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Redefining fatty liver disease: Understanding the shift from NAFLD (non-alcoholic fatty liver disease) to MASLD (metabolic dysfunction-associated steatotic liver disease)

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Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) represents the updated terminology replacing non-alcoholic fatty liver disease (NAFLD), reflecting a significant advancement in the understanding of fatty liver disorders. Introduced through an international consensus in 2023, MASLD emphasizes the central role of metabolic dysfunction rather than defining the condition by the absence of alcohol consumption. This change aims to reduce stigma, improve diagnostic accuracy, and align disease nomenclature with current scientific evidence. MASLD is characterized by hepatic steatosis in individuals with one or more cardiometabolic risk factors, including obesity, type 2 diabetes mellitus, dyslipidemia, hypertension, or insulin resistance. It is now recognized as the most common chronic liver disease globally and is closely associated with cardiovascular disease, chronic kidney disease, and metabolic syndrome. The transition from NAFLD to MASLD also introduces updated classifications, including metabolic dysfunction-associated steatohepatitis (MASH), replacing non-alcoholic steatohepatitis (NASH). This article discusses the rationale behind the nomenclature change, diagnostic criteria, epidemiology, pathophysiology, clinical implications, and future directions in the management of MASLD. Understanding this evolving terminology is essential for healthcare professionals, researchers, and policymakers to improve patient care and promote standardized clinical practice.

Keywords: MASLD, NAFLD, MASH, fatty liver disease, metabolic dysfunction, hepatic steatosis, metabolic syndrome, insulin resistance, liver disease, non-alcoholic steatohepatitis

Introduction

Fatty liver disease has emerged as one of the leading causes of chronic liver disease worldwide, affecting approximately one-third of the global adult population (Younossi *et al*., 2019) [37]. Traditionally, this condition was referred to as Non-Alcoholic Fatty Liver Disease (NAFLD), a diagnosis established when hepatic steatosis occurred in individuals without significant alcohol consumption or other secondary causes of liver fat accumulation (Hashimoto *et al*., 2015) [14]. While the term NAFLD has been widely used for decades, it has several limitations (Rinella and Sookoian, 2024) [28]. Primarily, it defines the disease by what it is not—rather than by its underlying cause—and places considerable emphasis on excluding alcohol use rather than identifying the metabolic abnormalities responsible for disease development.

Advances in clinical research have demonstrated that metabolic dysfunction, including obesity, insulin resistance, type 2 diabetes mellitus, dyslipidemia, hypertension, and central adiposity, plays a fundamental role in the initiation and progression of fatty liver disease (Zhao *et al*., 2023) [40]. These findings prompted international liver societies and experts to reconsider the disease nomenclature. In 2023[40], following a multidisciplinary Delphi consensus involving hepatologists, endocrinologists, gastroenterologists, and patient advocacy groups, the term Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) was formally adopted to replace NAFLD (Abaalkhail *et al*., 2025) [38].

The updated terminology reflects a more accurate understanding of disease pathogenesis by recognizing metabolic dysfunction as the primary driver of hepatic steatosis (Eslam *et al*., 2020) [11]. MASLD is diagnosed in individuals with evidence of liver steatosis and at least one cardiometabolic risk factor, irrespective of low or moderate alcohol intake. Additionally, the inflammatory subtype previously known as Non-Alcoholic Steatohepatitis (NASH) has been renamed Metabolic Dysfunction-Associated Steatohepatitis (MASH), emphasizing the metabolic basis of progressive liver injury (Tilg *et al*., 2026) [32].

The change from NAFLD to MASLD is more than a simple revision in terminology. It has important implications for clinical practice, research, epidemiological studies, patient communication, and healthcare policy. By focusing on metabolic health, the new nomenclature promotes earlier identification of at-risk individuals and encourages integrated management of metabolic disorders alongside liver disease.

Rationale for the Transition from NAFLD to MASLD

The transition from Non-Alcoholic Fatty Liver Disease (NAFLD) to Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) reflects a significant shift in the understanding of fatty liver disease, emphasizing its underlying pathophysiology rather than defining it by the absence of alcohol consumption (Huang *et al*., 2025) [16]. The term *NAFLD* was increasingly recognized as inadequate because it relied on excluding significant alcohol intake instead of identifying the primary drivers of the disease (Rinella and Sookoian, 2024) [28]. Additionally, the label

"non-alcoholic" often caused confusion among patients and healthcare providers, while the reference to alcohol contributed to unnecessary social stigma. Growing scientific evidence has established that metabolic dysfunction—including obesity, insulin resistance, type 2 diabetes mellitus, dyslipidemia, hypertension, and other cardiometabolic risk factors—is the principal cause of hepatic steatosis in most affected individuals. Consequently, the adoption of the term *MASLD* shifts the diagnostic focus toward the presence of metabolic abnormalities, providing a more accurate, inclusive, and clinically meaningful framework that aligns with current knowledge of disease mechanisms and supports improved patient care and research consistency (Rinella and Sookoian, 2026) [29].

