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Letters to the editor

Are we measuring fibrosis or just fluctuations? Rethinking liver stiffness measurement trajectories in chronic hepatitis B

To the Editor,

I read with great interest the recent report by Jiang et al. on using longitudinal liver stiffness measurements (LSM) trajectories to predict outcomes in chronic hepatitis B virus (HBV) with compensated advanced chronic liver disease (cACLD). The study's large cohort (1272 patients) and novel use of group-based trajectory modeling (GBTM) are commendable, providing robust statistical power. As the authors note, GBTM allowed stratification of patients into distinct stiffness trajectories, and these dynamic patterns were strongly linked to liver-related events (LREs) [1]. Importantly, those in high or fluctuating LSM trajectories (rapid decrease then increase, or high−stable) faced significantly higher risks of decompensation, hepatocellular carcinoma (HCC) and mortality. These findings are consistent with existing literature that supports the prognostic utility of noninvasive elastography. For instance, transient elastography has been described as a valuable modality for assessing the risk of HCC occurrence and recurrence [2]. Similarly, prior long-term studies indicate that patients with persistently elevated or variable fibrosis markers tend to experience more liver-related complications [3]. Therefore, Jiang et al. rightly emphasize the importance of monitoring LSM trends over time, rather than relying solely on a single FibroScan assessment, to enhance clinical decision-making.

I note several strengths of the study. First, the very large sample size – far larger than prior longitudinal FibroScan cohorts – gives confidence in the trajectory classifications and outcome associations. Second, the application of GBTM is innovative and conceptually appealing: it groups patients by their fibrosis evolution, a strategy previously applied (for example, to FibroTest-based trajectories in HIV-HBV coinfection) that similarly identified high−risk subgroups [3]. Third, the clinical implications are clear: if validated, dynamic LSM trajectories could help personalize surveillance and therapy. For instance, patients in low−stable trajectories might require less intensive monitoring, whereas those in high-risk trajectories could benefit from closer follow-up. These results reinforce that stiffness changes under treatment or over time carry independent prognostic weight – a notion supported by recent review literature highlighting the role of LSM in HCC surveillance [2].

Nevertheless, several limitations should be noted. As a retrospective study, the usual concerns of selection bias and unmeasured confounding apply. Moreover, as previously discussed by Patel and Sebastiani, noninvasive fibrosis tests were not initially designed to capture the dynamic nature of fibrogenesis and are subject to intrinsic variability [4]. In Jiang et al.'s cohort, the predominance of decreasing LSM patterns and the limited number of patients with increasing trajectories raise questions about the model's ability to capture true fibrosis progression [1]. Furthermore, FibroScan is known to have within-subject variability, especially in obese individuals, which may obscure biological signals [5]. Although the authors ensured a minimum number of reliable scans per patient, variability due to technical factors or transient hepatic inflammation could still influence trajectory interpretation. The absence of liver biopsy or another gold-standard fibrosis assessment represents another important limitation. As emphasized in the literature, noninvasive markers should complement, rather than replace, histologic evaluation [4]. Without histologic correlation, it remains unclear whether the LSM trends reflect genuine fibrotic remodeling or transient confounders such as ALT elevations or cholestasis. Finally, the lack of an actively rising trajectory group underscores the need for broader validation in more diverse cohorts [1].

Clinically, the findings suggest that serial elastography could augment standard care for chronic hepatitis B (CHB) / cACLD patients by identifying those at higher risk of decompensation or HCC. If validated prospectively, the trajectory classes might inform individualized surveillance intervals or prompt earlier intervention. Future studies should attempt prospective validation of these trajectory groups and their risk predictions. Incorporating paired biopsy or magnetic resonance (MR) elastography at baseline and follow-up would strengthen the link between stiffness trajectories and true fibrosis change. It would also be valuable to test the model in other etiologies (e.g., chronic hepatitis C, nonalcoholic steatohepatitis) and in different populations, to ensure generalizability. Furthermore, integrating clinical variables (ALT, fibrosis biomarkers, antiviral response) into the trajectory analysis could refine risk stratification.

In conclusion, Jiang et al. provide an innovative application of longitudinal LSM data and demonstrate clear differences in prognosis between stiffness trajectory groups [1,3]. I congratulate the authors on this substantial contribution. With further validation and expansion, dynamic LSM monitoring may become a powerful adjunct to liver disease management, guiding personalized patient care.

Authors' contributions

The author confirms that he is the sole contributor of this manuscript, and he has read and approved the final version for publication.

Declaration of competing interest

None.

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