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PRACTICE GUIDANCE

TASL practice guidance for the diagnosis and management of metabolic dysfunction-associated steatotic liver disease (MASLD)

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Points to Note

- **Synthesis of Current Evidence:** 99% of former NAFLD cases align with new MASLD criteria, and TASL 2026 guidance focuses on improving clinical approaches to management.
- **Major Controversies:** Debates continue over replacing liver biopsies with NITs (FIB-4/VCTE) and defining ideal patient profiles for new MASH therapies like resmetirom.
- **Future Directions:** Efforts focus on expanding Turkish epidemiological data, defining cancer screening strategies for non-cirrhotic MASLD, and monitoring long-term drug efficacy.

ABSTRACT

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease worldwide and represents a major and growing public health challenge in Türkiye. This guidance provides an updated, clinically oriented overview of the definition, epidemiology, screening, diagnosis, risk stratification, and management of MASLD, with particular emphasis on evolving nomenclature, non-invasive diagnostic pathways, and current treatment strategies. The document addresses the full clinical spectrum of disease, from steatosis and metabolic dysfunction-associated steatohepatitis (MASH) to advanced fibrosis, cirrhosis, hepatocellular carcinoma, and liver transplantation. The guidance also incorporates evidence and practice considerations relevant to the Turkish population, including local epidemiology, resource availability, and implementation challenges in real-world care. Finally, areas of uncertainty and evidence gaps are highlighted to support future research and locally relevant policy development.

Keywords: Cirrhosis, fibrosis, MASLD, MASH, metabolic dysfunction, steatotic liver disease.

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Guidance development and Methodology

The Turkish Association for the Study of the Liver (TASL) Governing Board commissioned the development of this guidance in February 2026. An Executive Committee was appointed by the TASL MASLD Special Interest Group and it comprised Turkish hepatologists with recognized clinical and academic expertise in MASLD, including clinical trials, ensuring balanced representation across different levels of clinical and academic experience, from early career investigators to senior experts in the field. An Advisory Board was subsequently selected by the TASL Governing Board based on prolonged clinical and academic expertise in hepatology and MASLD.

The guidance was developed in accordance with the methodological principles for trustworthy guidelines articulated by the National Academy of Medicine (formerly the Institute of Medicine), the Guidelines International Network (GIN)–McMaster Guideline Development Checklist, and the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument. The Executive Committee was responsible for formulating the clinical questions, supervising the evidence review, drafting the recommendations, and assigning the level of evidence and strength of the recommendations for each statement. The Advisory Board independently reviewed the full draft for scientific content, balance, and applicability to Turkish clinical practice. To mitigate intellectual and financial conflicts of interest, members who declared a relevant interest neither served as lead authors nor had a deciding vote on recommendations concerning the relevant product class.

The draft guidance was presented for open discussion at a hybrid TASL İstanbul meeting in April 2026 and was subsequently revised in response to feedback and suggestions received during the TASL National Congress in May 2026. Following the revision, the manuscript was circulated to the Advisory Board and finalized after incorporating additional comments and feedback.

The recommendations were developed independently and were not directly adopted from existing international guidance documents. Instead, the available evidence was identified, critically appraised, synthesized, and graded according to the standardized methodology detailed below, with particular consideration of its applicability to the Turkish population.

Scope and Target Audience

This practice guidance addresses the definition, epidemiology, screening, diagnosis, risk stratification, treatment, and long-term management of metabolic dysfunction-associated steatotic liver disease (MASLD) across its full clinical spectrum. It includes the use of non-invasive diagnostic tools, lifestyle and pharmacological treatment options, bariatric and endoscopic interventions, and the management of cirrhosis, hepatocellular carcinoma, and liver transplantation-related issues. The guidance is primarily intended for hepatologists, gastroenterologists, endocrinologists, internal medicine physicians, primary care physicians and other healthcare professionals involved in the multidisciplinary care of patients with MASLD in Türkiye.

Clinical Questions Addressed by this Guidance

This guidance was developed to address the following key clinical questions:

Each key question was structured a priori by the Executive Committee using the PICO framework (Population, Intervention or index test, Comparator, Outcome). Patient-important outcomes were prioritized and pre-specified, namely all-cause and liver-related mortality, progression to cirrhosis, hepatic decompensation, hepatocellular carcinoma, major adverse cardiovascular events, and diagnostic accuracy of non-invasive tests for advanced fibrosis. These PICO questions defined the eligibility criteria for the literature search and the structure of the corresponding recommendations.

- What is the current definition and classification of MASLD, including its relationship with steatotic liver disease (SLD), MASH, metabolic dysfunction and alcohol-related liver disease (MetALD)?
- Which individuals should be screened for MASLD and advanced fibrosis?
- What is the preferred diagnostic pathway for MASLD in routine clinical practice, including the role of non-invasive tests and liver biopsy?
- Which lifestyle interventions should be recommended, and what degree of weight loss is clinically meaningful?
- What is the role of liver-directed therapy, antidiabetic agents, lipid-lowering treatment, bariatric surgery, and endoscopic interventions?
- How should associated metabolic comorbidities and cardiovascular risk be assessed and managed?
- How should cirrhosis, portal hypertension, hepatocellular carcinoma risk, and liver transplantation-related issues be managed in patients with MASLD?

Literature Review

A structured literature review was conducted using PubMed/MEDLINE, Embase, Web of Science, and Scopus. The search strategy incorporated combinations of the following terms: MASLD, MASH, SLD, MAFLD, NAFLD, MetALD, fibrosis, cirrhosis, hepatocellular carcinoma, non-invasive tests, obesity, type 2 diabetes mellitus, dyslipidemia, hypertension, cardiovascular disease, chronic kidney disease, bariatric surgery, endoscopic therapy, and liver transplantation. All relevant evidence published up to April 2026 was considered.

Priority was given to systematic reviews, meta-analyses, randomized controlled trials, large observational cohort studies, and international clinical practice guidelines. Where available, particular consideration was given to epidemiological and clinical data from Türkiye to ensure the relevance and applicability of the recommendations to the Turkish population.

Search Strategy

The electronic search combined controlled vocabulary (MeSH/Emtree) with free-text keywords, linked by Boolean operators ("OR" with-

Table 1. Classification of evidence levels based on study designs and source types

Level	Definition (source types)
High	Consistent evidence from well-conducted randomized controlled trials, or systematic reviews/meta-analyses of such trials, or large robust prospective cohort studies; further research is unlikely to change confidence in the estimate.
Moderate	Real-world and registry data, retrospective cohorts, smaller or methodologically limited randomized trials, post-hoc or subgroup analyses, or indirect evidence; further research may change the estimate.
Low	Expert opinion, case series or case reports, mechanistic or physiological reasoning, narrative reviews, or substantial extrapolation from indirect populations.

in concepts, "AND" across concepts), and was adapted to the syntax of each database. The search covered the period from database inception to 30 April 2026, with no start-date restriction, and was limited to records in English. The electronic search was supplemented by (i) hand-searching of the reference lists of included articles and of relevant international guidelines, (ii) screening of recent congress proceedings (EASL, AASLD, and the TASL National Congress), and (iii) targeted searches of regulatory sources (EMA and FDA) and trial registries for the licensing status of MASH-directed therapies. Records were exported to a reference manager and de-duplicated prior to screening. The full database-specific search strings are available from the corresponding author upon request.

Study Selection and Screening

Titles and abstracts were screened against the pre-specified PICO criteria, and potentially eligible records were assessed in full text. Each step was performed by at least two committee members, with disagreements resolved through discussion or by a third reviewer. Studies were eligible if they reported on adults (or, where stated, children) with MASLD/MASH or its antecedent terms (NAFLD/NASH/MAFLD) and addressed one or more of the pre-specified questions and outcomes. Editorials, narrative commentaries without primary data, non-peer-reviewed preprints, and studies judged to be at high risk of bias were used only as supportive context and not as a basis for graded recommendations. When several studies addressed the same question, the evidence base was prioritized hierarchically: meta-analyses and systematic reviews, randomized controlled trials, large prospective cohorts, retrospective/real-world studies, and mechanistic data or expert opinion. Where contemporary international guidelines addressed an identical question, they were appraised as secondary sources and reinterpreted for the Turkish context rather than adopted verbatim.

Critical Appraisal and Evidence Synthesis

Included studies were critically appraised for methodological quality and risk of bias using design-appropriate considerations (randomization and blinding for trials; selection, attrition, and confounding for observational studies; spectrum, and reference-standard adequacy for diagnostic-accuracy studies). Because the body of evidence was clinically and methodologically heterogeneous, evidence was synthesized narratively rather than by *de novo* meta-analysis, and quantitative estimates were reported as published. For each PICO question, the committee summarized the direction, magnitude, consistency, and certainty of the effect, together with its directness and applicability to routine Turkish practice, and this structured summary formed the explicit basis for the level of evidence and the strength of the recommendation assigned below.

Rating the Level of Evidence

Because the guidance was finalized after the formal meetings and a further consensus/voting round could no longer be convened, the Executive Committee applied a structured, pre-defined framework—adapted from the GRADE approach and from the evidence-rating schemes of contemporary EASL and AASLD MASLD guidance—to grade every recommendation *post hoc*. Each recommendation was assigned one of three levels of evidence (High, Moderate, or Low), reflecting the certainty that the estimated effect is correct. The level reflects the study design as a starting point and is then modified by the risk of bias, inconsistency, indirectness, imprecision, and publication bias (which may lower it) and by a large, consistent effect or a clear dose–response relationship (which may raise it) (Table 1).

