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Does MAFLD really increase the severity of COVID-19?

Dear Editor,

We read with great interest the meta-analysis by Pan et al [1] entitled "Metabolic associated fatty liver disease increases the severity of COVID-19" published in Digestive and Liver Disease. The article provides new information on the risk of severe COVID-19. There is evidence suggesting that comorbidities such as hypertension, diabetes mellitus, and cardiovascular diseases are associated with COVID-19 severity (https://covid19.who.int/). In their article, the authors found that individuals with metabolic associated fatty liver disease (MAFLD) also have a high risk to develop a severe condition when infected by COVID-19, [odds ratio (OR): 2.93; 95% confidence interval (95%CI): 1.87, 4.60].

We found that the study has several limitations that should be clarified. First, the article includes several letters to the Editor. At least four [2–5] out of six papers [2–7] are letters to the Editor. Although the Newcastle-Ottawa scale (NOS) was used to assess the quality of the included papers, which had moderate to high quality, the vast majority of meta-analysis studies excluded letters to the Editor. Referring to guideline from Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [8], reviews, commentaries, and letters to the Editor should be excluded. Nevertheless, since they have moderate-high quality based on the NOS criteria, these articles might be tolerable for inclusion in the meta-analysis. Second, two [2,4] out of six papers [2-7] do not provide sufficient data for meta-analysis. The data of MAFLD prevalence in both severe and mild-moderate COVID-19 are insufficient to calculate the correlation and effect estimates. In the study by Zou et al [2] for example, the data are presented as total cases of severe COVID-19 and total cases of MAFLD. The data on how many MAFLD patients developed severe and mild - moderate COVID-19 were not presented. Therefore, the calculation of cumulative effect estimates, and the correlation was impossible to perform, and this article should be excluded. Moreover, in the study by Targher et al [4], the available data are only the number of MAFLD patients with neutrophil-to-lymphocyte ratio (NLR) $\leq$ 2.8 and NLR $>$ 2.8. NLR is not the indicator of COVID-19 severity. The indicators of COVID-19 severity include any of the following criteria: respiratory distress (RR $\geq$ 30/min), oxygen saturation $\leq$ 93% at rest, and arterial partial pressure of oxygen (PaO2) / fraction of inspiration O2 (FiO2) $\leq$ 300 mnHg [9]. Therefore, we consider that this article does not meet the criteria to define severe COVID-19 and should be excluded. We re-analyzed the data after excluding those two papers and found that patients with MAFLD had a 6-fold higher risk of developing severe COVID-19 compared to those without MAFLD,(OR: 6.66; 95%CI: 2.84, 15.64) (Fig 1). Although our analysis is consistent with Pan et al [1], our analysis highlights a higher risk.

We believe that study by Pan et al [1] provides important information on COVID-19 management, particularly in patients with MAFLD. This study suggests that MAFLD patients should be allocated to high monitoring due to the high likelihood of developing severe COVID-19.

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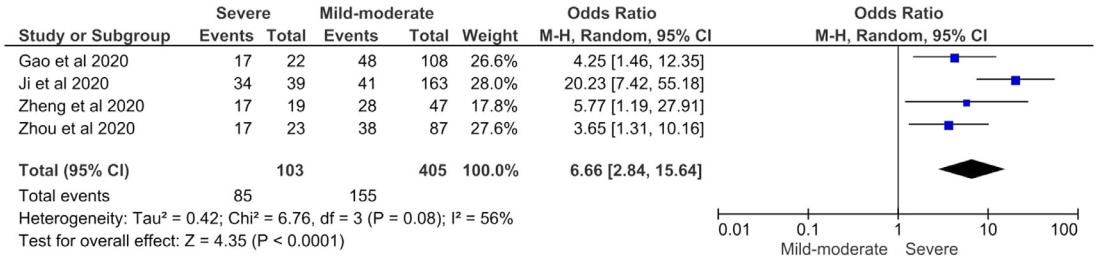

Fig. 1. Forest plot of the association between MAFLD and the risk of severe COVID-19 (OR: 6.66; 95%CI: 2.84, 15.64; *p*: <0.0001; p Heterogeneity: 0.0810; I squared: 56%; p Egger: 0.6440).

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Declaration of Competing Interest

None of the authors has any conflicts to declare.

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