DOI: 10.63583/cq45me13

Metabolic dysfunction-associated steatotic liver disease - masld

HA VU
University of Health Sciences, Vietnam National University, Ho Chi Minh City

Abstract

Objective: *Metabolic dysfunction-associated steatotic liver disease (MASLD) is a new nomenclature for Nonalcoholic Fatty Liver Disease (NAFLD) proposed by American Association for the Study of Liver Diseases and European Association for the Study of the Liver (AASLD and EASL) in 2023. Recent guidelines from AASLD 2024 and emerging updates from 2025 have redefined diagnostic and therapeutic approaches to MASLD. This article aims to summarize treatment objectives, patient selection, pharmacologic and non-pharmacologic therapies, and follow-up strategies.* ***Result****: Lifestyle modification remains the cornerstone of treatment. Pioglitazone and Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 receptor agonists), especially semaglutide, are the first-line pharmacotherapies in selected patients. Resmetirom, recently approved by the FDA and incorporated into the 2025 AASLD guideline, has become a promising therapeutic option for patients with Metabolic dysfunction-associated steatohepatitis (MASH) and fibrosis. Other emerging agents such as lanifibranor are still under investigation in phase III trials. Fibrosis risk stratification using Fibrosis-4 Index (FIB-4), Meta-analysis of Enhanced Liver Fibrosis and FIB-4 (MEFIB), Magnetic Resonance Imaging - Aspartate Aminotransferase Score(MAST) scores aids in determining treatment urgency and monitoring.* ***Conclusion:*** *With improved risk stratification and expanding therapeutic options, individualized care in MASLD will improve long-term outcomes.*

Keywords: steatotic liver disease, dysfunction-associated.

I. Introduction

Nonalcoholic Fatty Liver Disease (NAFLD) was a widely used term for decades to describe the accumulation of fat in the liver not caused by alcohol. However, since 2023, the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) have jointly agreed to replace the term NAFLD with Metabolic dysfunction-associated steatotic liver disease (MASLD) to more accurately reflect the pathophysiological basis linked to metabolic dysfunction [1,2].

MASLD results from fat accumulation in the liver in conjunction with one or more metabolic disorders such as obesity, type 2 diabetes, dyslipidemia, or metabolic syndrome.

MASLD is now the leading cause of progressive liver fibrosis, hepatocellular carcinoma (HCC), and is one of the most common indications for liver transplantation in many developed countries [1,3]. Epidemiological studies report a global prevalence of MASLD of approximately 25–30%, with a rapidly increasing trend among younger populations, particularly in Asia and Latin America [3]. However, MASLD progresses silently, and most patients are

Received: 31/6/2024, Accepted: 14/9/2024
Corresponding author: hvu@uhsvnu.edu.vn - University of Health Sciences, Vietnam National University, Ho Chi Minh City

DOI: 10.63583/cq45me13

diagnosed only after advanced liver damage or complications have occurred.

Therefore, updating approaches to diagnosis, risk stratification, and treatment options in accordance with the latest clinical guidelines is essential for mitigating the disease burden associated with MASLD.

II. Diagnosis

According to the 2024 AASLD guidelines, the diagnosis of Metabolic dysfunction-associated steatotic liver disease (MASLD) is based on two main criteria. First, there must be evidence of hepatic steatosis detected through imaging modalities such as ultrasound, FibroScan-CAP (Controlled Attenuation Parameter), or MRI-PDFF (Magnetic Resonance Imaging Proton Density Fat Fraction). Second, this must be accompanied by at least one metabolic abnormality, including: BMI ≥ 25 kg/m² (or ≥ 23 kg/m² for Asian populations), Type 2 diabetes mellitus, Elevated fasting glucose (≥ 100 mg/dL) or HbA1c ≥ 5.7%, Hypertriglyceridemia ≥ 1.7 mmol/L (150 mg/dL), Reduced HDL-C ≤ 1.0 mmol/L (40 mg/dL), Or hypertension [1,2].

In the absence of metabolic risk factors, secondary causes of hepatic steatosis must be excluded, such as: Excessive alcohol consumption (> 20 g/day for women and > 30 g/day for men), Chronic viral hepatitis, or autoimmune liver diseases.

III. Risk Stratification

Once MASLD is diagnosed, the next step is to stratify the risk of liver fibrosis in order to identify patients who require intensive treatment and close monitoring. One of the first recommended tools is the Fibrosis-4 (FIB-4) index, which is calculated based on age, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count. FIB-4 results are interpreted as follows: < 1.3: low risk of fibrosis, suitable for routine follow-up; 1.3–2.67: intermediate risk, further assessment with FibroScan (liver stiffness measurement – LSM) is advised; > 2.67: high risk, requiring referral to a hepatology specialist for further evaluation.