Rating the Strength of Recommendation and Verb Conventions

The strength of each recommendation was determined by integrating five domains: (1) level of evidence; (2) balance between desirable and undesirable effects (benefit–harm); (3) clinical necessity and impact on prognosis or patient-important outcomes; (4) applicability in Türkiye, including access, cost, tiered healthcare system, and practicality of implementation; and (5) availability of alternatives and burden imposed on the patient. Two strengths were used: Strong and Conditional. Consistent with the GRADE approach, a strong recommendation may accompany moderate- or low-level evidence when the benefit–harm balance or the imperative to avoid harm is decisive. Conversely, high-level evidence may yield only a conditional recommendation when applicability, cost, or patient burden is limited (Table 2).

Updating Policy

This guidance is intended to function as a living document. An update is planned after the initial approval of a MASH-specific pharmacological therapy in Türkiye or within 3 years of publication, whichever occurs first. Earlier revision may also be considered if major new evidence emerges that is likely to influence diagnostic pathways, treatment recommendations, or the management of metabolic comorbidities and long-term outcomes.

Table 2. Strength of recommendations, clinical interpretations, and corresponding operative wording

Strength	Interpretation	Operative wording (verb)
Strong	Desirable effects clearly outweigh undesirable effects and burden; applies to most patients in most circumstances.	"is recommended", "should", "must"
Conditional	Desirable effects probably outweigh undesirable effects, but the balance is closer, the evidence weaker, or the applicability/feasibility constrained; shared decision-making is appropriate.	"is suggested", "may be considered", "can be"
Conditional (against)	Undesirable effects probably outweigh desirable effects in most situations; however, exceptions exist.	"is not generally recommended", "is better avoided"
Strong (against)	The undesirable effects clearly outweigh the desirable effects; therefore, the intervention should not be used.	"is not recommended", "should not", "is contraindicated"

Conflict of Interest and Financial Disclosure

No external financial support was received for the preparation of this guidance. No pharmaceutical company or commercial entity had any role in the conception, drafting, review, or approval of this document. Yusuf Yilmaz has served as a consultant and/or advisory board member for Zydus, Echosens, and Novo Nordisk. All other authors declare that they have no conflicts of interest relevant to the content of this guidance.

In line with the conflict-of-interest management described above, authors with a declared relevant interest were recused from leading and from final adjudication of the recommendations addressing the corresponding product class (vibration-controlled transient elastography, GLP-1 receptor agonists, and saroglitazar/PPAR agents); these recommendations were drafted and graded by non-conflicted committee members.

Introduction

Since it was first defined in the 1980s, the term non-alcoholic fatty liver disease (NAFLD) has been used to describe a spectrum of conditions encompassing non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). However, in recent years, the terminology has been increasingly debated since it defines the condition by the absence of significant alcohol consumption rather than by its underlying pathophysiology. In 2020, a group of experts from 22 different countries reached a consensus and proposed renaming NAFLD as metabolic dysfunction-associated fatty liver disease (MAFLD).[1] In 2023, through a Delphi consensus, a group of researchers gathered all causes of metabolic fatty liver disease under the umbrella term "Steatotic Liver Disease" (SLD),[2] and reclassified the previously-defined MAFLD as Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Under this framework, the presence of intrahepatic fat accompanied by at least one cardiometabolic risk factor is defined as MASLD. This nomenclature has been accepted as a more affirmative and pathophysiologically relevant description of the disease. Similarly, for cases accompanied by an active inflammatory process, the term "MASH" (Metabolic Dysfunction-Associated Steatohepatitis) is used instead of "NASH".[3] The old term NAFLD has been abandoned due to both the exclusionary nature of the "non-alcoholic" expression and the stigmatizing effect of the word "fatty".[2]

In recent years, particularly following the change in nomenclature, our understanding of the disease has evolved substantially. Screening strategies have advanced, and we are now entering an era in which MASLD can also be treated pharmacologically. In light of these developments, an updated guidance tailored to the Turkish population is warranted. This guidance aims to provide a comprehensive overview of the current evidence on the diagnosis, screening, management, and treatment of MASLD, while addressing challenges specific to clinical practice in Türkiye. In addition, we discuss emerging therapeutic approaches and future directions in the field, with the goal of supporting healthcare professionals in the optimal care of individuals with MASLD.

Definition, Epidemiology, Natural Course and Risk Factors of MASLD

Definition

SLD is the umbrella term that encompasses MASLD, which refers to the accumulation of fat (steatosis) in the liver due to any cause and includes a broad spectrum of liver disorders (Fig. 1).[1] The primary goal of this terminological change was to define the disease through an affirmative approach based on the presence of existing metabolic dysfunction rather than solely on the absence of alcohol consumption. Simultaneously, with this new classification, alcohol-related liver disease and alcohol consumption have been more clearly defined, and steatosis due to other causes has been addressed.

Validation studies conducted during the transition to the new terminology have shown that most patients meeting the former NAFLD criteria are fully compatible with the new MASLD definition. In large-scale cohort analyses, 95% to 99% of patients previously diagnosed with NAFLD are directly included in the MASLD category because they present with at least one cardiometabolic risk factor.[4] This high concordance rate demonstrates that the change in terminology does not disrupt the continuity of past scientific data; on the contrary, it improves diagnostic accuracy by emphasizing the presence of metabolic risk factors.[5,6] While only 1–3% of patients previously diagnosed with NAFLD are reclassified into the "Cryptogenic SLD" category, the designation of patients with both metabolic dysfunction and moderate alcohol consumption as Metabolic dysfunction and alcohol-as-

sociated liver disease (MetALD) has enabled a clearer distinction for clinical management.[7]

Subcategories are defined according to the underlying etiology of steatosis, as outlined below.

MASLD

This category represents the largest subgroup of SLD.

- MASLD: This condition is defined by the presence of hepatic steatosis combined with at least one cardiometabolic risk factor. These risk factors include obesity, type 2 diabetes, hypertension, and dyslipidemia.
- MASH: Standing for metabolic dysfunction-associated steatohepatitis, is considered the more severe and progressive form of MASLD. While MASLD refers to the presence of fat, MASH occurs when fat is accompanied by liver inflammation and cellular damage, often characterized by "ballooning" of the liver cells.

MetALD

One of the most critical categories in the new terminology is MetALD, which describes individuals who simultaneously meet the criteria for MASLD and consume alcohol above specified thresholds. This category is unique because it recognizes the combined and potentially synergistic effects of metabolic dysfunction and alcohol consumption on liver health. The diagnosis specifically applies to individuals whose daily alcohol intake is between 20–50 g for women and 30–60 g for men. By establishing these clear alcohol thresholds alongside metabolic indicators, this classification allows clinicians to better identify and manage patients who face a "double hit" of liver injury from both lifestyle and metabolic sources.[8] The proposal of this subcategory has introduced a new diagnostic framework and addressed a previously unmet gap.

ALD (Alcohol-Associated Liver Disease)

This category defines a condition in which the primary driver of liver fat accumulation is excessive alcohol consumption rather than metabolic factors. To be classified in this category, alcohol intake must exceed the following high thresholds: >50 g/day for women and >60 g/day for men. Unlike the previous categories, this diagnosis focuses on the direct toxic impact of high-level alcohol use on the liver.

Specific Etiology SLD

This group includes cases where the underlying cause of liver fat is a specific condition other than metabolic factors or excessive alcohol use, as shown in Table 3.

Cryptogenic SLD

This category refers to cases in which hepatic steatosis is present, but the underlying cause remains unknown. It is characterized by the absence of identifiable factors; specifically, steatosis cannot be attributed to metabolic dysfunction, significant alcohol consumption, or any other known cause. Essentially, it serves as a classification for individuals who do not fit within the established metabolic, alcohol-associated, or specific etiological categories of steatotic liver disease.

Table 3. Secondary causes of hepatic steatosis

Category	Conditions
Infections	Chronic HCV infection
Nutritional/ Intestinal-related	• Coeliac disease • Small intestinal bacterial overgrowth
Endocrine disorders	• Polycystic ovary syndrome • Hypothyroidism • Hypopituitarism • Growth hormone deficiency
Genetic Diseases	• A1AT deficiency • Wilson's disease • Haemochromatosis • Congenital lipodystrophy • Abeta- and Hypobetalipoproteinemia • Familial hypercholesterolemia • Glycogen storage diseases • Cholesterol ester storage disease • Hereditary fructose intolerance
Pregnancy-associated	Acute fatty liver of pregnancy
Steatosis-associated risk gene variants	PNPLA3 p.I148M

HCV: Hepatitis C virus; A1AT: Alpha-1-antitrypsin.

Diagnosis of MASLD

The diagnosis of MASLD is established by the presence of hepatic steatosis detected by a validated method, together with at least one cardiometabolic risk factor. Accordingly, the diagnostic evaluation is based on three key components: the presence of hepatic steatosis, the identification of at least one cardiometabolic risk factor, and the assessment of other potential causes or contributors to liver disease.[2]

Assessment of Hepatic Steatosis

The first step in the diagnostic process is to establish the presence of hepatic steatosis. This can be achieved using the following methods:

- Non-invasive tests (NITs): Several diagnostic scores, including the fatty liver index, hepatic steatosis index, and triglyceride–glucose index, are available.[9,10] In settings where imaging modalities are not accessible, these blood-based NITs may be considered as alternative screening tools.
- Imaging Methods: Ultrasonography is the most used imaging modality. For more detailed assessment, Magnetic Resonance Imaging Proton Density Fat Fraction (MRI-PDFF), a non-invasive specialized MRI technique used to accurately quantify the fat fraction in the liver, or computed tomography (CT) may be used.

