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LETTER TO THE EDITOR

Letter: Metabolic Dysfunction–Associated Steatotic Liver Disease in Primary Biliary Cholangitis—Friend, Foe or Red Herring?

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Editors,

We read with interest the article by Hernández-Pérez et al. [1] on the coexistence of metabolic dysfunction–associated steatotic liver disease (MASLD) in primary biliary cholangitis (PBC). The recent recognition of MASLD as a distinct clinical entity underscores the importance of understanding its interaction with autoimmune liver diseases [2]. However, several methodological aspects warrant further consideration to ensure a balanced interpretation of the authors' findings. First, participants were diagnosed using histological evidence of PBC, but the manuscript lacked detailed information. Additionally, 17.1% of the cohort was antimitochondrial antibody (AMA) negative, exceeding the 5% reported in the literature [3]. Due to the small sample size and higher AMA-negative cases, the study population may not represent the general PBC population accurately. Second, 36% of the MASLD group had steatohepatitis (MASH), a severe form of MASLD linked to negative outcomes. While MASLD affects 25%–33% of the general population, MASH prevalence is only 3%–5% in patients diagnosed with MASLD [4]. The high MASH occurrence in the PBC + MASLD group complicates attributing worse liver outcomes solely to MASLD. In addition, multivariable analysis identified an independent association between treatment response and MASLD, but not with MASH. However, the limited number of patients with MASH (13 out of 129) may not provide sufficient power to rule out its potential impact on the outcomes. Third, patients with PBC + MASLD were 5.7 years older and had 3.5 years more accumulated follow-up time compared to patients with PBC alone. This asymmetry in the comparison of liver-related outcomes between the two groups limits the ability to definitively conclude that liver transplantation and liver-related mortality are more prevalent in the PBC + MASLD group. Importantly, the study provided a cross-sectional analysis of steatosis, but it did not clarify whether this condition throughout the follow-up period. Given the estimated incidence rate of MASLD at 46.9 cases per 1000 person-years [5], it remains uncertain whether any patients initially diagnosed with PBC alone subsequently developed MASLD during the median follow-up period of 10 years. Considering the small sample size of the cohort, even a limited number of new MASLD cases or the regression of steatosis in the PBC-only group could substantially impact the outcome comparison between the two groups. Interestingly, an analysis of our PBC cohort for MASLD and its effect on ursodeoxycholic acid (UDCA) response according to Paris II criteria yielded contrasting results. Specifically, we found that 83.0% of PBC + MASLD patients and 65.2% of PBC-only patients responded to UDCA ($p = 0.042$), with higher response rates in PBC patients with moderate-to-severe steatosis. This suggests that MASLD may not negatively impact, and could even benefit, UDCA response in PBC, aligning with previous reports that coexisting steatosis might improve treatment response and disease course [6].

In conclusion, while Hernández-Pérez et al.'s study provides valuable insights, the highlighted limitations necessitate cautious interpretation. Further research with larger, well-characterised cohorts and longitudinal assessments of steatosis is needed to understand the complex interplay between MASLD and PBC and its impact on treatment response and disease outcomes.

Author Contributions

Ilkay Ergenc: writing – original draft, conceptualization, resources. **Yusuf Yilmaz:** conceptualization, writing – original draft, writing – review and editing, supervision, investigation, methodology.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

Linked Content

This article is linked to Hernández-Pérez et al papers. To view these articles, visit https://doi.org/10.1111/apt.18134 and https://doi.org/10.1111/apt.18332.

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