Diagnostic Criteria and Classification of MASLD

The diagnosis of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is based on the presence of hepatic steatosis together with evidence of metabolic dysfunction (Tilg *et al*., 2026) [32]. Hepatic steatosis must be confirmed by imaging modalities such as ultrasonography, controlled attenuation parameter (CAP) using transient elastography, magnetic resonance imaging (MRI), histological examination, or validated non-invasive biomarkers (Martinou *et al*., 2022) [21]. In addition to liver fat accumulation, an individual must have at least one cardiometabolic risk factor, including overweight or obesity, type 2 diabetes mellitus, prediabetes, hypertension, dyslipidemia, increased waist circumference, or insulin resistance. Unlike the previous NAFLD definition, which required the exclusion of significant alcohol consumption, the MASLD criteria recognize that individuals with metabolic dysfunction may also consume small or moderate amounts of alcohol without excluding the diagnosis. This updated approach better reflects the multifactorial nature of fatty liver disease and provides a more practical and clinically relevant framework for identifying patients at risk of disease progression (Després *et al*., 2008) [9].

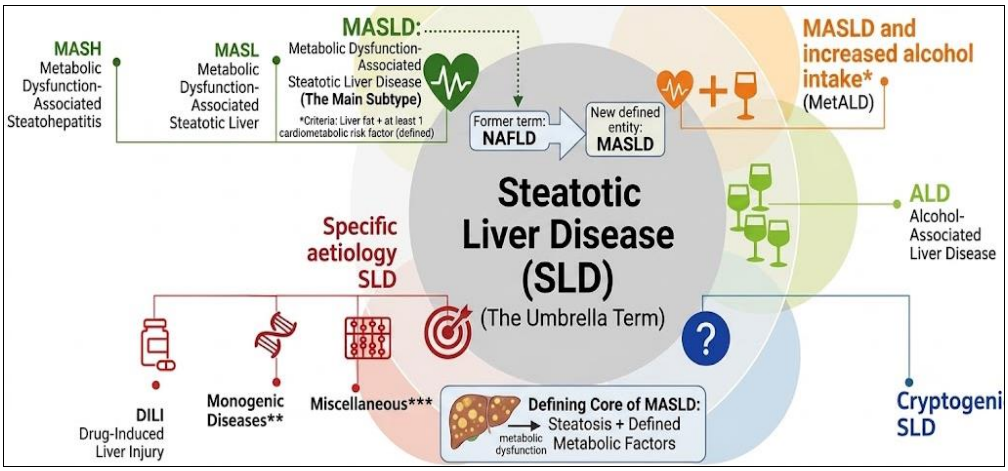

Fig 1: *Classification hierarchy of Steatotic Liver Disease (SLD) depicting the shift from NAFLD to MASLD and its sub-entities including MASH, MetALD, Specific Aetiology SLD, and Cryptogenic SLD*

Global Epidemiology and Disease Burden

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has emerged as one of the most prevalent and rapidly increasing chronic liver diseases worldwide, paralleling the global rise in obesity, type 2 diabetes mellitus, and metabolic syndrome (Portincasa *et al*., 2024) [26]. Current estimates indicate that MASLD affects approximately 30–38% of the adult population globally, making it a major public health concern (Miao *et al*., 2024) [23]. The prevalence is substantially higher among individuals with metabolic risk factors, exceeding 60–70% in those with obesity and affecting 70–80% of patients with type 2 diabetes mellitus (Nsiah *et al*., 2015) [25]. Alarmingly, MASLD is no longer confined to middle-aged adults; its incidence is rising among adolescents and young adults, largely driven by increasing rates of childhood obesity, sedentary lifestyles, and unhealthy dietary habits. As the disease progresses in a subset of patients to advanced fibrosis, cirrhosis, and hepatocellular carcinoma, MASLD has become one of the leading indications for liver transplantation in many countries. Given the continuing global epidemic of metabolic syndrome and related disorders, the burden of MASLD is projected to increase substantially over the coming decades, emphasizing the urgent need for effective prevention, early detection, and comprehensive management strategies (Xu *et al*., 2025).

Pathophysiology of MASLD

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) develops through a complex interplay of metabolic, genetic, inflammatory, and environmental factors that collectively promote hepatic fat accumulation and progressive liver injury (Sandireddy *et al*., 2024) [30]. The disease is primarily driven by insulin resistance, which increases the release of free fatty acids from adipose tissue and enhances their uptake by the liver, leading to excessive triglyceride deposition within hepatocytes. As lipid accumulation progresses, lipotoxicity, oxidative stress, and mitochondrial dysfunction trigger hepatocellular damage and activate inflammatory pathways, resulting in the release of pro-inflammatory cytokines and chemokines (Birkenfeld and Shulman, 2014) [3]. These inflammatory processes stimulate hepatic stellate cells, promoting fibrosis and, in advanced stages, cirrhosis. Alterations in the gut–liver axis, including changes in gut microbiota composition and increased intestinal permeability, further exacerbate liver inflammation through the translocation of bacterial endotoxins (Milosevic *et al*., 2019) [24]. In addition, genetic variants such as PNPLA3, TM6SF2, and MBOAT7

influence individual susceptibility to disease development and progression. Lifestyle factors, including calorie-rich diets, physical inactivity, and environmental influences, further contribute to disease onset and severity. Together, these multiple interacting mechanisms support the "multiple-hit" model of MASLD pathogenesis, explaining its heterogeneous clinical presentation and progression.