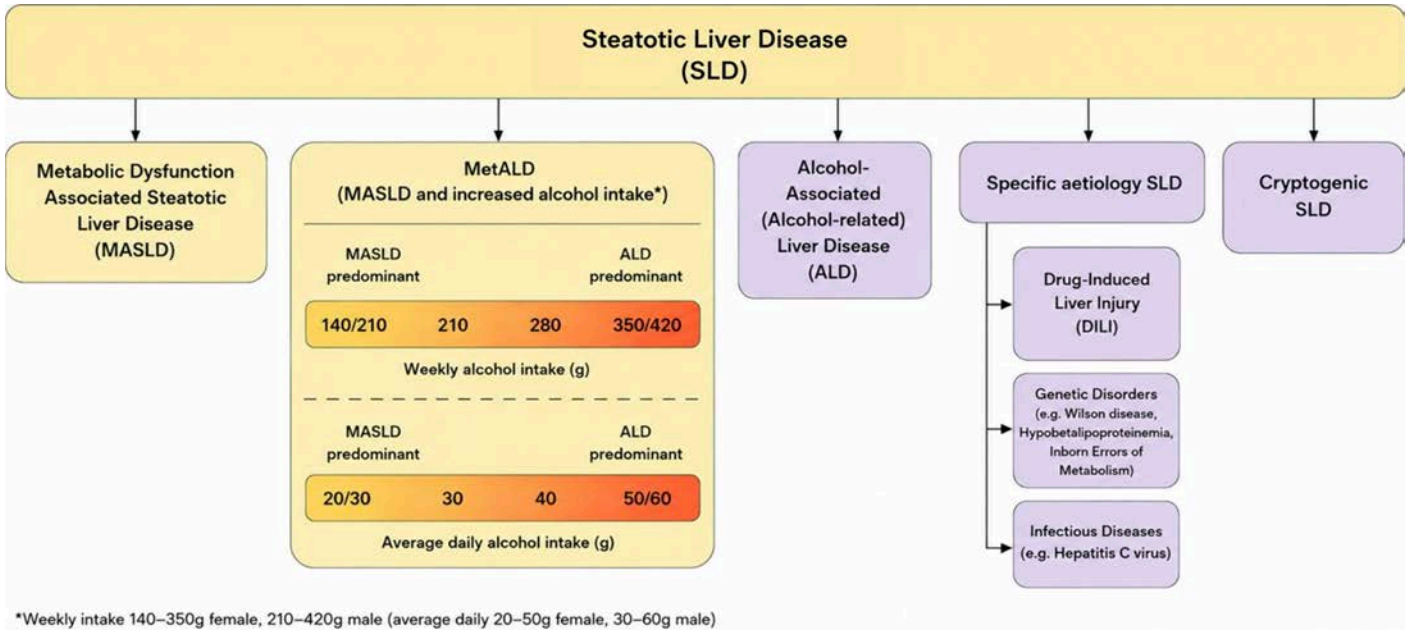


Figure 1. Classification of steatotic liver disease (SLD) according to the updated nomenclature. Adapted from [2].

SLD: Steatotic liver disease; MASLD: Metabolic dysfunction-associated steatotic liver disease; MetALD: Metabolic dysfunction and alcohol-related liver disease; ALD: Alcohol-related liver disease; DILI: Drug-induced liver injury.

- Vibration-Controlled Transient Elastography (VCTE): A non-invasive method that quantitatively assesses both hepatic steatosis through the Controlled Attenuation Parameter (CAP) and liver fibrosis through Liver Stiffness Measurement (LSM).
- Biopsy: Although considered the "reference standard" for definitive diagnosis, it is not routinely performed due to its invasive nature. It may be considered when accompanying causes of liver disease are suspected, or when there is concern regarding disease severity and progression.

Identification of Metabolic Risk Factors

The identification of at least one cardiometabolic risk factor is a prerequisite for the diagnosis of MASLD in individuals with hepatic steatosis. The five qualifying cardiometabolic risk categories and their respective diagnostic criteria are summarized in Figure 2:

Exclusion of Other Causes

To confirm a diagnosis of MASLD, alternative causes of hepatic steatosis should be excluded, including excessive alcohol consumption (defined as an average daily intake of ≥20 g for women and ≥30 g for men), viral hepatitis (e.g., hepatitis B or C), and drug-induced liver injury. The clinical algorithm for MASLD terminology is summarized in Figure 2.

Epidemiology

The prevalence of MASLD is increasing worldwide in parallel with the rising prevalence of obesity and other cardiometabolic risk factors. Current estimates suggest that approximately 1.3 billion people worldwide are affected by MASLD.[11–13] The disease is more common in men than in women, with reported prevalence rates of approximately 40% and 25%, respectively.[14] Furthermore, MASLD has emerged as one of the leading indications for liver transplantation in many parts of the world.[15] In 2021, mortality due to MASLD-related cirrhosis was reported as 97,403 cases, and hepatocellular carcinoma (HCC)-related deaths reached 40,925 cases.[11] This indicates that the incidence of the disease will continue to rise for both genders in the coming years. Projections suggest that an additional 667 million cases of MASLD will occur by 2045, highlighting the substantial and growing global burden of the disease.[16] Moreover, MASLD is not limited to adults but also affects children, with disease processes potentially beginning as early as the fetal stage and continuing throughout the lifespan into late adulthood. The global prevalence of MASLD in children is estimated to be approximately 7%, increasing to around 14% among adolescents.[17] A recent meta-analysis based on data from Turkish pediatric populations reported a markedly higher prevalence of up to 50%; however, this estimate was derived from cohorts of children with obesity or those with elevated liver transaminases. Consequently, these findings are not representative of the general pediatric population, for which robust prevalence data remain limited.[18] In contrast, a previous autopsy-based liver biopsy study conducted in children and adolescents aged 2–20 years reported a prevalence of approximately 6%, which is consistent with estimates from the broader literature.[19]

The prevalence of cardiometabolic risk factors, particularly type 2 diabetes mellitus (T2DM) and obesity, has increased substantially in Türkiye over recent decades. According to World Health Organization estimates, the age-standardized prevalence of obesity among adults in Türkiye was 33.3% in 2022.[20] Data from TURDEP-I and TURDEP-II,

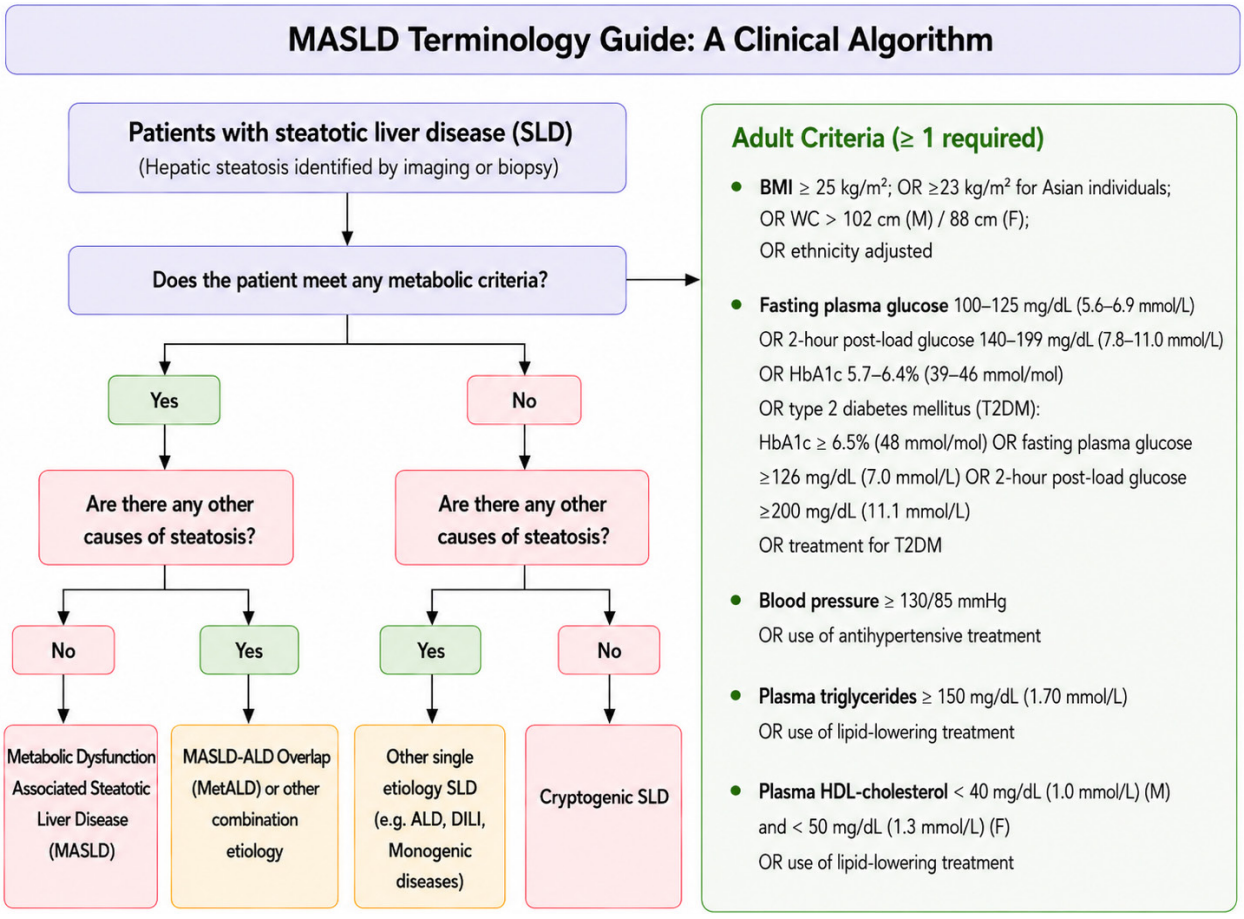


Figure 2. Clinical algorithm for the diagnosis and classification of steatotic liver disease (SLD) according to the MASLD nomenclature. Modified from [2].

