AI In Diagnosing Metabolic Dysfunction- Associated Steatotic Liver Disease (Masld): A Narrative Review

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Abstract

Formerly known as non-alcoholic fatty liver disease (NAFLD), metabolic dysfunction-associated steatohepatitis (MASH), fibrosis, cirrhosis, and hepatocellular carcinoma (HCC), MASLD is one of the most common diseases in the world, affecting 28% of adults and being the primary cause of chronic liver disease. Although the liver biopsy is the gold standard for diagnosing MASLD, the hunt for trustworthy non-invasive diagnostic techniques has been spurred by its invasive nature, sample inaccuracy, expenses, and consequences. For improving MASLD diagnosis, staging, and prognosis, artificial intelligence (AI) which includes machine learning, deep learning, radiomics, and digital pathology can be regarded as breakthrough technology. The current narrative review summarizes research on the use of AI-assisted techniques in comparison to histological, imaging, or clinical reference standards that was done between January 2018 and July 2026 and was found in PubMed, Embase, Scopus, Web of Science, ScienceDirect, and the Cochrane Library. With AUROCs ranging from 0.85 to 0.99 for steatosis diagnosis and 0.82 to 0.97 for fibrosis staging, AI-based imaging models utilizing ultrasound, computed tomography, magnetic resonance imaging, and elastography demonstrated exceptional diagnostic effectiveness. When it came to detecting clinically significant fibrosis and MASH, machine-learning algorithms that incorporated regular laboratory markers, metabolomics, proteomics, and data on the gut microbiome frequently outperformed conventional non-invasive algorithms like FIB-4 and the NAFLD Fibrosis Score. Diagnostic accuracy comparable to that of hepatopathologist experts was achieved by digitizing liver biopsies and used deep learning to analyse these images. HCC risk classification and surveillance were enhanced by using AI to create prediction models. The clinical use of these technologies is hampered by a number of factors, including inconsistent methodology, inadequate external validation, biases in data selection, and the interpretability of the results produced, despite the encouraging advancements made thus far. Because AI offers precise and minimally intrusive diagnoses, it generally has enormous potential for the treatment of MASLD.

Keywords: Metabolic dysfunction-associated steatotic liver disease (MASLD); Non-alcoholic fatty liver disease (NAFLD); Metabolic dysfunction-associated steatohepatitis (MASH); Artificial intelligence (AI); Machine learning; Deep learning; Liver fibrosis; Hepatocellular carcinoma (HCC).

1. Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the term used in 2023, following the multi-society Delphi Consensus, instead of non-alcoholic fatty liver disease (NAFLD)[1]. Despite the use of either NALFD or NAFLD terminology, this disease became the most common chronic liver disease worldwide affecting 25% to 30% of adults globally and continues to grow, following an increase in obesity and the incidence of type 2 diabetes mellitus (T2DM).

The definition of this condition is rather succinct: liver fat content is detected via imaging and/or biopsy together with at least one of the five cardiometabolic risk factors with exclusion of alcohol abuse and others that cause fatty liver disease[2,3].Thereafter follow several different options for the development of this disease ranging from MASL to MASH with hepatocellular injury and inflammation followed by progression to fibrosis, cirrhosis and sometimes hepatocellular carcinoma (HCC)[3].

