What is new in the 2025 APASL guidelines for metabolic dysfunction-associated fatty liver disease?

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As the global epidemics of obesity and type 2 diabetes mellitus (T2DM) continue to rise, metabolic dysfunction-associated fatty liver disease (MAFLD) has become the most common chronic liver disease globally. The Asia-Pacific region is particularly affected, accounting for a significant majority of global liver-related deaths (1). To address this, the Asian Pacific Association for the Study of the Liver (APASL) has released updated clinical practice guidelines in 2025 (2). This article is a commentary focusing on the key changes and new recommendations within those guidelines, which were published in *Hepatology International* (2).

Recognizing the limitations of the exclusionary diagnostic criteria for non-alcoholic fatty liver disease (NAFLD) and emphasizing the key role of metabolic dysfunction in disease pathogenesis, the introduction of the MAFLD definition in 2020 was a milestone in disease research and clinical practice (3-5). This shift reflects a significant evolution in our understanding of the disease, moving away from a diagnosis of exclusion towards one of inclusion based on metabolic dysfunction, recognizing the central role of metabolic factors and introducing the key concept of dual etiology, including alcohol consumption or coexisting liver diseases (6).

Over the past 5 years, there have been significant advancements in understanding the disease, culminating in new knowledge, the first approved treatment, and the beginning of a new era of artificial intelligence (AI) with potential promise for hepatology. These changes stimulate the need for an updated document of the APASL guidelines for the diagnosis and management of MAFLD, which was recently released in 2025 (2). This updated guideline provides a comprehensive framework for addressing the growing burden of MAFLD in the Asia-Pacific region. This commentary aims to highlight the key aspects in this landmark document and touch on the main changes from the 2020 version (7).

Nomenclature and diagnostic criteria

The APASL was the first pan-national society to endorse the redefinition of fatty liver disease from NAFLD to MAFLD in 2020 (7), and this is now firmly reinforced in the 2025

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guidelines (2), backed by robust evidence accumulated over recent years. This change has multiple positive implications for improving the identification of patients at risk of both hepatic and extra-hepatic complications, enhancing disease awareness, and favorable implications for International Classification of Diseases (ICD)-coding and clinical trials (8-11).

The MAFLD diagnostic criteria maintain the core components of overweight/obesity, T2DM, or evidence of metabolic dysfunction in lean individuals. This classification also represents an important initial step towards deconvoluting the heterogeneity of the disease, and some recent studies suggest that these subgroups might have distinct features and disease outcomes (12). Future efforts should be directed towards better stratification of these patients, with the potential to identify further subtypes of the disease and provide stratified management approaches tailored to these MAFLD subtypes, such as lean MAFLD or T2DM-predominant phenotypes, which may have distinct prognoses and therapeutic responses. By acknowledging different clinical presentations, such as lean individuals with metabolic dysfunction versus those with obesity or T2DM, the guideline highlights the need for future refinement in classifying disease subtypes, which paves the way for more personalized approaches in diagnosis, monitoring, and treatment.

Risk stratification and non-invasive testing

Both the 2020 and 2025 APASL guidelines emphasize risk stratification using non-invasive tests (NITs) to identify individuals at high risk of advanced fibrosis, facilitating targeted intervention and resource allocation. The updated guidelines provide more detailed recommendations for NIT utilization, balancing innovation with accessibility across diverse resource settings.

In the 2025 guideline, the Fibrosis-4 (FIB-4) index remains recommended as a readily available and cost-effective first-line test (13,14). Furthermore, the updated recommendations offer a practical, layered framework for risk stratification (2). This includes the use of advanced techniques like vibration-controlled transient elastography (VCTE), enhanced liver fibrosis (ELF), and magnetic resonance elastography (MRE), alongside emerging tools such as the FibroScan-AST (FAST) score. Notably, the guideline incorporates ethnic-specific data for Asian populations, demonstrating a commitment to regionally appropriate care. Another notable aspect in the guideline is discussing the age-adjusted cutoffs for FIB-4, with note of cautions that, in patients ≥65 years, raising the FIB-4 rule-out threshold from 1.3 to 2.0 may lower sensitivity from ~84% to ~36%, a clinically significant trade-off.

By endorsing both advanced technologies (MRE, FAST score) and accessible tools (FIB-4), the guidelines support widespread implementation and promote broader public health initiatives, aiding clinical trial design and fostering cross-disciplinary awareness of MAFLD as a systemic disease. The role of newer NITs, such as MRE and FAST score, has also been discussed based on emerging evidence regarding their performance in Asian populations.

Management recommendations

Lifestyle interventions, including dietary modification, regular exercise, and behavioral strategies, remain the cornerstone of MAFLD management in the updated guideline (2). The 2025 version provides simple and clinically applicable specific guidance on the types and intensity of exercise, recommending a range of 150–240 minutes of moderate-to-vigorous intensity aerobic exercise per week. The guideline also notes that benefits may be observed with as little as 135 minutes per week.