SLD: Steatotic liver disease; MASLD: Metabolic dysfunction-associated steatotic liver disease; MetALD: Metabolic dysfunction and alcohol-related liver disease; BMI: Body mass index; WC: Waist circumference; T2DM: Type 2 diabetes mellitus; HDL: High-density lipoprotein.

which monitored the course of metabolic diseases in the adult population of Türkiye, revealed that over a 12-year period between 1998 and 2010, the prevalence of T2DM increased from 7.2% to 16.5%, and the prevalence of obesity rose from 22% to 36%.[21,22]

Parallel to this metabolic increase in the population, MASLD prevalence in Türkiye is projected to exceed 30%. Türkiye has thus become one of the countries with the highest global prevalence of hepatic steatosis in the world in line with the increase in metabolic risk factors. In a community-based study, the ultrasonographic prevalence of SLD was reported as 60.1%, while a multi-center screening study found the MASLD prevalence to be 45.5%, another check-up study found that the overall prevalence of NAFLD as 48.3%.[23–25] Current histopathological data based on forensic autopsy series reveal that 43.3% of the population has steatotic liver disease, pointing to a prevalence that extends beyond clinical diagnosis rates.[26] This high prevalence is directly related to the dramatic upward trend in the frequency of obesity (36%) and T2DM (16.5%), which is also supported by epidemiological data (Table 4).

When the progressive course of the disease is examined, a significant proportion of MASLD cases in Türkiye carry the risk of hepatic inflammation and injury. An autopsy-based study confirmed the presence of MASH (steatohepatitis) in approximately 20.6% of individuals with steatosis.[26] Furthermore, MASLD prevalence is particularly higher in at-risk populations with existing cardiometabolic risk factors. Among adults with at least one cardiometabolic risk factor, the frequency of MASLD has been reported to be as high as 75.7%, while a high risk of advanced fibrosis, as defined by the FIB-4 score, has been identified in 12% of individuals.[27] Moreover, MASLD severity is known to increase with the cumulative burden of cardiometabolic risk factors, reaching its highest level in the presence of T2DM.[28] Another recent Turkish study reported a MASLD prevalence of 73.2% among patients with T2DM, with significant fibrosis identified in 14.1% of the cohort.[29] These data demonstrate that the burden of MASLD in our country extends beyond simple steatosis and represents a major public health concern, with the potential to progress to end-stage liver disease, including cirrhosis and hepatocellular carcinoma (HCC).

Natural Course and Risk Factors

Although MASLD is generally a slow-progressing disease, inflammation and progressive fibrosis develop in a small subset of patients

Table 4. Prevalence of steatotic liver disease and MASLD in Türkiye: summary of major epidemiological studies

Author (year)	Study type	Population/sample size	Diagnostic method	Prevalence (%)	Terminology used
Değertekin et al. (2021)[23]	Retrospective hospital-based study	6,567 check-up patients	US	48.3	NAFLD
Sezgin et al. (2023)[24]	Cross-sectional cohort study	2,797 individuals	US	60.1	SLD
Yilmaz et al. (2021)[25]	Multicenter, prospective cohort study	909 dyspeptic patients	US	45.5	MAFLD
Ergenc et al. (2024)[26]	Forensic autopsy study (cross-sectional)	62 autopsy cases (out of 1,797)	Histopathology	43.3	MASLD
Kirik et al. (2025)[27]	Cross-sectional multicenter study	14,371 adults with cardiometabolic risk factors	US	75.7	MASLD

US: Ultrasonography; SLD: Steatotic liver disease; NAFLD: Non-alcoholic fatty liver disease; MAFLD: Metabolic dysfunction-associated fatty liver disease; MASLD: Metabolic Dysfunction-associated steatotic liver disease.

Table 5. Modifiable and non-modifiable risk factors for MASLD and disease progression

Category	Risk factors	Description/clinical significance
Modifiable risk factors	Obesity/overweight	One of the strongest drivers of the disease; weight gain accelerates fibrosis progression.
	Insulin resistance, T2DM, prediabetes	Among the most important predictors of progression; increases the risk of HCC.
	Dyslipidemia	Atherogenic lipid profile increases hepatic steatosis.
	Hypertension	A component of metabolic syndrome; associated with fibrosis progression.
	Sedentary lifestyle	Lack of physical activity facilitates disease development.
	Unhealthy diet	Diets rich in fructose and saturated fats increase steatosis.
	Alcohol consumption (especially concomitant)	Exhibits a synergistic effect with metabolic factors.
	Smoking	Associated with HCC and fibrosis progression.
	Sarcopenia	Contributes to disease progression by increasing insulin resistance.
Non-modifiable risk factors	Genetic predisposition (PNPLA3, TM6SF2, MBOAT7, etc.)	Determinant in disease development and severity.
	Age (>50)	Risk of developing fibrosis and cirrhosis increases.
	Gender and hormonal status	Risk is higher in men and postmenopausal women.
	Ethnicity	Higher prevalence and severity in certain populations (e.g., Hispanic individuals).
	Family history	Reflects a combination of genetic and environmental factors.

T2DM: Type 2 diabetes mellitus; HCC: Hepatocellular carcinoma.

with MASLD. The rate of liver fibrosis progression is the most critical factor determining the prognosis of the disease. According to comprehensive paired-biopsy studies, the rate of fibrosis progression in patients with MASLD has been calculated at an average of one stage every 14 years.[30] However, this process is not linear; while some patients remain stable for a long time (non-progressors), others may exhibit a "fast-progressor" character. The risk factors for both the development and rapid progression of the disease are similar (Table 5).[31] In paired biopsy studies conducted in Türkiye, fibrosis progression was found to be significantly associated with baseline hypertension and elevated AST and ALT levels.[32]

The progression from simple steatosis to cirrhosis typically occurs over a period of 20–30 years. Population-based data show that approximately 3–5% of patients with MASLD progress to cirrhosis at the end of this process.[33] Once cirrhosis has developed, the annual risk of developing HCC is approximately 1–1.5%.[34] Notably, HCC associated with MASH can occur without the development of cirrhosis (non-cirrhotic HCC). In patients with MASLD, cardiovascular disease is the leading cause of death, followed by extrahepatic malignancies and liver-related complications.[33] Although the course of the disease varies on an individual basis, effective management of metabolic factors can slow down progression or allow for fibrosis regression.[35]

Recommendations

1. SLD should be used as a comprehensive umbrella term for all hepatic fat accumulation etiologies. Within this framework, MASLD (formerly NAFLD) represents the largest metabolic subgroup. Due to the high concordance rate (up to 99%) between NAFLD and MASLD, which ensures the continuity of existing scientific data while providing an affirmative and non-stigmatizing diagnosis, the updated nomenclature is preferred in clinical practice. [LoE: High; SoR: Strong]
2. Considering its high prevalence and disease burden in Türkiye, MASLD should be recognized as a major public health concern. Efforts should be made to increase both public and professional awareness, ensuring that MASLD is routinely considered in clinical practice by healthcare providers. [LoE: Moderate; SoR: Strong]
3. The presence of at least one cardiometabolic risk factor, such as obesity, T2DM, or hypertension, is the primary driver for MASLD diagnosis and serves as the most important critical predictor of disease progression. Consequently, all patients should undergo regular and systematic evaluations for all cardiometabolic risk factors. [LoE: High; SoR: Strong]

Screening and Diagnosis of MASLD

Although MASLD is a highly prevalent disorder affecting approximately 50% of the population in Türkiye, its diagnosis is not always straightforward.[25] This challenge can be attributed to limited physician awareness and delays in timely clinical action.[36] This section aims to outline a diagnostic pathway for physicians managing patients with MASLD in both primary and secondary care settings, incorporating non-invasive and invasive diagnostic strategies applicable to routine clinical practice in Türkiye.

Which Patients Should be Screened Primarily?

Given the high prevalence of MASLD, there is a need for cost-effective and patient-friendly screening strategies that can accurately identify individuals who require specialized care. These strategies should also minimize unnecessary healthcare utilization and expenditures. Screening is particularly recommended for individuals with concomitant comorbidities, as they are at greater risk of developing MASLD and its associated complications. Therefore, targeted screening of individuals at high risk for advanced fibrosis represents a justified and appropriate approach. MASLD is most commonly observed in individuals with metabolic comorbidities, including T2DM, obesity, hypertension, and hyperlipidemia.[12] T2DM is strongly associated with advanced fibrosis, the most important prognostic determinant of MASLD, affecting up to 17% of patients with MASLD and T2DM.[37] In addition to the high prevalence of advanced fibrosis in this group, individuals with T2DM exhibit the poorest survival outcomes compared with those with other metabolic risk factors, with a fourfold increase in overall mortality and a twentyfold increase in cardiovascular mortality.[28] These observations further support the rationale for targeted screening in this population. Indeed, screening high-risk individuals has been shown to be more cost-effective than no screening.[38,39] In particular, screening individuals with evidence of hepatic steatosis and a high cardiometabolic burden has been demonstrated to be both cost-effective and diagnostically efficient.[40,41]

As noted previously, the prevalence of MASLD among children with obesity or a high metabolic burden is comparable to that observed in adults and is associated with a lifelong disease burden.[18] Therefore, screening could be encouraged in these high-risk pediatric populations. Given the early onset of disease and its potentially prolonged course, affected individuals may require long-term follow-up throughout adulthood. Notably, pediatric MASLD is associated with a significantly higher likelihood of requiring liver transplantation compared with the general population.[42] However, screening strategies in children differ from those used in adults and are primarily based on ultrasonography, measurement of transaminase levels, and assessment of metabolic risk factors.[43]

Recommendations

1. Patients with T2DM, obesity + ≥1 cardiometabolic risk factor, or signs of hepatic steatosis should be screened for advanced liver disease. [LoE: Moderate; SoR: Strong]
2. Children with obesity, elevated transaminase levels, or conditions associated with a high metabolic burden should be screened for the presence of MASLD. These individuals should undergo regular long-term follow-up to monitor disease progression and liver-related outcomes. [LoE: Low; SoR: Strong]

