Received: 16 April 2022 | Accepted: 18 April 2022

DOI: 10.1002/hep.32563

CORRESPONDENCE

Letter to the editor: Pitfalls in the outcome differences between NAFLD and MAFLD

To the editor,

We read with interest the paper by Younossi et al.[1] on the differential impact of nonalcoholic fatty liver disease (NAFLD) and metabolic dysfunction associated fatty liver disease (MAFLD) definitions on long-term outcomes of mortality. We commend the authors for undertaking this study. However, we have several concerns with this work, specifically their findings and conclusion that there is no difference in outcomes between the two definitions. Numerous studies and meta-analyses are in concordance that the MAFLD definition has superior utility for identifying patients at high risk of advanced fibrosis, cardiovascular disease, chronic kidney disease, impaired lung function, impaired cognitive function, quality of life, and morality compared to NAFLD.[2–4]

The apparent contradiction in this report is likely due to a number of implicit biases. Firstly, for estimation of total causal effects, it is not only unnecessary but also likely harmful to adjust for a variable on a causal path from exposure to outcome, or to incorporate variables that are used in the MAFLD definition.[5] This has likely produced an overadjustment bias that typically biases toward the null-hypothesis and results in an imprecise relative risk with reduced statistical significance.[5] Overadjustment bias can be easily dealt with: the variables that are overadjusted should be removed from the multivariable analyses. We would be very interested in the results from a multivariable analysis that is unlikely to suffer from overadjustment. Dealing correctly with comorbidities is especially important when assessing the outcome of patients with MAFLD, as metabolic comorbidities are by definition, and in published reports, more prevalent in individuals with MAFLD compared to NAFLD. Notably, the authors did not show a similarly adjusted model for NAFLD.[3,4] In addition, analysis of the nonoverlapping patients between MAFLD only and NAFLD definitions is not presented—this is the group that is distinct between the two terms.

Space restrictions limit our ability to present all our concerns. However, based on the above errors, we have concerns about the validity, meaningfulness, and impact of this study.

CONFLICT OF INTEREST

Nothing to report.

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