The guidelines incorporate emerging evidence on the benefits of specific dietary patterns, such as the Mediterranean diet or intermittent fasting, and provide practical guidance on implementing these approaches in diverse cultural contexts.

Additionally, with the approval of resmetirom as the first drug for MAFLD (15), the 2025 APASL guidelines provide specific practical recommendations on its use, including clear patient selection criteria, optimal treatment duration, appropriate monitoring strategies, and considerations for drug combinations and sequential therapies. The document also discusses emerging pharmacological therapies targeting various pathways in MAFLD pathogenesis (16-19).

Emerging evidence also supports the use of semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, in managing MAFLD, particularly in patients with co-existing T2DM or obesity (20). While not specifically approved for MAFLD at the time of this guideline's release, semaglutide has demonstrated benefits in reducing liver fat and improving metabolic parameters in clinical trials and should be considered as part of a comprehensive treatment strategy. Further studies are needed to determine its optimal use in various MAFLD subtypes.

It is important to acknowledge the limited representation

of Asian populations in the clinical trials for emerging MAFLD therapies. Future research should prioritize the inclusion of diverse populations, particularly Asian individuals, to ensure the generalizability of trial results and the applicability of treatment recommendations across all ethnicities (21).

When metabolic surgery is being considered in MAFLD patients, several key factors warrant attention. Bariatric surgery is indicated in MAFLD patients with obesity [body mass index (BMI) ≥27.5 kg/m^2 in Asians] who have failed conventional weight loss strategies and is demonstrated to be effective in promoting histologic improvement (resolution of steatosis, ballooning degeneration, and inflammation), and reducing the 10-year cumulative incidence of major adverse liver outcomes (22). However, in patients with cirrhosis, particularly decompensated cirrhosis, bariatric surgery carries a significantly elevated risk (up to 18% reported mortality) (23,24). Thorough pre-operative assessment for portal hypertension and careful patient selection are paramount in minimizing risk and maximizing benefits.

Special populations

The 2025 guideline provides further emphasis on the unique characteristics and management considerations for special populations, including lean MAFLD, pediatric MAFLD, and those with dual etiologies (e.g., MAFLD with viral hepatitis or alcohol-related liver disease) (25).

Recent evidence suggests that lean-MAFLD may have a distinct but worse phenotype compared to non-lean MAFLD (26-28). This subgroup exhibits an elevated risk of cardiovascular disease (CVD) and chronic kidney disease (CKD), and increased all-cause mortality, similar to obese MAFLD, underscoring the systemic nature of the disease (29-31). Consequently, the guideline provides structured recommendations for managing lean MAFLD, emphasizing improved body composition (reducing fat mass while preserving muscle mass) and enhanced metabolic fitness. Proactive screening for CVD and CKD in lean MAFLD patients is also highlighted due to the potential for under recognition of these complications in the absence of obesity (30,32). The emphasis on cardiovascular and renal risk assessment in lean MAFLD further promotes a holistic approach to patient care.

In pediatric MAFLD, greater emphasis was placed on early lifestyle interventions, including family-based approaches, and the need for further research to evaluate the long-term efficacy of these interventions in preventing disease progression.

Patient-reported outcomes (PROs)

Another fundamental aspect of the APASL guidelines documents emphasizing the importance of understanding MAFLD from a patient perspective through PROs, particularly by validating culturally appropriate PRO measures for Asian MAFLD populations. This will enable empowering patients in their management, a better understanding of the patient experience, inform treatment decisions, and improve patient engagement in clinical trials and management strategies (33). Recognizing that most existing PRO tools were developed in Western contexts, the guideline underscores the need for measures that adequately address region-specific experiences and concerns. Integrating PROs into clinical care provides patients with an opportunity to participate in their management and equips clinicians with additional insights into the effects of the disease, including fatigue, psychological symptoms, and impacts on daily activities.

AI

Given the rapid advancement of AI in healthcare, the application of AI techniques in MAFLD management was first added to the 2025 guideline, including emphasizes AI's diverse and expansive scope, from predictive analytics and data mining to improved diagnostics, with potential for enhanced accuracy in predicting disease progression and identifying patients at risk for developing severe subtypes like metabolic dysfunction-associated steatohepatitis (MASH) or advanced fibrosis (34). To fully leverage this potential, future studies could include further exploration of AI-based tools, facilitate personalized risk assessment, identify novel therapeutic targets, and enhance clinical trials while addressing important ethical and logistical considerations surrounding AI implementation (35).

In conclusion, the 2025 APASL guidelines represent a significant step forward in the management of MAFLD, incorporating the latest evidence and addressing key challenges in the Asia-Pacific region. This document would undoubtedly be instrumental in improving the care of individuals affected by this increasingly prevalent liver disease.

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