A combined model that is gaining popularity is MEFIB (Meta-analysis of Enhanced Liver Fibrosis and FIB-4). Patients with FIB-4 > 1.6 and LSM > 8.6 kPa are considered at high risk for advanced fibrosis (≥ F2).

In centers with access to advanced imaging, the MRI-AST score a combination of MRI-PDFF and AST levels can be used to predict histological damage, particularly in patients with fibrosis ≥ F2.

In addition to these three main tools, other scoring systems such as the NAFLD Fibrosis Score (NFS), ELF (Enhanced Liver Fibrosis), FAST (FibroScan-AST), and FibroMeter are also recommended depending on the facility's available resources and expertise.

According to AASLD and EASL guidelines, the current clinical approach should begin with FIB-4 for all MASLD patients with metabolic risk factors, followed by non-invasive tools such as FibroScan or MRI as needed. Liver biopsy should only be indicated in unclear diagnostic cases or when precise histological assessment is necessary prior to initiating specific treatment.

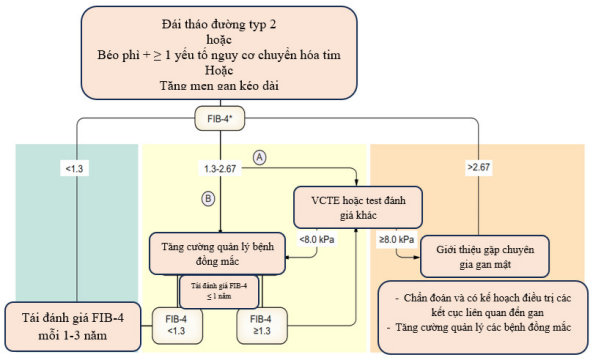

Figure 1. Proposed strategy for non-invasive assessment of advanced fibrosis risk and liver-

DOI: 10.63583/cq45me13

related outcomes in patients with MASLD (Source: EASL-EASD-EASO Clinical Practice Guidelines on the Management of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), 2024).

IV. Treatment goal

The treatment goals in Metabolic dysfunction-associated steatotic liver disease (MASLD) include: slowing or reversing the progression of steatohepatitis with fibrosis, improving insulin resistance, controlling blood glucose and lipid levels, and preventing serious complications such as cirrhosis, hepatocellular carcinoma (HCC), and cardiovascular mortality [3].

Among treatment strategies, weight loss is considered the most critical cornerstone. Numerous studies have demonstrated that: A weight loss of ≥ 5% can improve liver enzymes such as ALT and AST; A reduction of 7–10% can improve liver histology, including decreased inflammation and fat accumulation; And a loss of >10% may result in complete resolution of metabolic-associated steatohepatitis (MASH) and liver fibrosis [1, 5].

V. Treatment Strategy

The treatment of Metabolic dysfunction-associated steatotic liver disease (MASLD) consists of two main pillars: (1) lifestyle modification and (2) pharmacologic therapy. Among these, lifestyle changes are the foundation for all stages of the disease, while drug therapy is primarily reserved for patients with confirmed MASH or at risk of progressive fibrosis.

Non-pharmacologic treatment: Lifestyle modification

The recommended dietary approach is the Mediterranean diet, aiming to reduce intake of refined sugars and saturated fats, while increasing consumption of vegetables, whole grains, fatty fish, and olive oil. Caloric intake should be reduced by approximately 500-1000 kcal per day to achieve steady and sustainable weight loss [1].

In terms of physical activity, patients are advised to engage in at least 150 minutes per week of moderate aerobic exercises such as brisk walking or swimming, along with resistance training (e.g., light weights or endurance exercises) 2-3 times per week to improve insulin sensitivity and reduce hepatic and visceral fat [2,5].

Moreover, managing coexisting metabolic risk factors is essential, including achieving glycemic control (HbA1c < 7%), blood pressure < 130/80 mmHg, and LDL-C < 100mg/dL, or lower depending on the patient's overall cardiovascular risk.

Pharmacologic treatment

Medication is indicated for MASLD patients with histologically confirmed MASH with liver fibrosis stages F2–F3, determined via biopsy or validated non-invasive scores. Pharmacotherapy may also be considered for patients who cannot achieve weight loss goals through lifestyle changes alone [1,3].

According to AASLD guidelines, several medications are currently recommended for MASLD treatment: Pioglitazone, a thiazolidinedione, has demonstrated efficacy in improving MASH and liver fibrosis, both in diabetic and non-diabetic patients. The recommended dose is 15-45 mg/day. Caution is advised due to potential side effects, including weight gain, edema, and osteoporosis in postmenopausal women [3].