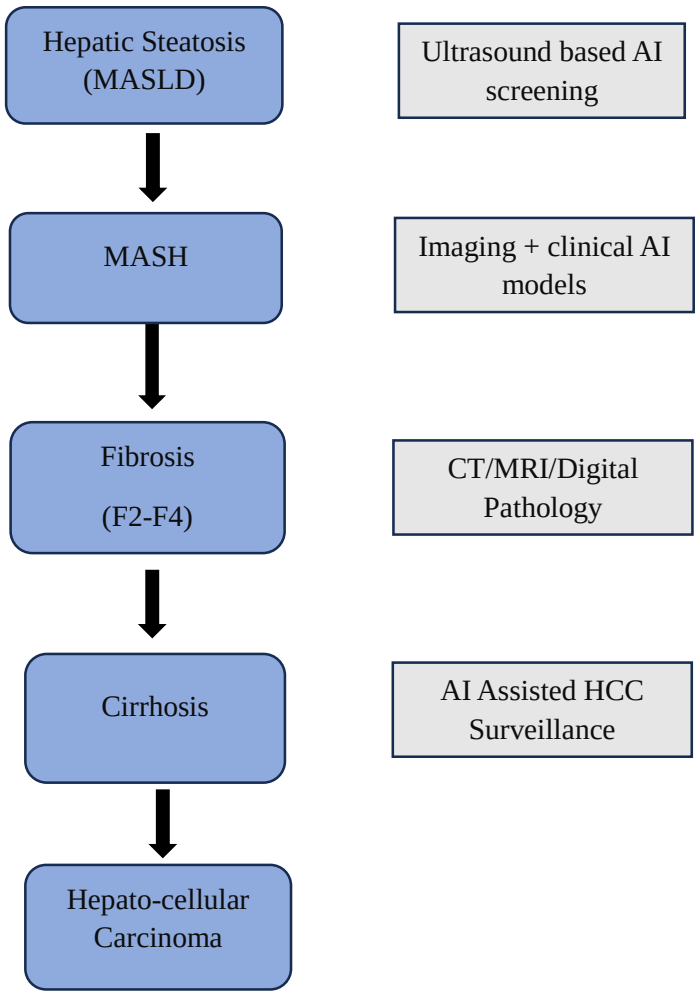


Figure 1: AI touchpoints across the MASLD diagnostic and diseases spectrum

At different stages, precise staging is essential. Early steatosis identification identifies people who will benefit more from risk factor therapy. MASH and severe fibrosis staging (F2 stage or higher) identifies patients who are most likely to benefit from monitoring or novel pharmaceutical therapy options that have recently become available. These patients are at a higher risk of developing disease and dying from liver problems. Lastly, since MASLD has emerged as one of the fastest-growing causes of HCC and its prognosis heavily depends on early identification, proper HCC surveillance is essential in cases with cirrhosis progression[3]. For all of these stages of MASLD, liver biopsy is the gold standard because it is the only test that can immediately assess all of the changes, including fibrosis, inflammation, ballooning, and steatosis. However, it is invasive, costly, and comes with procedural risks, as well as issues with sampling bias and inter-observer variability. Because of all the aforementioned characteristics, liver biopsy is not a good option for routine population screening[3].

Non-invasive testing (NITs), however, have assisted in addressing a portion of this issue. Although blood-based composite tests, like the FIB-4 index or the NAFLD fibrosis score (NFS), are readily available and reasonably priced, their accuracy is low, and a sizable percentage of results are still unclear and need additional testing, or simply aren't easily accessible outside of specialized hepatology facilities. HCC surveillance has a unique problem of its own. Due to low picture quality, the conventional ultrasound + serum alpha-fetoprotein (AFP) test is not very sensitive, particularly when used in obese and hepatic steatosis patients[4]. Due to its capacity to diagnostic patterns in imaging, histopathology, multiomics, or routine clinical data that would be challenging for humans to consistently locate, artificial intelligence (AI), including conventional ML and DL, has emerged as a potential solution to close these gaps. In recent years, there has been a rapid accumulation of literature on the use of CNNs, SVMs, GBMs, and similar machine learning tools in the diagnosis of MASLD. This involves the use of ultrasonography to detect steatosis, MRI and elastography to stage fibrosis, digital scoring of biopsy samples, and, most recently, HCC surveillance among patients with liver cirrhosis[5,6].

Despite this, the data are dispersed throughout the radiology, hepatology, pathology, and computational biology literature, and the research vary widely in terms of technique, references, and outcomes assessed. Reviews that have been done in the past have only included one stage of the disease or one diagnostic technique, such as the evaluation of fibrosis or the detection of steatosis. This review aims to address the need for a review that would concentrate on the literature currently available regarding the use of AI in diagnosing all stages of MASLD, from steatosis to MASH, fibrosis, cirrhosis, and hepatocellular carcinoma surveillance. It would also outline the benefits of the technology, the initial findings, and the difficulties encountered when implementing AI in hepatological practice.