Use of Non-Invasive Diagnostic Tests in Screening and Diagnosis

Although liver biopsy remains the reference standard for the diagnosis of MASLD, NITs have demonstrated strong performance in the initial risk stratification of the disease and enable more accurate identification of advanced disease in high-risk individuals.[44] Risk stratification for fibrosis can be performed using both blood-based biomarkers and imaging modalities. For the screening of high-risk individuals—such as those with T2DM, obesity with at least one additional cardiometabolic risk factor, or evidence of hepatic steatosis—the FIB-4 index is an appropriate and widely used first-line tool for risk stratification. Its reliance on routinely available clinical parameters and ease of calculation make it particularly well-suited for use in primary care settings. However, its performance may be limited in certain populations, including younger individuals, lean patients and those with severe obesity; therefore, results should be interpreted with caution in these groups.[45,46] Additionally, caution is required when interpreting these findings for children and pregnant women, as the performance is less reliable within these specific groups.[47,48]

A FIB-4 value <1.3 generally excludes a high risk of advanced fibrosis, whereas in individuals older than 65 years, a higher threshold of <2.0 is recommended for the same purpose. The utility of the FIB-4 index, including its diagnostic performance, has been validated across various clinical settings and comorbid conditions such as type 2 diabetes mellitus and obesity. Studies conducted in Turkish cohorts have demonstrated a high negative predictive value, supporting its effectiveness in

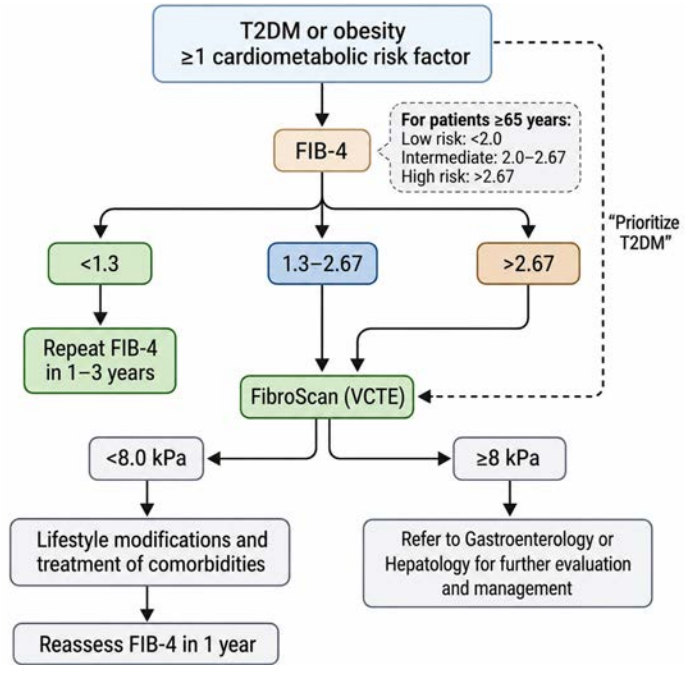


Figure 3. MASLD risk stratification and management algorithm.

MASLD: Metabolic dysfunction-associated steatotic liver disease; T2DM: Type 2 diabetes mellitus; VCTE: Vibration-controlled transient elastography; *: If available, MRE or ELF score can also be considered in the second step.

reliably excluding advanced fibrosis.[45,49,50] Although several alternative non-invasive scoring systems, such as the NAFLD Fibrosis Score (NFS), aspartate aminotransferase-to-platelet ratio index (APRI), and BARD score, are available, the FIB-4 index remains the most widely used for risk stratification. This preference is largely due to its ease of calculation and superior overall performance in identifying advanced fibrosis.[51]

For patients who are not classified as low-risk based on the initial FIB-4 assessment, further diagnostic work-up is required. Current recommendations support a two-step approach, in which individuals with a low probability of advanced fibrosis are first excluded, followed by a more detailed evaluation of those at an increased risk of advanced disease (Fig. 3). At this stage, a second-line assessment using either imaging-based modalities or more advanced blood-based algorithms with higher diagnostic accuracy is recommended. It should be noted that this algorithm is used in triage of the patients rather than evaluation for treatment. Suitable options include imaging techniques such as VCTE and magnetic resonance elastography (MRE), as well as blood-based tests such as the Enhanced Liver Fibrosis (ELF) test.[52–55] MRE has been shown to be particularly advantageous in individuals with obesity; however, owing to its limited availability, higher cost, and greater technical complexity, ultrasound-based techniques such as VCTE are more commonly utilized in clinical practice.[54,56] LSM is widely used as a non-invasive indicator of hepatic fibrosis. An LSM value <8 kPa generally rules out advanced fibrosis, whereas values >12 kPa are associated with a high likelihood of advanced fibrosis; higher values increase the likelihood of cirrhosis and should be interpreted in the appropriate clinical context.[57] With the use of the XL probe, VCTE has demonstrated acceptable performance in individuals with obesity. Conversely, measurement variability in patients with obesity remains a concern. To enhance reliability, performing repeat assessments at a one-week interval can be recommended for this population.[58,59] Moreover, as with other ultrasound-based techniques, accuracy is operator dependent.[60,61] Given the increased risk of advanced fibrosis in patients with T2DM, direct referral to hepatology for VCTE should be considered in this population.[62] This approach has been shown to rapidly reduce false-negative cases to near zero, albeit at the expense of an increased rate of false positives.[63] MRE may also be considered as a second-line assessment modality when available. MRI-based techniques offer advantages over ultrasound-based approaches due to lower operator dependency and reduced susceptibility to patient-related factors, including BMI.[64]

As mentioned previously, for the detection of hepatic steatosis, both blood-based indices, such as the Fatty Liver Index, and imaging modalities, including ultrasonography and FibroScan, can be utilized. MRI-PDFF is considered the reference standard; however, its use is largely confined to research settings and clinical trials.[65,66] Nevertheless, because hepatic steatosis is not the primary determinant of prognosis, screening strategies should not focus solely on its detection.

Role of Liver Biopsy

Although liver biopsy remains the reference standard, its routine use is not recommended because of its invasive nature, potential complications, and associated patient discomfort.[67,68] However, liver biopsy should be considered in selected clinical scenarios, including the following:

1. When the exclusion of concomitant or alternative etiologies is required
2. In the context of clinical trials
3. During bariatric surgery procedures
4. In cases of discordant results between NITs

Table 6 outlines the NITs utilized in the diagnosis and stratification of MASLD, as well as the indications for liver biopsy.

Recommendations

1. The FIB-4 index should be utilized as the first-line tool for risk stratification in patients with MASLD. [LoE: High; SoR: Strong]
2. Patients who are not classified as low risk in the initial step should undergo further evaluation, preferably with VCTE, or MRE if available. [LoE: High; SoR: Strong]
   a. Patients at higher clinical risk, including but not limited to those with type 2 diabetes mellitus, should be prioritized for second-line assessment using VCTE. [LoE: Moderate; SoR: Strong]
   b. Where available, VCTE may also be considered as a first-line risk assessment tool in high-risk populations. [LoE: Moderate; SoR: Conditional]
3. Liver biopsy is not routinely required in the diagnosis of MASLD and should be reserved for selected cases where clinically indicated. [LoE: Moderate; SoR: Strong]

Table 6. Use of NITs and liver biopsy in MASLD diagnosis

NIT	Utility	Setting	Cut-off	Advantages	Disadvantages
Ultrasonography	Detection of hepatic steatosis	Screening tool	Qualitative	Low cost, widely available, first-line screening	Low sensitivity for mild steatosis (<20%), operator-dependent, limited in severe obesity
MRI-PDFF	Detection of hepatic steatosis	Clinical trials	>5.5%	Highly accurate, quantifies fat across the whole liver, reference standard for research	High cost, limited availability, contraindicated in claustrophobia/implants
FIB-4	Estimation of advanced fibrosis	First line triaging of disease severity	<1.3 (Rule-out); >2.67 (Rule-in); <2.0 for age >65	Routine laboratory examination, well qualified for first line triaging	Age dependent, low performance in younger adults, lean and morbid obese patients, children and pregnant women
VCTE	Estimation of fibrosis status	Second step for triaging disease severity	<8.0 kPa (Rule-out F3); 12 kPa (Rule-in F3)	Point-of-care, validated extensively	Affected by BMI (requires XL probe), food intake, congestion, and operator experience
MRE	Estimation of fibrosis status	Second step for triaging disease severity, can be encouraged in obese individuals	F2: 3.14 kPa F3: 3.53 kPa F4: 4.45 kPa	Most accurate NIT for fibrosis staging, whole liver assessment, less affected by BMI/ascites	Very high cost, limited clinical availability, time-consuming
ELF	Estimation of fibrosis status	Second step for triaging disease severity	<7.7 (Rule-out F3); >9.8 (Rule-in F3)	Validated prognostic value for liver-related events	Proprietary test, costly, limited availability in routine clinical labs
Liver biopsy	Reference standard	Clinical trials, discordance in NITs, exclusion of alternative diagnoses	NA (Histological grading/staging)	Direct visualization of MASH activity, assesses co-pathologies, definitive staging.	Invasive, risk of complications (pain, bleeding), sampling error, inter-observer variability

NIT: Non-invasive test; MASLD: Metabolic dysfunction-associated steatotic liver disease; MASH: Metabolic dysfunction-associated steatohepatitis; FIB-4: Fibrosis-4 index; VCTE: Vibration-controlled transient elastography; MRI-PDFF: Magnetic resonance imaging proton density fat fraction; MRE: Magnetic resonance elastography; ELF: Enhanced liver fibrosis; NA: Not applicable.

Treatment of MASLD

The management of MASLD is primarily centered on weight reduction, encompassing lifestyle interventions, pharmacological therapies, and bariatric and endoscopic treatment options, all aimed at achieving meaningful and sustained weight loss. In recent years, clinical trials have led to the approval of therapies specifically targeting MASH, thereby expanding the therapeutic landscape.[69] This section outlines the current treatment approaches for MASLD.

