distribution in this study, which were expressed by means and standard deviation (SD). For example, the mean value of D-dimer in the No fibrosis group was 1606, while the SD value was 7055 (Table 2, $P=0.732$). Statistically, if the SD value is significantly greater than the mean value, suggesting that continuous variables might not conform to normal distribution. In that case, it is inappropriate to use mean and SD to describe that continuous variable, neither use *t*-test to compare the differences between groups. Similarly, according to the information provided in Table 2, it could be inferred that troponins and creatine phosphokinase (CPK) levels do not conform to the normal distribution with a high probability, yet inappropriate description methods and statistical analysis might be used.

Second, according to the description in Table 2, there were significant differences in some baseline characteristics between No fibrosis and Severe fibrosis patients. Additionally, those parameters with differences between groups in Table 2 have been confirmed by previous studies to be related to the prognosis of COVID-19 patients. For instance, there were significant differences in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) between patients without fibrosis and patients with severe fibrosis in Table 2 (45.8 ± 40.3 versus 67.7 ± 38.2 , 48.2 ± 38.3 versus 83.0 ± 30.3 , $P=0.005$ and $P=0.000$, respectively), and previous study displayed that high AST/ALT ratio is an important factor for the poor prognosis of COVID patients [2,3], suggesting that AST/ALT ratio could be used as a novel marker for predicting the poor prognosis of COVID-19 patients. However, although there were significant differences in AST and ALT levels between the two groups, the authors did not adjust these two variables as confounding factors

in subsequent logistic regression analysis, nor did they describe the exact reasons why AST and ALT were not considered as confounding factors.

Third, it should be emphasized that the severity of COVID-19 disease is also associated with poor prognosis. Currently, according to the severity of COVID-19 disease, it could be divided into the following four types: mild, moderate, severe, and critical [4,5]. Undoubtedly, higher COVID-19 disease severity is associated with poorer prognosis. It would be an interesting result to conduct subgroup analysis according to the severity of COVID-19 disease and then explore the relationship between liver fibrosis and the prognosis of COVID-19 patients.

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Declaration of Competing Interest

None.

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References

- [1] Campos-Murguía A, Román-Calleja BM, Toledo-Coronado IV, et al. Liver fibrosis in patients with metabolic associated fatty liver disease is a risk factor for adverse outcomes in COVID-19. *Dig Liver Dis* 2021;53(5):525–33.
- [2] Qin C, Wei Y, Lyu X, et al. High aspartate aminotransferase to alanine aminotransferase ratio on admission as risk factor for poor prognosis in COVID-19 patients. *Sci Rep* 2020;10(1):1–10.
- [3] Fu L, Fei J, Xiang HX, et al. Influence factors of death risk among COVID-19 patients in Wuhan, China: a hospital-based case-cohort study. *MedRxiv* 2020.
- [4] Zhang J, Wang X, Jia X, et al. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. *Clin Microbiol Infect* 2020;26(6):767–72.
- [5] Targher G, Mantovani A, Wang XB, et al. Patients with diabetes are at higher risk for severe illness from COVID-19. *Diabetes Metab*. 2020;46(4):335.

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