Received: 19 April 2023 | Accepted: 19 April 2023

DOI: 10.1097/HEP.0000000000000442

CORRESPONDENCE

Reply: Is there survival bias? The etiologic analysis for the negative association between fatty liver and mortality in the elderly populations

We thank Hu et al[1] for their interest in our study demonstrating that fatty liver disease was not associated with an increased risk of all-cause mortality among community-dwelling elderly population.[2] In their letter, they raised the issue of survival bias being dependent on and potentially different across different etiologies of steatosis in the investigated participants.

First of all, it needs to be stressed that this study was designed to assess the clinical relevance of fatty liver disease among community-dwelling elderly population and whether early detection or screening is warranted. Our data convincingly demonstrate that fatty liver disease, regardless of the definition used (ultrasound-steatosis, NAFLD, or metabolic associated fatty liver disease), was not associated with increased mortality, which therefore strongly indicates that fatty liver disease among the elderly general population is not clinically relevant. Although this may indeed be explained by healthy survivor bias and/or competing mortality risks, this would still implicate that this investigated population comprises healthy survivors and individuals whose survival is not dependent on the presence of fatty liver disease. As a result, this only underscores that policy-makers and health care professionals should not focus on early detection of fatty liver disease among the elderly population but rather on younger populations for whom hepatic steatosis is a risk factor for adverse outcomes.[3]

Although we demonstrated consistent results among several clinically relevant subgroups, we cannot rule out that there might be an etiology of fatty liver disease associated with increased mortality risk among the elderly general population; the most likely example would be alcohol-associated liver disease. In the current cohort, metabolic dysfunction associated with fatty liver disease—unquestionably the dominant etiology—was not associated with increased mortality. Moreover, it is important to note that metabolic associated fatty liver disease and alcohol consumption are 2 independent risk factors for all-cause mortality among the general population.[4] Further studies should focus on whether alcohol-associated liver disease–related steatosis is a determinant of outcomes in the elderly. Furthermore, we endorse further studies including participants from all age groups focussing identifying at which age fatty liver disease ceases to be a risk factor for mortality, which should help guide screening strategies.

In conclusion, fatty liver disease does not impact survival among community-dwelling elderly population and should therefore not be screened for.

AUTHOR CONTRIBUTIONS

Writing of the manuscript: Laurens A. van Kleef, and critical review of the manuscript, approval of final version, and approval of submission: All authors.

FUNDING INFORMATION

Financial support was provided by the Foundation for Liver and Gastrointestinal Research, Rotterdam, the Netherlands. The funding source did not influence either the study design, data collection, analysis, and interpretation of the data or the writing of the report and decision to submit for publication.

CONFLICTS OF INTEREST

Milan J. Sonneveld consults for and received grants from Gilead. He consults for Albireo. He received grants from Fujirebio. Robert J de. Knegt consults for, advises, and received grants from AbbVie. He advises and received grants from Gilead. He is on the speakers' bureau for and received grants from Echosens. He is on the speakers' bureau for Norgine. He received grants from Janssen, Inventiva, and GSK. The remaining author has no conflicts to report.

Laurens A. van Kleef
Milan J. Sonneveld
Robert J. de Knegt

Departments of Gastroenterology and Hepatology, Erasmus MC University Medical Centre, Rotterdam, The Netherlands

Correspondence
Laurens A. van Kleef, Department of Gastroenterology and Hepatology, Erasmus MC University Medical Centre, Room Na-602, Postbus 2040, 3000 CA Rotterdam, The Netherlands.
Email: l.vankleef@erasmusmc.nl

ORCID
Laurens A. van Kleef https://orcid.org0000–0002–2333–1182

REFERENCES

1. Hu Y, Li Z, He W, Wang X, Cheng X. Letter to the Editor: Is there survival bias? The etiologic analysis for the negative association between fatty liver and mortality in the elderly populations. Hepatology. 2023 May 11. doi: 10.1097/HEP.0000000000000441. Epub ahead of print.
2. van Kleef LA, Sonneveld MJ, Kavousi M, Ikram MA, de Man RA, de Knegt RJ. Fatty liver disease is not associated with increased mortality in the elderly—a prospective cohort study. Hepatology. 2023;77:585–93.
3. Dunn W, Xu R, Wingard DL, Rogers C, Angulo P, Younossi ZM, et al. Suspected nonalcoholic fatty liver disease and mortality risk in a population-based cohort study. Am J Gastroenterol. 2008;103:2263–71.
4. van Kleef LA, de Knegt RJ, Brouwer WP. Metabolic dysfunction-associated fatty liver disease and excessive alcohol consumption are both independent risk factors for mortality. Hepatology. 2023;77:942–8.