GLP-1 receptor agonists (e.g., semaglutide) have shown significant weight reduction, improvement in liver histology, and reduced insulin resistance. Starting dose is 0.25mg per week, gradually increasing to 1.0-2.4mg per week. Common side effects include nausea, vomiting, and reduced appetite [4,6]. SGLT2

DOI: 10.63583/cq45me13

inhibitors (e.g., empagliflozin, dapagliflozin) have limited evidence for improving fibrosis but may benefit MASLD patients with diabetes by improving glycemic control and lowering liver enzymes [3]. Vitamin E at 800 IU/day may be beneficial for non-diabetic patients with MASH; however, long-term use should be approached cautiously due to risks of hemorrhage and prostate cancer [1,5].

Resmetirom, a thyroid hormone receptor β agonist, has demonstrated histologic and MRI-based improvements in liver fat and fibrosis. Approved by the FDA in 2025, it is now included in AASLD treatment guidelines as an evidence-based option. The recommended dose is 80 or 100 mg orally per day, depending on patient response and tolerability. Liver enzymes, lipid profile, and fibrosis markers should be monitored regularly during treatment [1].

Additional investigational therapies include: Lanifibranor, a pan-PPAR α/δ/γ agonist, which has shown multi-targeted histologic benefits in the liver. Obeticholic acid, an FXR agonist, which has demonstrated antifibrotic effects but may cause pruritus and increased LDL-C in some patients [6].

VI. Treatment Monitoring and Response Evaluation

Following treatment initiation, patients should be monitored every 3-6 months to assess efficacy and adjust therapy as needed. Monitoring includes both clinical and laboratory evaluations. Clinically, weight, waist circumference, blood pressure, and gastrointestinal symptoms should be tracked. Laboratory monitoring should include periodic assessments of ALT, AST, HbA1c (in diabetic patients), and FIB-4 every 6-12 months.

For patients at high risk or with fibrosis stage ≥ F2, additional imaging such as FibroScan or liver ultrasound is recommended annually [1,2]. For those with advanced fibrosis (F3-F4) or LSM ≥ 15kPa, hepatocellular carcinoma (HCC) surveillance should be performed using ultrasound combined with alpha-fetoprotein (AFP) testing every 6 months [1].

Treatment should be discontinued or adjusted if no biochemical response is observed after 12 months or if severe adverse effects occur. The optimal treatment goals include normalization of ALT, reduction of FIB-4, and maintenance of target weight.

VII. Conclusion

The 2024-2025 AASLD guidelines provide a comprehensive approach to the management of Metabolic dysfunction-associated steatotic liver disease (MASLD), encompassing updated diagnostic criteria, risk stratification, and personalized treatment strategies. Lifestyle modification remains the cornerstone of therapy, while pharmacologic agents such as pioglitazone, GLP-1 receptor agonists, and resmetirom are recommended for high-risk patient groups. The integration of non-invasive tools like FIB-4, MEFIB, and MAST enhances clinical decision-making and helps improve long-term outcomes for patients with MASLD.

References

1. AASLD Practice Guidance on MASLD and MASH. American Association for the Study of Liver Diseases; 2024-2025. Available from: https://www.aasld.org/
2. Rinella ME, Sanyal AJ, Wong VW, et al. AASLD–EASL joint guidance on MASLD: redefinition, diagnosis and management. Gastroenterology. 2024;166(1): 36-52.
3. Eslam M, Newsome PN, Anstee QM, et al. MASLD: a unified terminology for metabolic-associated fatty liver disease. Nat Rev Gastroenterol Hepatol. 2024; 21(2):87-101.
4. Loomba R, Neuschwander-Tetri BA, Sanyal AJ, et al. Resmetirom for the treatment of MASH

DOI: 10.63583/cq45me13

with liver fibrosis. N Engl J Med. 2023;388(5): 421-432.

5. Younossi ZM, Stepanova M, Henry L, et al. Epidemiology and economic burden of MASLD. J Hepatol. 2023;79(1): 66-80.
6. Armstrong MJ, Gaunt P, Aithal GP, et al. The effectiveness of obeticholic acid in MASH: results from the REGENERATE trial. Lancet. 2024; 403(10388): 104-115.
7. U.S. National Library of Medicine. ClinicalTrials.gov. Clinical trials of resmetirom and lanifibranor in MASLD. Accessed 2025. Available from: https://clinicaltrials.gov/
8. EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD), Journal of Hepatology, September 2024. vol. 81, 492–542