Role of Lifestyle Modifications

Lifestyle modifications, including a healthy diet promoting weight loss and regular physical activity, represent both the initial and fundamental components of MASLD management for any patient group including children. Successful weight loss is defined as achieving a minimum 5% reduction from baseline weight at the sixth month and maintaining it for at least 12 months.[70] Therefore, an evaluation for therapy success can be recommended after six months of lifestyle interventions. A paired liver biopsy study demonstrated that a weight loss of ≥5% of body weight is associated with improvement in hepatic steatosis, 7–10% with resolution of inflammation, and ≥10% with improvement in fibrosis. Notably, nearly all patients who achieved ≥10% weight loss exhibited resolution of MASH, with approximately half also showing regression of fibrosis.[71] Consequently, lifestyle modifications targeting weight loss represent the cornerstone of MASLD management and should be implemented alongside any other therapeutic interventions. However, the long-term sustainability of lifestyle modifications is limited, as they are frequently associated with weight regain; in many cases, substantial or even complete weight regain can occur within slightly more than one year.[72,73] However, even when weight regain occurs, the beneficial effects of prior weight loss, particularly in terms of reductions in hepatic steatosis and improvements in insulin resistance, may persist.[74] Notwithstanding the benefits of weight loss in individuals with obesity, even lean patients with hepatic steatosis may benefit from modest weight reduction, particularly in terms of improvement in hepatic fat content.[75] Therefore, recommending a weight loss of at least 5% of body weight is beneficial for all patients, whereas for lean individuals, a 3–5% target is appropriate.

Lifestyle modifications should aim not only for weight loss (including a hypocaloric diet) but also extend beyond it; specific recommendations regarding dietary composition and types of physical activity should be provided to patients. The Mediterranean diet, characterized by a high intake of olive oil, vegetables, and seafood, and limited consumption of ultra-processed foods, has consistently demonstrated broad health benefits, including improvements in liver health.[76–78] The Mediterranean diet may improve MASLD even in the absence of weight loss. Evidence suggests that adherence to this dietary pattern can reduce hepatic steatosis and improve cardiometabolic health through mechanisms independent of weight reduction, including improvements in insulin sensitivity.[79] Although less extensively studied than the Mediterranean diet, a low-fat diet may also serve as an equally effective dietary pattern providing similar health benefits, particularly for individuals who find the Mediterranean diet less palatable.[77,80] Another commonly adopted dietary approach is intermittent fasting; however, its benefits are less consistently established compared to the Mediterranean diet.[81] Nevertheless, some studies, particularly those evaluating Ramadan fasting, have reported potential metabolic and hepatic benefits.[82] Avoiding sarcopenia is also an important aspect of management, particularly in patients with established cirrhosis or in the elderly. These patients should be prescribed a high-protein diet (1.0–1.5 g/kg/day), ideally combined with resistance training to preserve muscle mass and function.[83] A late-evening snack is another effective nutritional strategy that may help prevent sarcopenia by reducing overnight muscle catabolism.[84]

The consumption of ultra-processed foods has been associated not only with MASLD but also with the development of hepatocellular carcinoma.[85,86] Moreover, improvements in hepatic steatosis have been shown to correlate with the extent of reduction in ultra-processed food intake,[87] suggesting a dose–response relationship in which lower consumption is associated with greater benefits. In addition, the consumption of sugar-sweetened beverages has been associated with an approximately twofold increased risk of MASLD.[88] This effect is largely attributed to their high fructose content. Notably, fructose restriction, even within an isocaloric diet, has been associated with the resolution of hepatic steatosis.[89] As previously reported, there is no established safe threshold for alcohol consumption; therefore, abstinence should be recommended for patients with MASLD.[90] In contrast, regular coffee consumption—particularly an intake of more than two cups per day, ideally three to four cups—has been associated with beneficial effects on liver health.[91,92] Although evidence regarding the impact of brewing methods is limited, traditional preparation techniques, such as filtered coffee, French press, and Turkish coffee, are known to contain compounds with potential hepatoprotective properties.[91] Although direct evidence regarding their effects on liver health is limited, black and green tea may also exert hepatoprotective effects, potentially linked to their well-established cardiovascular benefits.[93,94]

Regular physical activity is an essential component of MASLD management. Notably, moderate- and vigorous-intensity exercise have been shown to confer similar benefits in reducing hepatic steatosis, as assessed by MRI-PDFF.[95] Current recommendations suggest engaging in moderate-to-vigorous physical activity for at least 150 minutes per week to achieve meaningful benefit. However, individuals who concentrate their activity into fewer sessions so-called "weekend warriors" may attain comparable benefits to those exercising more regularly.[96] Both aerobic exercise and resistance training have been shown to reduce hepatic steatosis. Therefore, resistance training may be particularly suitable for patients with limited cardiorespiratory capacity. However, combined exercise programs incorporating both aerobic and resistance components appear to provide synergistic benefits and are preferable when feasible.[97–99]

Recommendations

1. Lifestyle modifications aiming for a weight loss of at least 5% of body weight should be recommended for all patients with MASLD, with an optimal target of ≥10%. For lean individuals, a weight loss target of 3–5% of body weight should be aimed. [LoE: High; SoR: Strong]
2. The Mediterranean diet should be the preferred dietary approach. Consumption of ultra-processed foods and sugar-sweetened beverages should be minimized or avoided. [LoE: Moderate; SoR: Strong]
3. Coffee intake may be encouraged for patients without contraindications, provided that it is well tolerated. [LoE: Moderate; SoR: Conditional]
4. Physical activity combining aerobic exercise and resistance training should be encouraged and tailored to the patient's individual lifestyle and functional capacity. [LoE: High; SoR: Strong]
5. A high-protein diet and resistance training can be encouraged, particularly in elderly patients and those with MASH-related cirrhosis, to preserve skeletal muscle mass and prevent the development of sarcopenia. [LoE: Moderate; SoR: Strong]

Pharmacologic Treatment Options

We have now entered an era in which MASLD is no longer managed solely through lifestyle modification, owing to the recent approval of pharmacological therapies targeting the disease. This development has expanded therapeutic options and raised expectations for the approval of additional agents in the near future. Importantly, not only MASH-specific therapies but also treatments targeting associated comorbidities can contribute to disease improvement through indirect hepatic benefits. This section reviews the current treatment options and outlines future perspectives on the management of MASLD (Fig. 4, Table 7).

Liver-Targeted Therapies

Resmetirom is a liver-directed thyroid hormone receptor-β agonist that reduces hepatic steatosis and inhibits fibrogenesis. Owing to its high selectivity for the β receptor, it minimizes the off-target effects typically associated with thyroid hormones. It is currently the only liver-targeted therapy option[100] approved by both the European Medicines Agency (EMA) and Food and Drug Administration

Table 7. Therapeutic indications and contraindications of medications beneficial in MASLD

Medication	Indication	Cautions/contraindications
Resmetirom (NA in Türkiye)	MASH+F2-F3	Cirrhosis
GLP-1 receptor agonists	T2DM, obesity Can be safely used in MASH	History of medullary thyroid cancer, MEN 2, history of pancreatitis, Child B and C cirrhosis
SGLT2 inhibitors	T2DM, chronic heart and kidney disease	Child C cirrhosis
PPAR	MASH	Heart failure, osteoporosis, weight gain, oedema
Metformin	T2DM	Cirrhosis
Statins	Dyslipidemia	Decompensated cirrhosis, acute liver failure

GLP-1: Glucagon-like peptide-1; MASH: Metabolic dysfunction-associated steatohepatitis; MEN 2: Multiple endocrine neoplasia type 2; NA: Not available; PPAR: Peroxisome proliferator-activated receptor; SGLT2: Sodium-glucose cotransporter 2; T2DM: Type 2 diabetes mellitus.

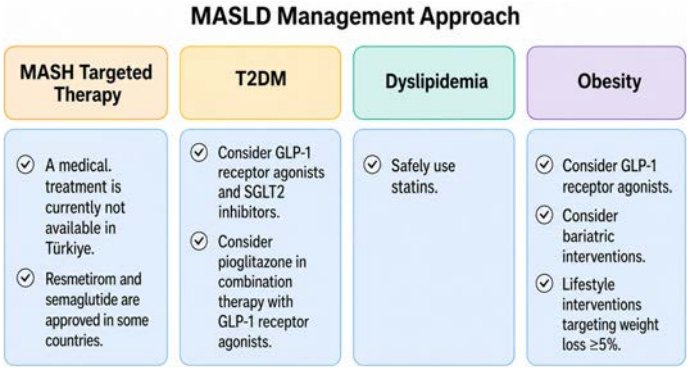


Figure 4. Pharmacotherapy in MASLD considering the comorbidities.

MASLD: Metabolic dysfunction-associated steatotic liver disease; T2DM: Type 2 diabetes mellitus; GLP-1: Glucagon-like peptide-1.

