



Letter to the Editor



# Expanding the Horizon: A Roadmap for Artificial Intelligence Integration in Metabolic Dysfunction-associated Steatotic Liver Disease

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Dear Editors,

We read with pleasure Zhu *et al.*'s recent review,<sup>1</sup> "Applications of Artificial Intelligence and Smart Devices in Metabolic Dysfunction-associated Steatotic Liver Disease", which we believe is very timely. Recently, significant updates have occurred in the field of hepatology, including nomenclature changes from nonalcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease and now metabolic dysfunction-associated steatotic liver disease (MASLD). Hence, it is important to find, in parallel, a thorough review summarizing the role of artificial intelligence (AI) and smart devices in this complex pathology.

Zhu *et al.* conducted a comprehensive review that included topics ranging from imaging analysis to patient self-management. Moreover, the authors also referred to debatable ethical aspects related to the use of AI. This article provides a state-of-the-art overview of the current status of the field. The review also provides recommendations related to the implementation of AI in the management of MASLD. Zhu *et al.* described the diagnostic accuracy of AI models, as well as ongoing concerns related to transparency and data privacy.

Nevertheless, another perspective is also worth discussing in regard to last-mile difficulties and challenges. Integrating cutting-edge algorithms into routine clinical practice and workflows remains uncertain. At present, a disparity exists between current literature on AI and actual endorsement by major societal guidelines. Although multiple studies have reported significant accuracy using these models, the use of AI for diagnosing or staging MASLD is not yet recommended in several societies, including the AASLD Practice Guidance (2023) and the EASL-EASD-EASO Clinical Practice Guidelines (2024).<sup>2,3</sup> Most clinics still rely on traditional non-invasive tests, such as FIB-4 and vibration-controlled transient

elastography. To transition AI from a research novelty to a guideline-endorsed tool, we need to bridge the gap between promising "in silico" results and real-world clinical impact.

To move beyond a purely conceptual framework, it is crucial to recognize recent milestones in AI applications that are already bridging this gap. In the realm of large-scale screening, machine learning models leveraging easily accessible clinical data have demonstrated high accuracy and robustness. For instance, an international validation study by Ye *et al.*<sup>4</sup> recently highlighted how such models can effectively screen for steatosis in MASLD across diverse populations, offering a scalable and cost-effective tool for primary care. Furthermore, AI is significantly improving current imaging modalities by enhancing diagnostic yield and reducing operator dependency. While traditional vibration-controlled transient elastography is the current standard, integrating AI into point-of-care transient elastography systems has been shown by Huang *et al.*<sup>5</sup> to markedly improve the simultaneous identification of both hepatic steatosis and fibrosis, bringing standard imaging closer to the precision of a digital biopsy.

Concept drift is a major hurdle and is often neglected. Zhu *et al.* point out that nearly 99% of NAFLD patients meet MASLD criteria.<sup>1</sup> Therefore, old datasets remain largely suitable for use. However, in machine learning, shifting inclusion criteria does not solely represent a linguistic change. NAFLD was previously defined by the presence of hepatic steatosis with no significant alcohol consumption. Nevertheless, MASLD now refers to hepatic steatosis in addition to metabolic risk factors. Therefore, models trained on NAFLD data can experience two major errors: they may wrongly label "cryptogenic steatotic" cases as MASLD or miss MASLD with increased alcohol intake (MetALD) patients who were previously excluded because of moderate alcohol consumption. To overcome this obstacle, it is necessary to re-phenotype previous datasets or use transfer learning to adapt existing models to the new definitions.

Zhu *et al.* also refer to wearables for continuous monitoring, which is a step forward.<sup>1</sup> A major goal in hepatology is to model patient trajectories, as it is essential to identify which patients with simple steatosis will progress and develop metabolic dysfunction-associated steatohepatitis (MASH) or decompensate within 3–5 years.<sup>6</sup> This requires time-series models with the ability to incorporate temporal data points, instead of the current standard cross-sectional convolutional neural networks.

Moreover, "explainable AI" remains essential to address

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**Table 1. A proposed roadmap for translating AI research into clinical hepatology**

Focus Area	Current State (as reviewed)	Proposed Future Direction (The "Phase 2" Agenda)
Guideline Status	Current AASLD/EASL clinical practice guidelines do not refer to AI tools <sup>2,3</sup>	Evidence Generation: Conduct multi-center, prospective randomized trials comparing AI care vs. standard care to obtain Level 1 evidence needed for guideline inclusion
Data Phenotyping & Concept Drift	Utilization of mixed "NAFLD" (exclusion-based) and "MASLD" (inclusion-based) cohorts creates label noise	Domain Adaptation: Use transfer learning to adapt old NAFLD models to MASLD; build "MASLD-native" registries including MetALD patients
Model Architecture	Predominantly static classifiers identified by the presence vs. absence of disease	Dynamic Forecasting: Implement longitudinal models (RNNs) that predict disease course and how patients respond to current therapies
Interpretability	High-accuracy "Black Box" models (DL)	Trust-Based Design: Require XAI features like SHAP values and saliency maps to demonstrate why a risk score is given
Data Sources	Unimodal analysis such as only histology, only ultrasound, or only labs	Multi-Modal Fusion: Create "digital twins" that process genomics, pathology, and EMR data simultaneously to mimic real clinician reasoning

AI, artificial intelligence; AASLD, American Association for the Study of Liver Diseases; DL, deep learning; EASL, European Association for the Study of the Liver; EMR, electronic medical record; MASLD, metabolic dysfunction-associated steatotic liver disease; MetALD, MASLD with increased alcohol intake; NAFLD, nonalcoholic fatty liver disease; RNN, recurrent neural network; SHAP, SHapley Additive exPlanations; XAI, explainable AI.

the "black box" nature of deep learning.<sup>1</sup> Multidisciplinary tumor boards and liver clinics make decisions based on more than numbers; therefore, it is important to demonstrate the reasoning behind a risk score. If a model provides both a probability and a heatmap showing its reasoning, adoption can be accelerated. Moreover, Popa *et al.*<sup>7</sup> reported that automated diagnosis can compete with human experts. Nevertheless, precise validation is still needed to confirm that AI can adequately differentiate between simple steatosis and MASH.

In Zhu *et al.*'s review, a strong foundation was provided.<sup>1</sup> Furthermore, we have proposed a framework (Table 1) summarizing the next steps as a "Phase 2" roadmap for translating these technologies from research to real clinical use.<sup>2,3</sup>

Finally, Zhu *et al.* provided an important starting point. Now it is up to clinicians, data scientists, and industry to build on this and turn AI into a real, clinic-ready tool.

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