Major pathogenic mechanisms include:

1. Insulin Resistance

Insulin resistance is widely recognized as the central pathogenic mechanism underlying Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) (Bo *et al*., 2024) [2]. In insulin-resistant states, particularly those associated with obesity and type 2 diabetes mellitus, the normal inhibitory effect of insulin on adipose tissue lipolysis is impaired (Zhao, 2020) [39]. Consequently, excessive amounts of free fatty acids (FFAs) are released from adipose tissue into the bloodstream and transported to the liver (Jensen, 2006) [17]. Simultaneously, insulin resistance stimulates hepatic *de novo* lipogenesis through activation of lipogenic transcription factors such as sterol regulatory element-binding protein-1c (SREBP-1c), while reducing fatty acid oxidation and impairing very-low-density lipoprotein (VLDL) secretion. These metabolic disturbances result in excessive triglyceride accumulation within hepatocytes, leading to hepatic steatosis. Persistent insulin resistance also contributes to hyperglycemia, hyperinsulinemia, and chronic low-grade inflammation, thereby accelerating disease progression from simple steatosis to metabolic dysfunction-associated steatohepatitis (MASH), fibrosis, and ultimately cirrhosis.

2. Lipotoxicity

While triglyceride accumulation is a hallmark of MASLD, it is the accumulation of toxic lipid metabolites, rather than triglycerides themselves, that plays a pivotal role in hepatocellular injury (Kuchay *et al*., 2025) [18]. Lipotoxicity results from the excessive deposition of harmful lipid species such as free fatty acids, ceramides, diacylglycerols, and free cholesterol within hepatocytes (Branković *et al*., 2022) [5]. These toxic lipids disrupt cellular homeostasis by inducing endoplasmic reticulum stress, mitochondrial dysfunction, oxidative damage, and activation of apoptotic pathways (Wang *et al*., 2023) [34]. They also stimulate inflammatory signaling cascades through activation of nuclear factor-kappa B (NF-κB) and c-Jun N-terminal kinase (JNK), leading to hepatocyte ballooning and cell death. The persistent lipotoxic environment promotes recruitment of inflammatory cells and activation of hepatic stellate cells, contributing to progressive liver injury, fibrosis, and the transition from simple steatosis to MASH.

3. Oxidative Stress

Oxidative stress is a major contributor to liver injury and disease progression in MASLD. Excessive accumulation of hepatic lipids increases mitochondrial β-oxidation and overwhelms the electron transport chain, resulting in the generation of reactive oxygen species (ROS). Additional sources of ROS include peroxisomal oxidation, cytochrome P450 enzymes (particularly CYP2E1), and activated inflammatory cells. Elevated ROS levels damage cellular proteins, lipids, and DNA through lipid peroxidation and oxidative modification, leading to mitochondrial dysfunction, impaired ATP production, and hepatocyte apoptosis. Oxidative stress also activates inflammatory and fibrogenic signaling pathways, including transforming growth factor-beta (TGF-β), thereby promoting collagen deposition and fibrosis. Thus, oxidative stress represents a crucial "second hit" that drives the progression of hepatic steatosis toward advanced liver disease (Svobodová *et al*., 2025) [38].

4. Chronic Inflammation

Chronic low-grade inflammation is a defining feature of MASLD and plays a critical role in disease progression. Hepatocyte injury caused by lipid accumulation and oxidative stress leads to the release of damage-associated molecular patterns (DAMPs), which activate resident liver macrophages (Kupffer cells) and recruit circulating immune cells (Mejía-Guzmán *et al*., 2025) [22]. These activated immune cells produce pro-inflammatory cytokines and chemokines, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β), and monocyte chemoattractant protein-1 (MCP-1) (Habanjar *et al*., 2023) [12]. Persistent inflammatory signaling promotes hepatocyte apoptosis and stimulates hepatic stellate cells, the principal fibrogenic cells of the liver. Activated stellate cells produce excessive extracellular matrix proteins, resulting in fibrosis and, eventually, cirrhosis. Therefore, chronic inflammation serves as a critical link between metabolic dysfunction, hepatocellular injury, and progressive liver fibrosis (Hammerich and Tacke, 2023) [13].

5. Gut Microbiota

Increasing evidence highlights the significant role of the gut–liver axis in the pathogenesis of MASLD. Alterations in the composition and diversity of the intestinal microbiota, known as gut dysbiosis, increase intestinal permeability, allowing bacterial products such as lipopolysaccharide (LPS) and other endotoxins to enter the portal circulation. These microbial-derived molecules activate hepatic immune cells through Toll-like receptors, triggering inflammatory responses and cytokine production within the liver (Benedé-Ubieto *et al*., 2024) [2]. Dysbiosis also influences bile acid metabolism, short-chain fatty acid production, choline metabolism, and endogenous ethanol generation, all of which contribute to hepatic lipid accumulation, insulin resistance, and inflammation. Consequently, the gut microbiota has emerged as an important therapeutic target, with interventions such as dietary modification, probiotics, prebiotics, synbiotics, and fecal microbiota transplantation being investigated for their potential role in MASLD management (Di Ciaula *et al*., 2020) [10].

