MASH Diagnosis: Non-Invasive Markers Show Promise at EASL 2026

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The accurate diagnosis of metabolic dysfunction-associated steatohepatitis (MASH) remains a clinical challenge, primarily relying on invasive liver biopsy to confirm inflammation and fibrosis.1 New data presented at EASL Congress 2026 suggests that a panel of non-invasive biomarkers could significantly reduce the need for biopsy in specific patient populations, streamlining diagnostic pathways.

KEY TAKEAWAYS

- The Pivot: Non-invasive biomarker panels are demonstrating sufficient accuracy to potentially defer or replace liver biopsy for MASH diagnosis in certain contexts.
- The Data: A composite score achieved a negative predictive value of 92% for advanced fibrosis (F3-F4) and a positive predictive value of 78% for MASH activity score e4.
- The Action: Clinicians should consider incorporating validated non-invasive scores into their MASH diagnostic algorithms, particularly for screening and monitoring, while awaiting further validation for definitive diagnosis.

MASH, previously known as non-alcoholic steatohepatitis (NASH), is characterised by hepatic steatosis, inflammation, and hepatocyte ballooning, often progressing to fibrosis and cirrhosis.1 The current gold standard for diagnosis and staging of MASH is liver biopsy, which carries risks including pain, bleeding, and, rarely, mortality.2 Furthermore, biopsy is subject to sampling variability and inter-observer differences in histological interpretation.3 The need for less invasive, more accessible diagnostic tools is substantial, particularly given the rising global prevalence of MASH.4 MASH affects a significant proportion of individuals with metabolic syndrome, type 2 diabetes, and obesity, conditions that are themselves increasing worldwide. Early and accurate diagnosis of MASH, especially advanced fibrosis, is crucial for timely intervention and management to prevent progression to end-stage liver disease, including hepatocellular carcinoma and the need for liver transplantation. The economic burden associated with MASH and its complications is also considerable, further underscoring the urgency for improved diagnostic pathways.

What the Liver Could Have Told Us Sooner

At EASL Congress 2026, researchers presented findings from a multicentre prospective study (N=2,850) evaluating the diagnostic performance of a novel panel of serum biomarkers for MASH and advanced fibrosis. The study enrolled adults with suspected MASH, defined by metabolic risk factors and imaging evidence of hepatic steatosis. All participants underwent a liver biopsy, which served as the reference standard. The biomarker panel included established markers such as AST, ALT, platelet count, albumin, and novel proteomic and metabolomic markers.5 The proteomic markers were

identified through mass spectrometry-based analysis of serum samples, focusing on proteins involved in inflammation, extracellular matrix remodeling, and lipid metabolism. Metabolomic markers were identified using nuclear magnetic resonance spectroscopy, targeting specific lipid species, amino acids, and organic acids known to be altered in MASH pathogenesis. Participants were recruited from tertiary care centres specializing in hepatology across several European countries, ensuring a diverse clinical representation of MASH severity.

The primary endpoint was the diagnostic accuracy of the biomarker panel for MASH (defined as NAFLD Activity Score (NAS) ≥4 with inflammation and ballooning) and for advanced fibrosis (F3-F4) as per the MASH Clinical Research Network scoring system. Secondary endpoints included correlation with histological features and prediction of clinical outcomes over a 2-year follow-up period.5 Histological assessments were performed by expert pathologists blinded to the biomarker results, using standardized scoring systems to ensure consistency and minimize bias. Clinical outcomes monitored during the follow-up period included liver-related mortality, liver transplantation, hepatic decompensation events (ascites, variceal bleeding, hepatic encephalopathy), and development of hepatocellular carcinoma.

The study demonstrated that the composite biomarker score achieved an area under the receiver operating characteristic curve (AUROC) of 0.87 (95% CI 0.85-0.89) for the diagnosis of MASH and an AUROC of 0.91 (95% CI 0.89-0.93) for advanced fibrosis. For advanced fibrosis (F3-F4), a predefined cut-off yielded a sensitivity of 85% and a specificity of 88%, with a negative predictive value (NPV) of 92% and a positive predictive value (PPV) of 78%. For MASH activity score ≥4, the sensitivity was 79%, specificity 82%, NPV 88%, and PPV 70%. The p-value for all primary and secondary endpoints was 0.001.6 These robust statistical measures underscore the potential clinical utility of the panel.

These results indicate that the non-invasive panel could effectively rule out advanced fibrosis in a significant proportion of patients, potentially reducing the number of biopsies required. The panel also showed a strong correlation with histological inflammation and ballooning, suggesting its utility in identifying active MASH. During the 2-year follow-up, patients classified as high-risk by the non-invasive panel had a significantly higher incidence of liver-related events (HR 2.87, 95% CI 2.15-3.83; P0.001) compared to those classified as low-risk.6 This predictive capability for clinical outcomes further enhances the value of the biomarker panel, moving beyond mere diagnostic accuracy to prognostic assessment.

While promising, the study acknowledged limitations, including the need for external validation in diverse populations and the fact that the PPV for MASH diagnosis, while substantial, still leaves a proportion of patients requiring biopsy for definitive confirmation. The study population was predominantly of European descent, and further research is needed to assess the panel's performance in other ethnic groups. The cost-effectiveness of integrating this panel into routine clinical practice also warrants further investigation. Future research will focus on refining the panel and exploring its role in monitoring treatment response.7 The current panel, while effective, may benefit from the inclusion of additional markers or the application of machine learning algorithms to optimize its predictive power. The logistical challenges of implementing novel proteomic and metabolomic assays in standard clinical laboratories also require consideration for widespread adoption.

For a comprehensive and foundational understanding of liver and biliary system diseases, which informs these emerging diagnostic strategies, consult Sherlock's Diseases of the Liver and Biliary System.

CLINICAL IMPLICATIONS

The data from EASL 2026 on non-invasive MASH diagnostics offers a tangible step towards reducing the reliance on liver biopsy. For general practitioners and specialists managing patients with metabolic syndrome, the prospect of a highly accurate negative predictive value for advanced fibrosis means fewer patients will need to undergo an invasive procedure. This is not merely a comfort factor; it translates to reduced healthcare costs, fewer procedure-related complications, and a more efficient diagnostic pathway for a condition with a rapidly expanding patient base. The challenge now lies in integrating these validated panels into clinical guidelines, ensuring that clinicians are equipped to interpret and act upon these scores appropriately.

The pharmaceutical industry, heavily invested in MASH therapeutics, will undoubtedly welcome these advancements. A more accessible and less burdensome diagnostic process could significantly broaden the pool of patients identified for potential treatment, accelerating recruitment for clinical trials and facilitating earlier intervention once therapies are approved. Companies developing MASH drugs, such as Madrigal Pharmaceuticals with resmetirom, or those with pipeline candidates, will benefit from a clearer, faster path to patient identification. However, the moderate positive predictive value for MASH activity itself suggests that biopsy will retain its role for definitive diagnosis in a subset of patients, particularly those with equivocal non-invasive results or where precise staging is critical for therapeutic decisions.

From a patient perspective, this represents a substantial improvement in their diagnostic journey. The anxiety and discomfort associated with liver biopsy are considerable, and any validated method that can reduce its necessity is a significant win. While the panel may not entirely eliminate the need for biopsy, it offers a triage mechanism that can spare many from an invasive procedure, allowing for earlier risk stratification and potentially earlier access to lifestyle interventions or emerging pharmacological treatments. The next iteration of guidelines from bodies like AASLD or EASL will need to provide clear recommendations on how these non-invasive tools should be deployed in routine practice, balancing diagnostic accuracy with patient convenience and resource allocation.

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