(FDA) for the treatment of noncirrhotic MASH with fibrosis F2 or F3. In the MAESTRO-NASH trial, the drug achieved MASH resolution in approximately 30% of patients and fibrosis improvement in approximately 25% of patients, both significantly higher than the placebo.[101] Following the positive results of this study, resmetirom has been approved in certain regions; however, it is not yet available in Türkiye. Given the FDA's accelerated-approval framework for noncirrhotic MASH with F2–F3 fibrosis, resmetirom's long-term clinical benefit remains to be confirmed in ongoing confirmatory outcome trials, the results of which are not yet available. Additionally, current approaches for determining treatment eligibility rely on NITs, which may have limitations in accurately identifying the most appropriate patients for therapy. Treatment eligibility is largely based on a VCTE-driven algorithm. Other diagnostic methods, such as MRE, may also be considered prior to initiating therapy. These diagnostic algorithms incorporate pharmacologic treatment decisions based on fibrosis assessment; for example, VCTE values above 10 kPa may support inclusion of patients with F2–F3 fibrosis, whereas values below 20 kPa may be used to help exclude cirrhosis (Fig. 5). However, validation in a Turkish MASLD cohort demonstrated significant limitations, with approximately 40% of patients being overprescribed and another 40% underdiagnosed, reflecting a very low level of agreement. Therefore, if the drug becomes available in our country, liver biopsy could be considered prior to treatment initiation in selected cases to ensure appropriate patient

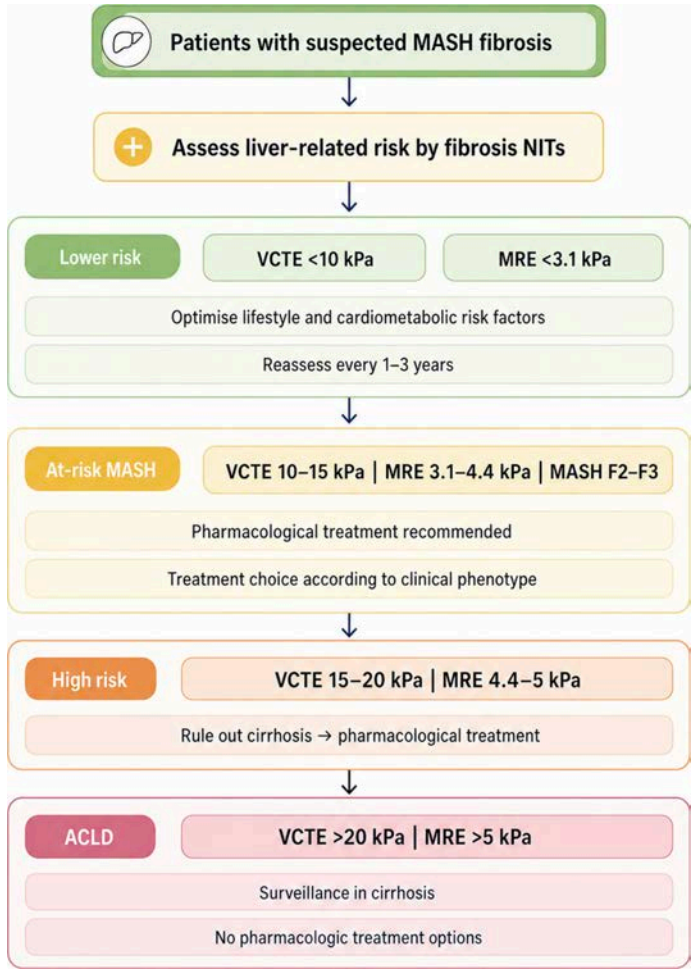


Figure 5. Algorithm for identifying adults with MASLD eligible for pharmacotherapy.

MASH: Metabolic dysfunction-associated steatohepatitis; VCTE: Vibration-controlled transient elastography; MRE: Magnetic resonance elastography; ACLD: advanced chronic liver disease.

selection and avoid unnecessary economic burden.[102] Furthermore, because resmetirom has only recently entered clinical practice, long-term real-world effectiveness, safety, and cost-effectiveness data remain limited, and further post-marketing studies are needed to better define optimal patient selection and treatment outcomes.

Antidiabetic Agents

Metformin is the most commonly prescribed first-line agent for the treatment of type 2 diabetes mellitus. Its principal hepatic benefit lies in reducing the risk of hepatocellular carcinoma by approximately 30%.[103] However, it does not appear to confer significant histological improvement in MASLD, including steatosis, inflammation, or fibrosis. In contrast, some evidence suggests a potential increase in lobular inflammation; therefore, metformin is not recommended as a direct treatment for MASLD.[104] Moreover, it should be avoided in decompensated cirrhosis due to a higher risk of lactic acidosis.[105]

SGLT2 inhibitors (empagliflozin, dapagliflozin) are antidiabetic agents that are preferentially used in patients with cardiovascular and renal disease, owing to their beneficial effects in reducing cardiovascular risk, slowing the progression of nephropathy, and promoting favorable metabolic and tissue-level changes.[106] SGLT2 inhibitors have also been shown to reduce hepatic fat content and lower transaminase levels, supporting their preferential use in patients with comorbid conditions such as cardiovascular or renal disease.[107,108] In addition, they demonstrated improvements in non-invasive markers of liver fibrosis.[109] Furthermore, their use has been associated with improved overall, cardiovascular, and liver-related outcomes in patients with MASLD and diabetes.[110]

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are antidiabetic agents that promote significant weight loss and reduce food intake by delaying gastric emptying and modulating central satiety pathways, in addition to their glucose-lowering effects.[111] Liraglutide was initially evaluated in patients with MASH in the phase 2 LEAN clinical trial. The study met its primary endpoint, with 39% of patients achieving resolution of MASH without worsening of fibrosis. Although significant improvements in liver enzyme levels were not observed, the treatment was associated with weight loss. Furthermore, liraglutide demonstrated a favorable safety profile, with predominantly mild to moderate adverse events.[112] However, its overall efficacy in reducing hepatic steatosis remains uncertain, with conflicting evidence reported in the literature.[113] In contrast, semaglutide appears to have a more favorable profile for the treatment of MASLD than other GLP-1 receptor agonists. In the SWITCH-SEMA trial, switching from liraglutide or dulaglutide to semaglutide resulted in a significant improvement in the Fatty Liver Index.[114] Moreover, following the ESSENCE trial, semaglutide has been approved for the treatment of MASLD due to its significant efficacy in achieving key histological endpoints.[115] However, similar benefits have not been demonstrated in patients with MASH-related cirrhosis, thereby limiting its utility in advanced stages of the disease.[116]

Pioglitazone represents a potentially cost-effective option for the treatment of MASLD, particularly in light of the high costs associated with newer therapies such as GLP-1 receptor agonists. It acts as a peroxisome proliferator-activated receptor (PPAR)-γ agonist with partial PPAR-α activity, thereby improving insulin sensitivity and contributing to reductions in plasma triglyceride levels. Pioglitazone has been shown to exert beneficial effects in MASLD, including reductions in hepatic fat content and inflammation.[117] Accumulating evidence, supported by meta-analyses, indicates its efficacy in improving liver fibrosis.[118] However, its use should be approached with caution due to potential adverse effects, including weight gain, an increased risk of bone fractures, particularly in postmenopausal women and cardiovascular complications related to fluid retention.[119–121] On the other hand, considering their beneficial effects on liver health, combination therapy with other antidiabetic agents, such as GLP-1 receptor agonists or dual GLP-1/GIP agonists, should be considered, particularly in patients with more severe disease. This approach may help minimize weight gain while optimizing liver-related benefits. For these reasons, the use of pioglitazone in MASH settings has already been recommended in T2DM guidelines.[122] Moreover, pioglitazone has been reported to reduce major vascular events, including stroke, and to improve insulin resistance, which further supports its use in appropriate patients.[123] Saroglitazar, another dual PPAR-α/γ agonist currently approved in India, has also demonstrated efficacy in the treatment of MASLD, with a generally favorable safety profile and predominantly mild adverse effects.[124]

Lipid Lowering Agents

Although the safety of statins in patients with MASLD, with the exception of decompensated cirrhosis, has been well established, concerns regarding potential hepatotoxicity persist, leading to the undertreatment of many individuals.[125–127] Statin use can lead to mild elevations in liver transaminases in over 15% of patients; however, clinically significant increases—defined as ALT levels greater than three times the upper limit of normal—are rare, occurring in less than 1% of cases. Consequently, treatment discontinuation is typically not warranted unless this threshold is exceeded. Furthermore, routine serial monitoring of liver enzymes is not required during statin therapy.[128] Statins may exert dose-dependent beneficial effects on liver fibrosis; however, the current evidence remains insufficient to draw definitive conclusions.[129]

Antioxidants

In patients with MASH and advanced liver disease, case–control studies have suggested that long-term vitamin E use is associated with a reduced risk of mortality and liver-related mortality.[130] In addition, the largest randomized controlled trial to date demonstrated that vitamin E supplementation (800 IU daily for two years) in non-diabetic patients with MASH led to significant improvements in hepatic steatosis and overall disease activity, accompanied by reductions in liver enzyme levels.[131] However, the effects of vitamin E on liver outcomes remain inconsistent across studies. In addition, safety concerns have been raised, including potential associations with hemorrhagic stroke, increased all-cause mortality, and prostate cancer.[132–134] Therefore, we do not recommend use of vitamin E in MASLD treatment.

Future Therapies

The therapeutic landscape for metabolic dysfunction-associated steatohepatitis (MASH) is evolving rapidly, with recent advances in pharmacologic options. Specifically, the accelerated approval of resmetirom (Rezdiffra) and semaglutide (Wegovy) now provides clinical pathways for patients with non-cirrhotic MASH and moderate-to-advanced fibrosis (F2–F3).

Beyond these initial approvals, a diverse pipeline of novel therapeutic agents is currently undergoing rigorous evaluation in phase 2 and phase 3 clinical trials. These emerging candidates are designed to target the

complex, multifaceted pathophysiology of MASH, including insulin resistance, obesity, hepatic inflammation, and fibrogenesis. Of particular note are the incretin-based multi-agonists, which include dual GLP-1/GIP agonists (e.g., tirzepatide), dual GLP-1/glucagon receptor agonists (e.g., cotadutide, survodutide, efinopegdutide), and triple GLP-1/GIP/glucagon receptor agonists (e.g., retatrutide). Parallel research continues to explore pathways involving bile acid signaling and lipid metabolism, with promising candidates such as the pan-PPAR α/δ/γ agonist lanifibranor and various FGF21 analogs, including efruxifermin, pegozafermin, and efimosfermin alfa.[135–138]

Clinical data indicate that both FGF21 analogs and incretin-based multi-agonists demonstrate robust histologic and non-invasive responses within a 24–52 week treatment window, frequently outperforming the substantial placebo responses observed in prior MASH clinical trials.[135] These multi-faceted therapeutic approaches reflect an increased capacity to address the complex underlying mechanisms of disease pathogenesis.