6. Genetic Susceptibility

Although metabolic dysfunction is the primary driver of MASLD, genetic susceptibility significantly influences individual risk, disease severity, and progression. Several genetic variants have been identified that alter hepatic lipid metabolism and inflammatory responses. Among these, polymorphisms in the patatin-like phospholipase domain-containing protein 3 (PNPLA3) gene, particularly the I148M variant, are strongly associated with increased hepatic fat accumulation, steatohepatitis, fibrosis, and hepatocellular carcinoma (Valenti *et al*., 2011) [33]. Variants in the transmembrane 6 superfamily member 2 (TM6SF2) gene impair very-low-density lipoprotein secretion, leading

to intracellular triglyceride accumulation, while mutations in the membrane-bound O-acyltransferase domain-containing 7 (MBOAT7) gene influence phospholipid remodeling and hepatic inflammation (Weiskirchen and Lonardo, 2026) [35]. Other genes, including GCKR, HSD17B13, and MARC1, have also been implicated in modifying disease susceptibility and progression. Understanding these genetic determinants may facilitate precision medicine approaches by enabling early risk stratification, personalized monitoring, and the development of targeted therapeutic interventions for patients with MASLD (Zhang *et al*., 2025) [19].

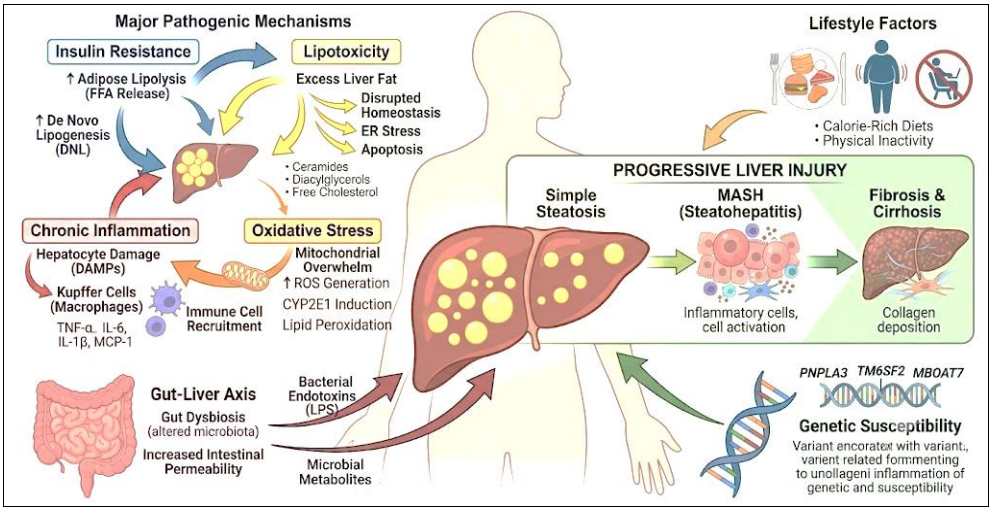

Fig 2: Pathophysiology and Progression Continuum of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Showing the interplay between primary drivers, cellular mechanisms of liver injury, and disease advancement to MASH and cirrhosis

Clinical Spectrum of MASLD

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) encompasses a broad clinical spectrum ranging from simple hepatic fat accumulation to advanced liver disease and malignancy. The earliest stage is simple steatosis (MASLD) (De *et al*., 2025) [38], characterized by excessive triglyceride accumulation in hepatocytes without significant inflammation or cellular injury, and many individuals remain asymptomatic at this stage. A subset of patients progresses to Metabolic Dysfunction-Associated Steatohepatitis (MASH), which is marked by hepatic steatosis accompanied by hepatocellular injury, inflammation, and varying degrees of fibrosis (Tilg *et al*., 2026) [32]. Persistent inflammation can lead to fibrosis, in which excessive extracellular matrix deposition results in progressive scarring of the liver. If fibrosis advances unchecked, it may culminate in cirrhosis, characterized by extensive architectural distortion, impaired liver function, portal hypertension, and an increased risk of liver failure. In the most advanced stage, patients may develop hepatocellular carcinoma (HCC), the primary form of liver cancer, which can occur in the setting of cirrhosis and, in some cases, even in its absence. This broad disease spectrum highlights the importance of early diagnosis and timely intervention to prevent progression to irreversible liver damage and its associated complications.