2. Main Review

2.1 Literature Search and Review Approach

This is a narrative review thus such type of a review does not have a specific set of procedures or protocol that one follows while performing a systematic review or meta-analysis. In the process of the review, one needs to perform an extensive literature search of PubMed/MEDLINE, Embase, Scopus, Web of Science, ScienceDirect, and Cochrane Library databases for articles from January 2018 till July 2026 based on keywords and references from recent reviews. Key words used included both controlled and uncontrolled terms describing the disease being considered ("MASLD", "NAFLD", "MAFLD", "metabolic dysfunction-associated steatohepatitis", "MASH",

"NASH", "hepatic steatosis", "liver fibrosis", "cirrhosis", "hepatocellular carcinoma") combined with controlled or uncontrolled terms defining the technology ("artificial intelligence", "machine learning", "deep learning", "neural network", "radiomics", "digital pathology", "computer-aided diagnosis"), as well as diagnostic context ("diagnosis", "detection", "staging", "screening", "surveillance", "ultrasound", "MRI", "computed tomography", "elastography", "biopsy", "biomarker"). Such literature search was not aimed at collecting all the articles but rather selecting them as examples for the current status and limitations of artificial intelligence in MASLD diagnostics.

Preference was given to works using an AI/ML/DL technique to detect or assess any component of the MASLD spectrum - steatosis, MASH, fibrosis, MASLD/cirrhosis complications, or HCC on MASLD/cirrhosis background in adults and providing a diagnostic measure (AUROC, sensitivity, specificity, accuracy) in relation to a clear reference standard like biopsy, imaging or a known clinical scoring system. Studies involving children, exclusively preclinical models with no translational value, treatment-response prediction or prognosis in the absence of diagnostic information, and opinion pieces that do not present original performance results even though some of them were included for additional context were given lower priority.

2.2 AI for Detecting Hepatic Steatosis

The initial task when using the MASLD paradigm is identifying whether steatosis exists at all and this area has had the biggest amount of AI research effort committed to it thus far, partly owing to the low cost and extensive availability of the modality, even though it is inherently operator-dependent[7]. Systematic evaluation and meta-analysis of CNN classifiers of hepatic steatosis utilizing B-mode ultrasound images, together with external validation within a community environment, has demonstrated very good diagnostic accuracy and generalisability[8]. Multi-layered pipelines of AI models that segment hepatic and renal anatomical features, identify capsule boundaries and grade steatosis have exhibited accuracy higher than 99% in internal tests but statistics of this size arguably do more to indicate curating data [8,9].

Another type of AI-based technologies that becomes increasingly popular does not use any imaging and relies solely on regular lab data, metabolomics/proteomics and gut microbiota biomarkers. One of the examples of this approach is ALADDIN machine learning-based model for fibrosis prediction in MASLD patients based on clinical data. This technology has proven to perform better than traditional serum-based models[4]. Another example of such tool is LIVERSTAT machine learning-based score for fibrosis prediction in fatty liver disease due to metabolic disorders[4]. In the field of metabolomics there were some successful attempts as well: a simple to use machine learning model based on clinical and metabolomic features has successfully identified non-invasive MASH with fibrosis stage F2-F3; additionally, a machine learning-based metabolomic score for predicting both MASH and liver disease mortality was developed [4,10]..

Machine learning based on gut microbiome signatures has also been established to help differentiate between alcohol-related and metabolic dysfunction-related steatosis in liver disease patients, which is actually an effective tool for differential diagnosis of patients with mixed risk factors[4], along with a serum protein risk stratification score designed to assess MASH[10]. Moreover, hub gene discovery utilizing bioinformatics, coupled with machine learning, has helped identify the pathogenic pathways of MASLD along with producing classifiers[11].

