Annals of Hepatology 30 (2025) 102121

Contents lists available at ScienceDirect

Annals of Hepatology

journal homepage: www.elsevier.es/annalsofhepatology

Letters to the editor

Refining fibrosis risk stratification in CHB–MASLD: methodological considerations

Dear Editor,

We read with interest the study by Hong *et al.* [1] investigating fibrosis risk in chronic hepatitis B (CHB) patients with metabolic dysfunction-associated steatotic liver disease (MASLD). The large biopsy-confirmed cohort provides valuable insights into dual liver disease burden. However, three methodological aspects warrant clarification to strengthen the conclusions.

First, the CHB control group included patients with steatosis <5% or >5% without cardiometabolic risk factors (CMRFs). This combines distinct populations: those without steatosis and those with steatosis lacking metabolic dysfunction. The authors note that steatosis grade did not correlate with fibrosis ($r = -0.077$, $p = 0.016$), yet subgroup analyses comparing these cohorts are absent. Prior work confirms that isolated steatosis (without CMRFs) may still influence fibrosis progression [2]. Re-analyzing fibrosis prevalence across steatosis subgroups (e.g., 0%, 1–5%, >5% without CMRFs) would clarify whether metabolic dysfunction, not steatosis alone, drives risk.

Second, multivariate analysis of significant fibrosis in CHB+MASLD patients omitted adjustment for steatosis severity (Table 3). While MASLD diagnosis requires ≥5% steatosis, higher grades (e.g., >33%) correlate with accelerated fibrosis in viral hepatitis [3]. The reported odds ratio for CMRF ≥3 (aOR = 3.234) might partially reflect unmeasured steatosis effects. Incorporating steatosis grade into the model would isolate the independent contribution of metabolic dysregulation.

Third, non-invasive tools (e.g., FIB-4) showed suboptimal performance for significant fibrosis (AUC = 0.679). The authors did not explore combining FIB-4 with liver stiffness measurement (LSM), which was strongly associated with fibrosis (aOR = 1.259). Transient elastography-based algorithms (e.g., Agile-3+) improve accuracy in metabolic liver disease [4]. Validating such models in this cohort could enhance clinical applicability.

To address these gaps, we suggest stratifying the CHB group by steatosis severity to quantify metabolic-independent effects, re-running multivariate models including steatosis grade as a covariate, and testing combined LSM/FIB-4 scores for fibrosis prediction.

These steps would refine risk stratification and align with emerging MASLD subphenotyping frameworks [5]. We commend the authors' focus on early intervention and welcome their perspectives on these points.

Conflicts of Interest

None.

Funding

This study was supported by the National Natural Science Foundation of China (82274260).

References

[1] Hong S, Hao Y, Sun L, Li P, Yang J, Zhang F, et al. Prevalence and risk factors of significant fibrosis in chronic hepatitis B patients with concurrent metabolic dysfunction-associated steatotic liver disease. Ann Hepatol 2024;30(2):101589. https://doi.org/10.1016/j.aohep.2024.101589.

[2] Zheng Q, Zou B, Wu Y, Yeo Y, Wu H, Stave CD, et al. Systematic review with meta-analysis: prevalence of hepatic steatosis, fibrosis and associated factors in chronic hepatitis B. Aliment Pharmacol Ther 2021;54(9):1100–9. https://doi.org/10.1111/apt.16595.

[3] Chan KE, Koh TJL, Tang ASP, Quek J, Yong JN, Tay P, et al. Global Prevalence and Clinical Characteristics of Metabolic-associated Fatty Liver Disease: A Meta-Analysis and Systematic Review of 10 739 607 Individuals. J Clin Endocrinol Metab 2022;107(9):2691–700.

[4] Pennisi G, Enea M, Pandolfo A, Celsa C, Antonucci M, Ciccioli C, et al. AGILE 3+ Score for the Diagnosis of Advanced Fibrosis and for Predicting Liver-related Events in NAFLD. Clin Gastroenterol Hepatol 2023;21(5):1293–1302.e5. https://doi.org/10.1016/j.cgh.2022.06.013.

[5] Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Ann Hepatol 2024;29(1):101133. https://doi.org/10.1016/j.aohep.2023.101133.

Chao Wan
Department of Infectious Diseases, The No. 967 Hospital of PLA Joint Logistics Support Force, Dalian, Liaoning, 116041, China

Mingjie Xie
Department of Pharmacy, Dalian University Affiliated Xinhua Hospital, Dalian, Liaoning, 116000, China

Ying Zhu*
Department of Infectious Diseases, The First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning, 116001, China

*Corresponding author.
E-mail address: zhuying20250730@163.com (Y. Zhu).

https://doi.org/10.1016/j.aohep.2025.102121