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Correspondence

Correspondence to editorial on “Risk stratification by noninvasive tests in patients with metabolic dysfunction-associated steatotic liver disease”

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Dear Editor,

We sincerely thank Dr. Goh and colleagues for their thoughtful and constructive editorial,¹ “Risk stratification of metabolic dysfunction-associated steatotic liver disease: The KASL pathway,” which highlights key aspects of our recent publication in *Clinical and Molecular Hepatology*.²

We are truly pleased that the editorial authors recognized the clinical value of our proposed two-step risk stratification strategy using Fibrosis-4 (FIB-4) followed by liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) for patients with metabolic dysfunction-associated steatotic liver disease (MASLD). As underscored, this sequential approach is both practical and effective in identifying at-risk patients while minimizing unnecessary referrals within healthcare systems. These features are particularly critical given the rising global burden of MASLD and the urgent need for more efficient resource allocation in clinical practice.

The editorial thoughtfully captured the robustness of our findings, especially regarding the predictive performance

of non-invasive tests. We fully agree with the editorial authors’ observation that the relatively lower prognostic accuracy of the FAST score, as demonstrated in our cohort, is consistent with previous results from previous studies.^{3,4} This consistency reinforces the rationale behind the KASL-endorsed pathway, which prioritizes LSM over FAST as a second-line evaluation after FIB-4. Despite the emergence of alternative scoring systems such as Agile 3+ and Agile 4+, these models have not consistently demonstrated clear advantages over LSM in predicting clinical outcomes, supporting the continued practical utility of LSM in everyday practice.

We also deeply appreciate the editorial’s discussion regarding age-related considerations in FIB-4 interpretation. As age is incorporated into the FIB-4 calculation, older adults may be inadvertently classified into higher fibrosis risk categories.⁵ In our study, we proactively addressed this by applying an age-adjusted FIB-4 cutoff (>2.0 for those aged ≥65 years), aiming to prevent unnecessary referrals and anxiety. Nonetheless, as recent research suggests, even more refined age-specific thresholds may be needed

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for elderly populations. We believe that additional external validation across diverse populations is essential to optimize risk stratification, and novel composite algorithms may further enhance accuracy in elderly MASLD patients without clinical signs of advanced disease.

Importantly, the editorial raises a critical point regarding longitudinal monitoring. Although our study did not include longitudinal follow-up data, previous research has demonstrated that patients transitioning from low to higher risk categories are at increased risk of liver-related events.⁶ This dynamic risk progression strongly emphasizes that a single-point assessment is insufficient for long-term management of MASLD. In real-world settings where LSM may not always be available, FIB-4 offers a simple and accessible means for risk monitoring. Meanwhile, serial LSM assessments in specialized centers could provide even greater precision for risk refinement.⁷⁻⁹ We firmly believe that incorporating routine, dynamic monitoring into MASLD care pathways will be key to improving patient outcomes.

Beyond clinical validation, successful implementation of the two-step pathway must also consider operational and health system factors, including infrastructure, accessibility to VCTE, and varying epidemiological contexts. Healthcare settings differ widely in terms of resources, technology access, and clinical workflows, and these variations can significantly influence the feasibility and effectiveness of the two-step strategy. In resource-limited environments, streamlined approaches that prioritize low-cost, widely available tests like FIB-4 are particularly valuable. On the other hand, in tertiary centers with access to VCTE, incorporating serial LSM can refine prognostication and guide more personalized interventions. Tailoring the KASL pathway to local healthcare realities will be essential for maximizing its impact.

Moreover, the broader impact of this strategy on healthcare costs, patient outcomes, and system efficiency must not be overlooked. We believe that future cost-effectiveness analyses will be essential to quantify the benefits of early risk stratification, including its potential to prevent cirrhosis and hepatocellular carcinoma, reduce long-term healthcare expenditures, and improve overall quality of life.

Preliminary modeling studies have suggested that early identification of high-risk patients through non-invasive tests could substantially decrease downstream complications and associated costs. However, real-world data assessing the economic and clinical outcomes of implementing the two-step pathway at scale are urgently needed to inform policy decisions and optimize resource allocation. To facilitate the practical implementation of this strategy, integrating the two-step strategy into electronic medical records could help increase its use and simplify clinical workflows. Automated algorithms that flag patients with elevated FIB-4 scores and recommend subsequent LSM assessments could facilitate early detection of at-risk individuals, reduce clinician burden, and ensure consistent application of the risk stratification pathway across different care settings.

Finally, we strongly concur with the editorial's call for large-scale, real-world studies to validate and refine the two-step risk stratification approach. As non-invasive technologies and biomarkers continue to evolve, it will be imperative to continuously update risk prediction algorithms to reflect new knowledge. International collaboration across diverse cohorts and healthcare systems will be crucial for developing robust, globally applicable strategies that can truly improve MASLD outcomes. Harmonizing definitions, standardizing measurement techniques, and sharing real-world evidence will accelerate progress toward universally accepted, evidence-based risk stratification pathways for MASLD.

Once again, we sincerely thank Dr. Goh and colleagues for their thoughtful and supportive editorial. We are honored to contribute to this evolving discussion on MASLD risk stratification and look forward to future collaborations that will further advance the care of patients with steatotic liver disease.

Authors' contribution

H.W.L and S.U.K contributed equally to the conception, drafting, and critical revision of the correspondence.

Abbreviations:

FIB-4, fibrosis-4; LSM, liver stiffness measurement; MASLD, metabolic dysfunction-associated steatotic liver disease; VCTE, vibration-controlled transient elastography

Conflicts of Interest

The authors have no conflicts to disclose.

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