2.4 AI in Digital Pathology for MASLD/MASH

Reducing reliance on biopsy to diagnose MASLD is one of the primary goals of this entire research field, but digital pathology remains important in this context not only as a method for validating imaging- and biomarker-derived models in comparison to actual ground truth, but also as an opportunity to standardize histological scoring .The manual application of the NASH Clinical Research Network (NASH CRN) scoring system, which independently evaluates steatosis, lobular inflammation, hepatocellular ballooning, and fibrosis, requires a significant amount of work from pathologists and is prone to genuine inter- and intra-observer variability[12].

In particular, multi-instance deep learning techniques applied to Sirius Red-stained sections that effectively handle the sparsity and uneven distribution of fibrotic tissue and exhibit excellent accuracy in retrospectively studied patients have advanced fibrosis staging[13]. Similar patch-based CNN workflows trained with thousands of image patches have achieved AUROCs greater than 0.90 and reasonable concordance with the pathologists' assessment of the degree of fibrosis; however, staining artifacts may result in false-positive fibrosis predictions, and patch-level classification may fail to capture architectural patterns, like bridging, that a pathologist may easily identify[13,14]. Prior research using second harmonic generation microscopy in conjunction with conventional and deep learning methods for collagen quantification and classification has been equally successful[14].

2.5 AI for Hepatocellular Carcinoma Surveillance in MASLD

The AI techniques for risk prediction and surveillance of HCC among such persons have garnered significant attention since MASLD has become one of the major and quickly expanding causes of cirrhosis and HCC[4 ,5]. There are a number of issues with the current HCC surveillance strategy, which includes bimonthly ultrasonography and AFP in cirrhotic patients, particularly with regard to poor imaging quality brought on by obesity or steatohepatitis and AFP-negative tumors[15]. In order to distinguish AFP-negative HCC from other benign focal liver lesions such as FNH in high-risk, hepatitis-B-infected patients who are challenging to screen with conventional techniques, deep-learning algorithms based on the analysis of B-mode ultrasound images have been created[15].

Patients with cirrhosis have been used in laboratories to predict the occurrence of HCC using machine learning based on longitudinal data. In terms of risk stratification for the development of HCC, a highly cited deep learning algorithm based on data from patients diagnosed with hepatitis C-related cirrhosis through electronic health records was found to outperform standard risk scores. This innovation has been increasingly used for patients diagnosed with cirrhosis as a result of MASLD. In order to improve discriminating beyond AFP, machine learning-based predictors for early HCC diagnosis have used clinical, biochemical, and image-based indicators[11]. Non-invasive molecular methods have also been suggested for the early identification of HCC, such as enzymatic methylation sequencing of cell-free DNA combined with pre-trained neural networks[11]. In addition to ongoing work on risk-stratified surveillance strategies suited to the expanding MASLD-driven HCC population, broader reviews of AI across the HCC care pathway point to additional roles in radiological lesion characterization, histopathological differentiation of liver tumors, and multiomics biomarker discovery[6 ,16, 17].