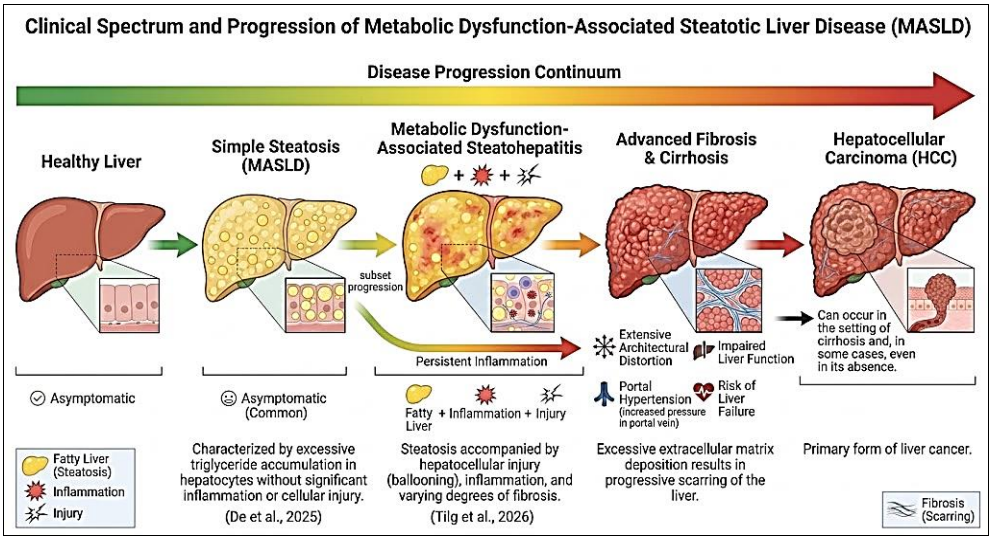

Fig 3: Clinical Continuum and Histological Stages of MASLD. Illustration of the disease continuum from simple steatosis to MASH, progressive fibrosis, cirrhosis, and end-stage complications including hepatocellular carcinoma (HCC)

Clinical Presentation and Diagnosis

The clinical presentation of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is often insidious, with many patients remaining asymptomatic during the early stages of the disease (Li *et al*., 2025) [16]. Consequently, MASLD is frequently detected incidentally through abnormal liver function tests or imaging studies performed for unrelated medical conditions. When

symptoms occur, they are generally nonspecific and may include fatigue, malaise, and mild discomfort or a dull aching pain in the right upper quadrant of the abdomen. Physical examination may reveal hepatomegaly, while laboratory investigations commonly demonstrate mild elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST), although normal liver enzyme levels do not exclude the diagnosis (Malakouti *et al*., 2017) [20]. Most patients exhibit one or more cardiometabolic risk factors, including central obesity, insulin resistance or type 2 diabetes mellitus, hypertension, dyslipidemia, and increased waist circumference. In advanced disease, progressive fibrosis and cirrhosis may lead to hepatic decompensation, manifested by jaundice, ascites, portal hypertension, hepatic encephalopathy, and gastrointestinal bleeding. The diagnosis of MASLD is based on evidence of hepatic steatosis together with the presence of at least one cardiometabolic risk factor. Initial evaluation includes laboratory tests such as liver function tests, lipid profile, fasting plasma glucose, glycated hemoglobin (HbA1c), and non-invasive fibrosis assessment using scoring systems such as the Fibrosis-4 (FIB-4) index and the NAFLD Fibrosis Score. Imaging modalities, including abdominal ultrasonography, vibration-controlled transient elastography with controlled attenuation parameter (FibroScan-CAP), and magnetic resonance imaging–proton density fat fraction (MRI-PDFF), are widely used to detect hepatic steatosis and assess fibrosis. Although liver biopsy remains the gold standard for confirming steatohepatitis and staging fibrosis, its invasive nature limits its use to selected cases where the diagnosis is uncertain or when accurate histological assessment is clinically warranted.

Current Management Strategies

The management of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is primarily directed toward improving metabolic health, preventing disease progression, and reducing liver-related as well as cardiovascular morbidity and mortality (Chan *et al*., 2023) [6]. Lifestyle modification remains the cornerstone of therapy and is recommended for all patients regardless of disease severity. Sustained weight loss of 7–10% of body weight has been shown to improve hepatic steatosis, resolve steatohepatitis, and reduce liver fibrosis in many individuals. Dietary interventions, particularly adherence to the Mediterranean diet, which is rich in fruits, vegetables, whole grains, legumes, fish, olive oil, and nuts, are associated with improvements in liver fat content and cardiometabolic risk factors. Regular physical activity, including at least 150 minutes of moderate-intensity aerobic exercise per week combined with resistance training, is recommended to enhance insulin sensitivity, reduce hepatic fat accumulation, and improve overall metabolic health. Patients are also advised to avoid excessive alcohol consumption and maintain healthy lifestyle habits.

Pharmacological therapy is primarily indicated for selected patients with biopsy-proven metabolic dysfunction-associated steatohepatitis (MASH), advanced fibrosis, or significant metabolic comorbidities (Chan *et al*., 2023) [6]. Current therapeutic approaches focus on managing the underlying metabolic abnormalities while reducing liver inflammation and fibrosis (Horn and Tacke, 2024) [15]. Agents such as glucagon-like peptide-1 (GLP-1) receptor agonists have demonstrated beneficial effects on weight reduction, glycemic control, and hepatic steatosis. Pioglitazone has shown efficacy in improving liver histology, particularly in patients with type 2 diabetes mellitus, whereas vitamin E may be considered in carefully selected non-diabetic patients with MASH (Choi *et al*., 2025) [7]. Sodium-glucose cotransporter-2 (SGLT2) inhibitors have also shown promise in reducing liver fat and improving metabolic outcomes. In addition, several novel antifibrotic agents and metabolic-targeted therapies are currently under clinical investigation (Zhou *et al*., 2026) [42].

Optimal management of associated comorbidities is an essential component of MASLD treatment. Effective control of obesity, type 2 diabetes mellitus, hypertension, dyslipidemia, and other components of metabolic syndrome reduces the risk of liver disease progression while simultaneously lowering the incidence of cardiovascular disease, which remains the leading cause of mortality among patients with MASLD. Consequently, a multidisciplinary approach involving hepatologists, endocrinologists, cardiologists, primary care physicians, dietitians, and other healthcare professionals is recommended to achieve comprehensive and individualized patient care.