2.6 Comparative Diagnostic Performance Against Conventional Tools

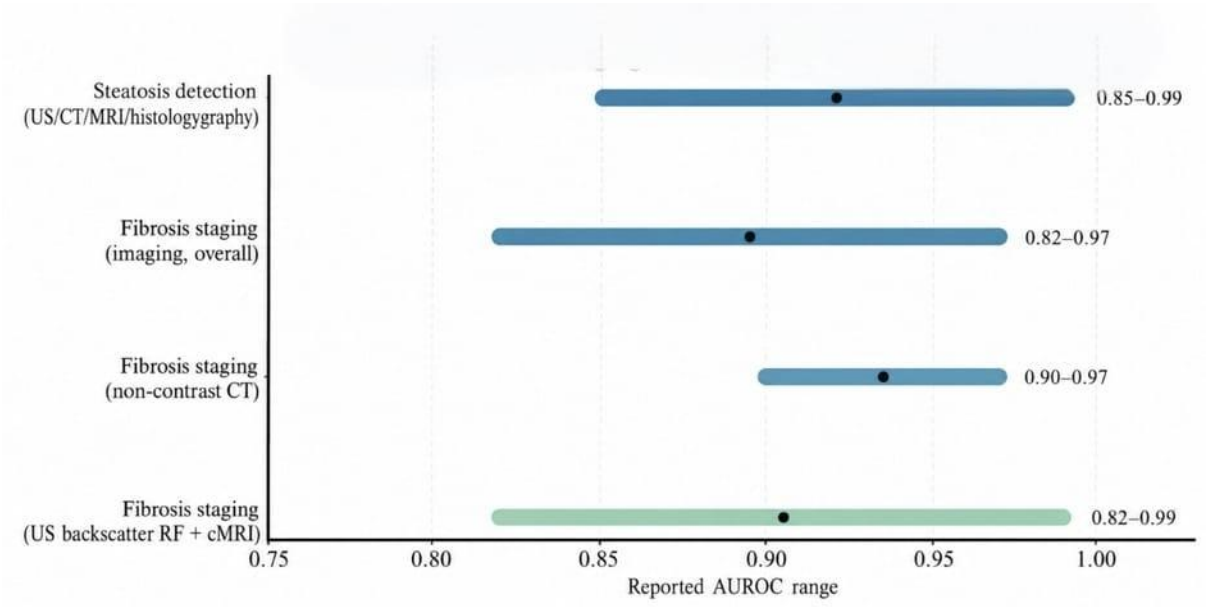


Figure 2

With regard to the detection of steatosis, fibrosis grading, MASH diagnosis, and HCC risk prediction, the common thread that is evident in this literature is that the AI methods generally tend to not only match the performance of the current methodologies in place including visual ultrasonography grading, serum biomarkers such as FIB-4 and NFS, histological grading of samples done manually, and AFP-based HCC surveillance but also surpass them by virtue of their reliability and scalability. As per a systematic review on the application of AI technology for fibrosis grading in MASLD comprising data from more than nineteen thousand patients and twenty-one studies, AI models have consistently outperformed FIB-4 and NFS[5]. In a similar sway, another meta-analysis on AI-enhanced abdominal imaging for liver fibrosis and MASLD also demonstrated high pooled accuracy using ultrasound, CT, and MRI scans[8]. This is indeed in line with other reviews of AI-powered automated diagnosis and staging of NAFLD/MASLD based on imaging, digital pathology, and biomarkers.

However, just how much AI outperforms traditional technology depends greatly on the imaging modality, population being studied, and reference standard used, and very few have made a true apples-to-apples comparison in clinically similar settings. The majority of the available AUROCs have been obtained from retrospective and single-center cohorts in which the reference standard is obtained concomitantly with the AI algorithm’s predictions, an arrangement that would tend to inflate the results compared to actual screening or surveillance in a prospective manner[5,8].

2.7 Explainability and Clinical Trust

Model complexity and interpretability is a persistent problem in imaging, pathology, and biomarker modelling. Deep learning architectures, especially those utilizing CNNs for imaging or histopathology, are often "black boxes," making it difficult for doctors to understand any given choice or spot any potential flaws, including the model's dependence on imaging artifacts. To get around this problem, MASLD diagnosis models are increasingly

using XAI techniques including saliency maps, attention mechanisms, and feature importance techniques like SHAP (SHapley Additive exPlanations).

In the process of MASLD steatosis staging in particular, explainable machine learning techniques have been developed for the analysis of potential biomarkers, including extracellular vesicles, in order to make the model's reasoning understandable to the clinician without significantly reducing the model's discriminative power[17]. These opinions about explainability's significance are reflected in more general hepatology-focused research, where explainability is practically considered a prerequisite for the model's approval[18].

2.8 Challenges and Limitations

Despite the consistently positive results, there are a number of methodological flaws that should prevent any rapid clinical use. First, studies vary greatly in terms of population type, imaging method, biomarkers, and outcome measures; several recent systematic reviews on the use of AI approaches for MASLD fibrosis and steatosis evaluation openly acknowledge this[5,6]. Second, the majority of the research is done retrospectively at a single location with inadequate external validation in various population settings, raising concerns about the results' applicability to different ethnic groups, disease stages, imaging machine manufacturers, and healthcare settings[5,8]. Lastly, the flawless accuracy of some ultrasound-based research may be primarily owing to the fact that many of the top-performing imaging models were trained and tested on relatively short datasets that were likely heavily pre-processed[19].

Fourth, the regulatory frameworks for validating and tracking constantly changing diagnostic software are still in their infancy, interpretability is still an unresolved issue, and clinical end users frequently lack an established methodology for incorporating model explanations into their diagnostic reasoning.[17,18]. Fifth, the large consortia and biomarker-discovery programs working on data standardization harmonized imaging protocols, consistent histological grading, interoperable laboratory and multiomics data structures remain a significant obstacle to pooling data across institutions for model training and validation[3,18].

Furthermore, sixth, with regards to the HCC surveillance, most of the studies were conducted on viral-hepatitis-associated cirrhosis, and there is a need to evaluate the performance of these models in the growing population of MASLD-associated cirrhosis that will be encountered in the future due to the different ethnical and metabolic risk factor profiles[15,20]. Finally, the most importantly, there is a lack of evidence on the benefit of artificial intelligence-driven diagnostic algorithms on downstream clinically relevant outcomes or cost-effectiveness after their implementation in the clinic, which was noted in almost all of the included studies.

2.9 Future Directions

A few developments seem likely to influence the future of AI-based MASLD diagnostics. In particular, multimodal studies utilizing fusion of imaging, histopathological, multiomics, and longitudinal data alongside clinical phenotyping in a single model likely represents the most physiologically plausible approach, given the multifactorial and protracted nature of the disease process. Similarly, federated learning appears to be a pragmatic solution to the challenge of achieving external validity in diagnostic AI while respecting the privacy and governance needs of participating centres.

The value of the described diagnostic accuracy in retrospective studies should be validated prospectively in prospective multinational studies in the real-world diagnostic pathway, namely, in the setting of screening, staging, or hepatocellular carcinoma (HCC) surveillance in primary care and hepatology clinics rather than tertiary care settings, if possible. The diagnostic accuracy of the technologies for HCC surveillance should also be validated in populations of patients with MASLD-related cirrhosis. Furthermore, the development of methods for providing an appropriate level of explainability and quantification of uncertainty in AI diagnostic models is critically needed to facilitate their potential deployment as aids in the diagnostic pathway, ranging from the initial suspicion of steatosis to cancer surveillance.

3. Conclusion

Artificial intelligence has demonstrated a substantial and broadly consistent diagnostic value across the continuum of clinical manifestations of MASLD: from the initial suspicion of hepatic steatosis on ultrasound to non-invasive diagnosis of MASH and the estimation of fibrosis using imaging, metabolomic, proteomic, and microbiome-based models; from digital pathology-based scoring of liver biopsy to computer-assisted surveillance of hepatocellular carcinoma in cirrhosis. In almost all these areas, the diagnostic performance of artificial intelligence approaches, either stand-alone or in combination with routine laboratory tests, appears to be consistent or exceed that of the currently used diagnostic paradigms in terms of overall accuracy, applicability, scalability, and reduced need for invasive procedures.

That said, the evidence base is predominantly retrospective, single center, inconsistent in design, limited in external validity, and poorly reported with many areas in which to improve clinical applicability and regulatory approval. There is an immediate and pressing need to evaluate the diagnostic performance of hepatocellular carcinoma surveillance algorithms in MASLD-associated versus viral-hepatitis-associated cirrhosis, given the rapid epidemiological transition underway in liver cancer etiology. The optimal deployment of artificial intelligence in MASLD requires a concerted effort in multi and federated center studies, standardized reference standards and reporting, development of mechanistic interpretability, and prospective incorporation into clinical pathways from first contact with the primary care provider across the spectrum of cancer surveillance in hepatology.

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- Visualization
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- Literature search
- screening

VSK:

- Writing original draft
- Methodology

SAH:

- Writing review
- Editing
- Formal analysis

VVK:

- Supervision
- Validation

MJU:

- Resources and final approval

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