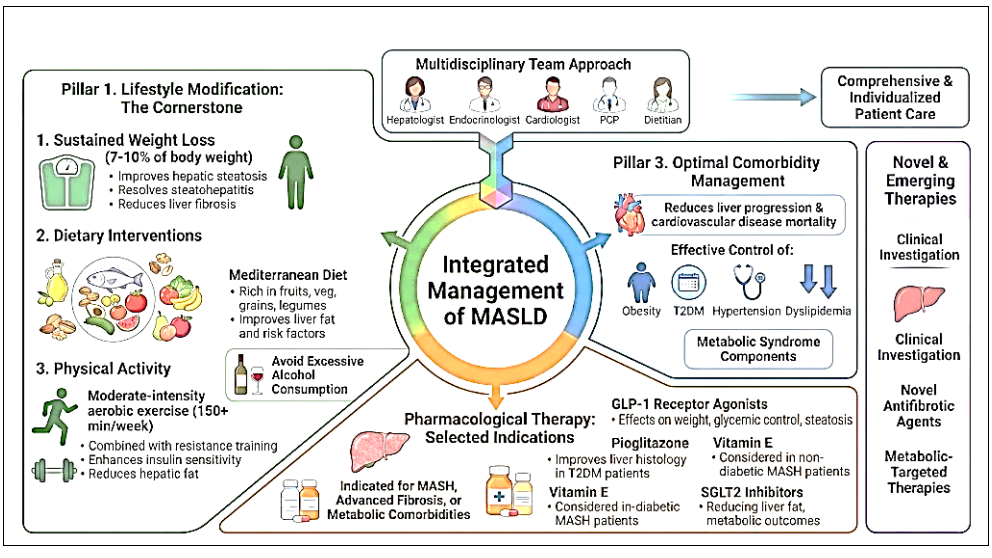

Fig 4: Management Strategies for MASLD

Clinical and Research Implications of the New Nomenclature

The adoption of the term Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) represents a significant advancement in the classification of fatty liver disease, offering several important clinical, scientific, and societal benefits. Unlike the previous term Non-Alcoholic Fatty Liver Disease (NAFLD), which defined the condition by the absence of alcohol consumption, MASLD more accurately reflects the current understanding that metabolic dysfunction is the principal driver of hepatic steatosis and disease progression (Rinella and Sookoian, 2024) [28]. This updated terminology reduces the alcohol-related stigma associated with the former name, thereby improving patient acceptance, communication, and engagement in medical care. By emphasizing underlying metabolic risk factors such as obesity, insulin resistance, type 2 diabetes mellitus, hypertension, and dyslipidemia, the MASLD framework encourages a more comprehensive, multidisciplinary approach involving hepatologists, endocrinologists, cardiologists, primary care physicians, dietitians, and other healthcare professionals. Furthermore, the standardized nomenclature enhances consistency in clinical practice, epidemiological studies, and international research collaborations, facilitating the comparison of study outcomes and the development of evidence-based guidelines. Importantly, the shift to MASLD also supports the advancement of precision medicine by promoting risk stratification and individualized treatment strategies based on metabolic profiles and disease severity, ultimately improving patient outcomes and public health strategies (Portincasa and Baffy, 2024) [26].

Future Directions and Emerging Research

The future of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) research is directed toward improving early detection, refining risk stratification, and developing more effective therapeutic strategies. Advances in non-invasive biomarkers and serum-based diagnostic panels, combined with imaging techniques such as transient elastography and magnetic resonance imaging, are expected to facilitate earlier diagnosis and reduce the need for liver biopsy. The integration of artificial intelligence (AI)-assisted imaging and machine learning algorithms has the potential to enhance the accuracy of detecting hepatic steatosis, fibrosis, and disease progression while enabling personalized risk prediction. Growing knowledge of the genetic and molecular mechanisms underlying MASLD is paving the way for precision medicine, where treatment can be tailored according to an individual's genetic profile, metabolic characteristics, and disease severity. In addition, several novel antifibrotic agents, metabolic-targeted therapies, and combination pharmacotherapies are currently under investigation to halt or reverse liver fibrosis and improve clinical outcomes. At the population level, public health initiatives focusing on the prevention of obesity, type 2 diabetes mellitus, and metabolic syndrome through healthy dietary habits, regular physical activity, and lifestyle modification will remain fundamental in reducing the global burden of MASLD. Continued collaboration among researchers, clinicians, policymakers, and patient advocacy groups, together with increased awareness among healthcare professionals and the general public, will be essential for improving early diagnosis, optimizing treatment, and ultimately reducing the incidence and long-term complications of this increasingly prevalent liver disease.

Conclusion

The transition from Non-Alcoholic Fatty Liver Disease (NAFLD) to Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) represents a significant milestone in hepatology. Rather than defining the disease by the absence of alcohol consumption, the new terminology recognizes metabolic dysfunction as the principal driver of hepatic steatosis and disease progression. This updated nomenclature aligns more closely with contemporary scientific knowledge, reduces stigma associated with the previous terminology, and facilitates more accurate diagnosis and patient-centered communication.

MASLD highlights the close relationship between liver disease and systemic metabolic disorders such as obesity, insulin resistance, type 2 diabetes mellitus, dyslipidemia, and hypertension. Recognizing these interconnected conditions encourages a multidisciplinary approach to patient care, focusing not only on liver health but also on reducing cardiovascular, renal, and metabolic complications. Early diagnosis through non-invasive assessment, combined with lifestyle modification and targeted management of metabolic risk factors, remains the cornerstone of therapy.

As research advances, the development of novel pharmacological agents, improved biomarkers, and precision medicine approaches is expected to transform the management of MASLD. Widespread adoption of the updated terminology in clinical practice, education, and research will promote standardized communication, enhance global collaboration, and ultimately improve patient outcomes. The shift from NAFLD to MASLD is therefore not merely a change in nomenclature but a reflection of a broader, evidence-based understanding of one of the most prevalent chronic liver diseases worldwide.

References

1. Abaalkhail F, Sanai FM, AlSwat K, Alzanbagi A, Aljedai A, Alshehri A, *et al*. Metabolic dysfunction-associated steatotic liver disease management in Saudi Arabia: A modified Delphi-based adaptation of international standards. Saudi Journal of Gastroenterology,2025:10-4103.
2. Benedé-Ubieto R, Cubero FJ, Nevzorova YA. Breaking the barriers: the role of gut homeostasis in Metabolic-Associated Steatotic Liver Disease (MASLD). Gut Microbes,2024:16(1):2331460.
3. Birkenfeld AL, Shulman GI. Nonalcoholic fatty liver disease, hepatic insulin resistance, and type 2 diabetes. Hepatology,2014:59(2):713–723.
4. Bo T, Gao L, Yao Z, Shao S, Wang X, Proud CG, *et al*. Hepatic selective insulin resistance at the intersection of insulin signaling and metabolic dysfunction-associated steatotic liver disease. Cell Metabolism,2024:36(5):947–968.
5. Branković M, Jovanović I, Dukić M, Radonjić T, Oprić S, Klašnja S, *et al*. Lipotoxicity as the leading cause of non-alcoholic steatohepatitis. International Journal of Molecular Sciences,2022:23(9):5146.
6. Chan WK, Chuah KH, Rajaram RB, Lim LL, Ratnasingam J, Vethakkan SR. Metabolic dysfunction-associated steatotic liver disease (MASLD): a state-of-

the-art review. Journal of Obesity & Metabolic Syndrome,2023:32(3):197.
7. Choi R, Vemuri J, Poloju A, Raj R, Mehta A, Asgharpour A, *et al*. Current and emerging treatments for metabolic associated steatotic liver disease and diabetes: a narrative review. Endocrines,2025:6(2):27.
8. De A, Panigrahi M, Duseja A, Singh SP. Metabolic-dysfunction associated steatotic liver disease (MASLD). In Hepatology. Academic Press,2025:861–888.
9. Després JP, Poirier P, Bergeron J, Tremblay A, Lemieux I, Alméras N. From individual risk factors and the metabolic syndrome to global cardiometabolic risk. European Heart Journal Supplements,2008:10(suppl_B):B24–B33.
10. Di Ciaula A, Baj J, Garruti G, Celano G, De Angelis M, Wang HH, *et al*. Liver steatosis, gut-liver axis, microbiome and environmental factors. A never-ending bidirectional cross-talk. Journal of Clinical Medicine,2020:9(8):2648.
11. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, *et al*. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. Journal of Hepatology,2020:73(1):202–209.
12. Habanjar O, Bingula R, Decombat C, Diab-Assaf M, Caldefie-Chezet F, Delort L. Crosstalk of inflammatory cytokines within the breast tumor microenvironment. International Journal of Molecular Sciences,2023:24(4):4002.
13. Hammerich L, Tacke F. Hepatic inflammatory responses in liver fibrosis. Nature Reviews Gastroenterology & Hepatology,2023:20(10):633–646.
14. Hashimoto E, Tokushige K, Ludwig J. Diagnosis and classification of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis: current concepts and remaining challenges. Hepatology Research,2015:45(1):20–28.
15. Horn P, Tacke F. Metabolic reprogramming in liver fibrosis. Cell Metabolism,2024:36(7):1439–1455.
16. Huang DQ, Wong VW, Rinella ME, Boursier J, Lazarus JV, Yki-Järvinen H, *et al*. Metabolic dysfunction-associated steatotic liver disease in adults. Nature Reviews Disease Primers,2025:11(1):14.
17. Jensen MD. Adipose tissue as an endocrine organ: implications of its distribution on free fatty acid metabolism. European Heart Journal Supplements,2006:8(suppl_B):B13–B19.
18. Kuchay MS, Choudhary NS, Ramos-Molina B. Pathophysiological underpinnings of metabolic dysfunction-associated steatotic liver disease. American Journal of Physiology-Cell Physiology,2025:328(5):C1637–C1666.
19. Li Y, Li L, Zhang Y, Lu J, Tang X, Bi C, *et al*. Clinical and pathological characteristics of metabolic dysfunction-associated steatotic liver disease and the key role of epigenetic regulation: implications for molecular mechanism and treatment. Therapeutic Advances in Endocrinology and Metabolism,2025:16:20420188251321602.
20. Malakouti M, Kataria A, Ali SK, Schenker S. Elevated liver enzymes in asymptomatic patients–what should I do? Journal of Clinical and Translational Hepatology,2017:5(4):394.
21. Martinou E, Pericleous M, Stefanova I, Kaur V, Angelidi AM. Diagnostic modalities of non-alcoholic fatty liver disease: from biochemical biomarkers to multi-omics non-invasive approaches. Diagnostics,2022:12(2):407.
22. Mejía-Guzmán JE, Belmont-Hernández RA, Chávez-Tapia NC, Uribe M, Nuño-Lámbarri N. Metabolic-dysfunction-associated steatotic liver disease: molecular mechanisms, clinical implications, and emerging therapeutic strategies. International Journal of Molecular Sciences,2025:26(7):2959.
23. Miao L, Targher G, Byrne CD, Cao YY, Zheng MH. Current status and future trends of the global burden of MASLD. Trends in Endocrinology & Metabolism,2024:35(8):697–707.
24. Milosevic I, Vujovic A, Barac A, Djelic M, Korac M, Radovanovic Spurnic A, *et al*. Gut-liver axis, gut microbiota, and its modulation in the management of liver diseases: a review of the literature. International Journal of Molecular Sciences,2019:20(2):395.
25. Nsiah K, Shang VO, Boateng KA, Mensah FO. Prevalence of metabolic syndrome in type 2 diabetes mellitus patients. International Journal of Applied and Basic Medical Research,2015:5(2):133–138.
26. Portincasa P, Baffy G. Metabolic dysfunction-associated steatotic liver disease: Evolution of the final terminology. European Journal of Internal Medicine,2024:124:35–39.
27. Portincasa P, Khalil M, Mahdi L, Perniola V, Idone V, Graziani A, *et al*. Metabolic dysfunction–associated steatotic liver disease: from pathogenesis to current therapeutic options. International Journal of Molecular Sciences,2024:25(11):5640.
28. Rinella ME, Sookoian S. From NAFLD to MASLD: updated naming and diagnosis criteria for fatty liver disease. Journal of Lipid Research,2024:65(1).
29. Rinella ME, Sookoian S. Therapeutic targets for metabolic dysfunction-associated steatohepatitis: a personalized approach to disease management. Nature Reviews Gastroenterology & Hepatology,2026:23(6):460–474.
30. Sandireddy R, Sakthivel S, Gupta P, Behari J, Tripathi M, Singh BK. Systemic impacts of metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH) on heart, muscle, and kidney related diseases. Frontiers in Cell and Developmental Biology,2024:12:1433857.
31. Svobodová G, Horní M, Velecká E, Boušová I. Metabolic dysfunction-associated steatotic liver disease-induced changes in the antioxidant system: A review. Archives of Toxicology,2025:99(1):1–22.
32. Tilg H, Petta S, Stefan N, Targher G. Metabolic dysfunction–associated steatotic liver disease in adults: a review. JAMA,2026:335(2):163–174.
33. Valenti L, Rumi M, Galmozzi E, Aghemo A, Del Menico B, De Nicola S, *et al*. Patatin-like phospholipase domain-containing 3 I148M polymorphism, steatosis, and liver damage in chronic hepatitis C. Hepatology,2011:53(3):791–799.
34. Wang B, Wang Y, Zhang J, Hu C, Jiang J, Li Y, *et al*. ROS-induced lipid peroxidation modulates cell death outcome: mechanisms behind apoptosis, autophagy,

and ferroptosis. Archives of Toxicology,2023:97(6):1439–1451.
35. Weiskirchen R, Lonardo A. Relevance of lipid droplets in metabolic dysfunction-associated steatotic liver disease. Expert Opinion on Therapeutic Targets,2026:30(5):473–497.
36. Xu B, Li H, Pi Y, Li K. Global, regional and national burden of metabolic dysfunction-associated steatotic liver disease in adolescents and adults aged 15–49 years from 1990 to 2021: Results from the 2021 global burden of disease study. Frontiers in Medicine,2025:12:1568211.
37. Younossi Z, Tacke F, Arrese M, Chander Sharma B, Mostafa I, Bugianesi E, *et al*. Global perspectives on nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Hepatology,2019:69(6):2672–2682.
38. Zhang X, Chang KM, Yu J, Loomba R. Unraveling Mechanisms of Genetic Risks in Metabolic Dysfunction–Associated Steatotic Liver Diseases: A Pathway to Precision Medicine. Annual Review of Pathology: Mechanisms of Disease,2025:20(1):375–403.
39. Zhao J, Wu Y, Rong X, Zheng C, Guo J. Anti-lipolysis induced by insulin in diverse pathophysiologic conditions of adipose tissue. Diabetes, Metabolic Syndrome and Obesity,2020:1575–1585.
40. Zhao X, An X, Yang C, Sun W, Ji H, Lian F, *et al*. The crucial role and mechanism of insulin resistance in metabolic disease. Frontiers in Endocrinology,2023:14:1149239.
41. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nature Reviews Endocrinology,2018:14(2):88–98.
42. Zhou XD, Lazarus JV, Krittanawong C, Targher G, Byrne CD, Younossi ZM, *et al*. Pharmacotherapy for metabolic dysfunction-associated steatohepatitis: heart–liver co-management. The Lancet Gastroenterology & Hepatology, 2026.