Recommendations

1. Pharmacological therapy is not a substitute for lifestyle interventions and should only be used as an adjunct when clinically indicated. Lifestyle modifications should be actively encouraged in all patients receiving pharmacotherapy. [LoE: High; SoR: Strong]
2. Pharmacological therapy with a MASH indication should be targeted at patients with clinically significant fibrosis and should exclude patients with cirrhosis. Treatment eligibility should be based primarily on non-invasive assessment, with VCTE as the preferred modality where available. [LoE: High; SoR: Strong]
    a. Patients with VCTE liver stiffness values in the 10–15 kPa range may be considered a priority group for consideration of pharmacological therapy. [LoE: Moderate; SoR: Conditional]
    b. In patients with VCTE liver stiffness values in the 15–20 kPa range, pharmacological therapy may be considered only if cirrhosis has been confidently excluded through clinical assessment, laboratory parameters, and imaging findings. In cases of diagnostic uncertainty, liver biopsy should be considered. [LoE: Moderate; SoR: Conditional]
3. Patients with MASLD and T2DM should be considered for antidiabetic pharmacotherapies with potential hepatic benefits:
    a. Pioglitazone may be encouraged in patients with type 2 diabetes mellitus and coexisting MASLD, where clinically appropriate and as a combination therapy. [LoE: Moderate; SoR: Conditional]
    b. SGLT2 inhibitors should be considered in patients with MASLD and type 2 diabetes mellitus, particularly in the presence of established or high-risk cardiovascular and/or renal disease. [LoE: High; SoR: Strong]

c. GLP-1 receptor agonists should be considered in patients with MASLD and type 2 diabetes mellitus, particularly in patients with coexisting obesity and/or in whom weight reduction is the key therapeutic target. [LoE: High; SoR: Strong]

Treatment of MASLD: Surgical and Endoscopic Therapy

Obesity has emerged as a critical global health crisis. Obesity is a major risk factor for metabolic syndrome and MASLD. While the prevalence of obesity among patients with MASLD is 50%, this figure reaches as high as 80% in biopsy-proven steatohepatitis cases. Conversely, among patients with obesity, the prevalence of MASLD is reported to be 75%, while that of MASH is 34%.[139]

Lifestyle modifications are recommended as the first-line treatment for obesity in all individuals and should not be abandoned under any circumstances. However, the impact of these approaches on sustainable weight loss remains limited. Pharmacological and bariatric treatments are recommended for patients who fail to achieve weight loss or demonstrate suboptimal weight loss despite at least six months of effort. Bariatric treatments contribute to MASH resolution and fibrosis regression by reducing hepatic inflammation, mitochondrial dysfunction, and endoplasmic reticulum stress, while increasing insulin sensitivity and promoting beneficial gut bacteria.[140] This section highlights the role of endoscopic and surgical interventions in MASLD treatment.

The indications for endoscopic and surgical therapies are defined as follows:[141]

- BMI ≥30 kg/m^2 and the presence of at least one obesity-related comorbidity (T2DM, obstructive sleep apnea (OSA), hyperlipidemia, hypertension, MASH, gastroesophageal reflux disease, asthma, osteoarthritis, polyendocrine metabolic ovarian syndrome (PMOS)).
- BMI ≥35 kg/m^2 (independent of the presence of obesity-related comorbidities).
- Endoscopic treatments are indicated for patients who are not eligible for surgery or who decline surgical intervention.

The contraindications are as follows:[141]

- Untreated major depression or psychosis
- Bulimia nervosa, Anorexia Nervosa
- Drug and alcohol use disorders
- Severe cardiac disease and coagulopathy
- Large Hiatal Hernia (>5 cm), active ulcer disease, severe GERD

Several endoscopic and surgical therapy options are available, and the choice of treatment should be individualized through shared decision-making with the patient. The most commonly preferred methods are illustrated in Figure 6.

Endoscopic Treatment Options

Endoscopic Sleeve Gastroplasty (ESG)

ESG is based on the principle of reducing gastric volume by endoscopic access to the patient's stomach via the transesophageal route and performing full-thickness sutures progressing from the antrum

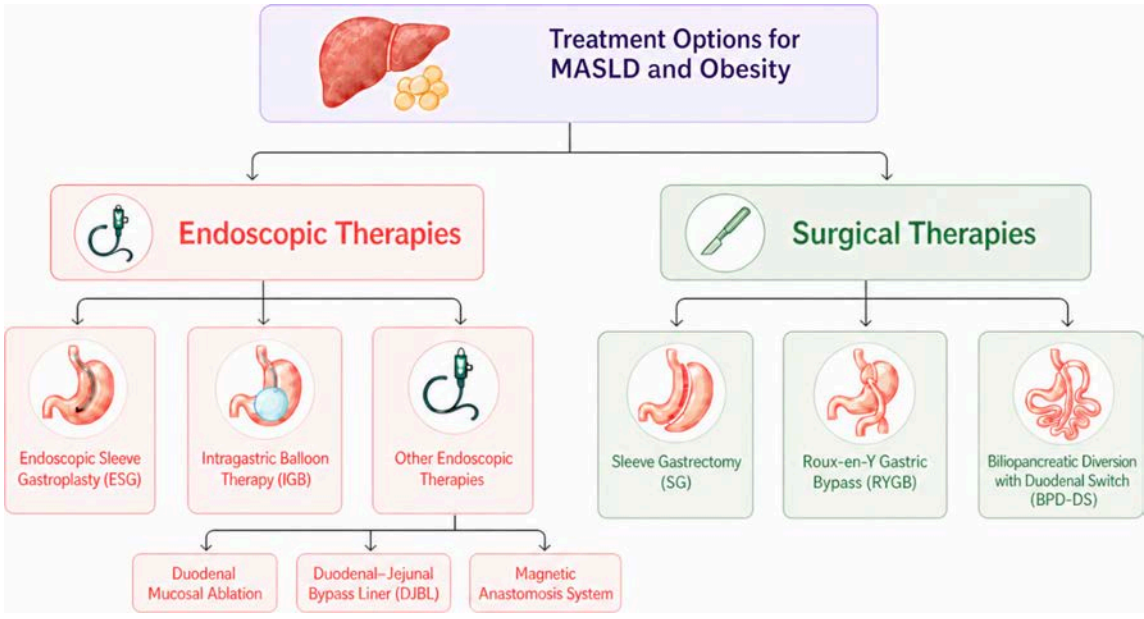


Figure 6. Endoscopic and surgical bariatric treatment options for MASLD and obesity.

toward the fundus. Weight loss following ESG appears sustainable in the long term. A recent meta-analysis demonstrated that at 6 months post-ESG, excess weight loss (EWL) was 48% and total body weight loss (TBWL) was 15.6%; at 60 months, EWL was 45.3% and TBWL was 15.9%.[142] In another meta-analysis evaluating the effects of ESG on patients with MASLD using non-invasive methods, ESG was associated with significant improvements in hepatic steatosis and fibrosis markers.[143]

Intragastric Balloon Therapy (IGB)

The working principle involves a balloon inflated with air or saline to a volume of at least 400 mL, which remains in the stomach for 6–12 months to promote early satiety and delay gastric emptying. The literature reports a TBWL ranging between 7.5% and 14% with this treatment. A meta-analysis of 442 patients found that IGB application resulted in a 79.2% improvement in steatosis and an 83.5% improvement in the MASLD activity score. Additionally, follow-up CT scans showed a reduction in liver volume in 93.9% of the patients. Furthermore, a biopsy-proven study observed an improvement of ≥2 points in the NAS score in 73% of patients and an improvement in fibrosis in 20%.[144]

Other Endoscopic Treatments

A method developed for treating metabolic diseases, such as type 2 DM and MASLD, involves the ablation of the duodenal mucosa between the Ampulla of Vater and the ligament of Treitz using thermal, radiofrequency, or steam therapy. The Duodenal-Jejunal Bypass Liner (DJBL) is designed to reduce nutrient absorption by placing a food-impermeable sleeve approximately 60 cm long into the duodenum. The Magnetic Anastomosis System aims to create a bypass by placing magnets in the duodenum and ileum to interact and form an anastomosis through tissue necrosis, thereby inducing weight loss via malabsorption.[145]

Surgical Methods

Sleeve Gastrectomy (SG)

SG is based on surgical excision of the gastric fundus and corpus to create a tubular gastric sleeve. This significantly reduces gastric volume; furthermore, neurohormonal modulation and changes in gastric emptying emerge as primary mechanisms for weight loss. A review of 3,542 patients found a one-year post-surgical TBWL of 29.5%. Literature evaluation indicates that during 1–3-year follow-ups post-SG, more than 50% of patients show histological and clinical improvement or resolution of MASLD.[146]

Roux-en-Y Gastric Bypass (RYGB)

RYGB is a highly effective and complex surgical method that aims to reduce food intake and nutrient absorption by creating a small gastric pouch and rerouting nutrients through a new path within the small intestine. Patients experience 60–70% EWL after RYGB, with a TBWL of 31.9% reported at the end of the first year. One review demonstrated a 53% reduction in steatohepatitis activity (NAS score) and a 26% reduction in liver fibrosis severity after RYGB. This protective effect persists during long-term follow-up.[147]

Biliopancreatic Diversion – Duodenal Switch (BPD-DS)

BPD-DS combines restrictive and malabsorptive mechanisms by delaying the mixing of bile and pancreatic enzymes with nutrients, resulting in superior long-term weight loss compared with other bariatric procedures. Excess weight loss approaches 80% at 2 years, while biopsy-based studies have reported MASH resolution in 70% of patients and fibrosis improvement in 32%. However, another study found fibrosis improvement in 27% of patients, whereas 40% experienced worsening, which was associated with low albumin levels, uncontrolled diarrhea, and menopausal status.[148–150]

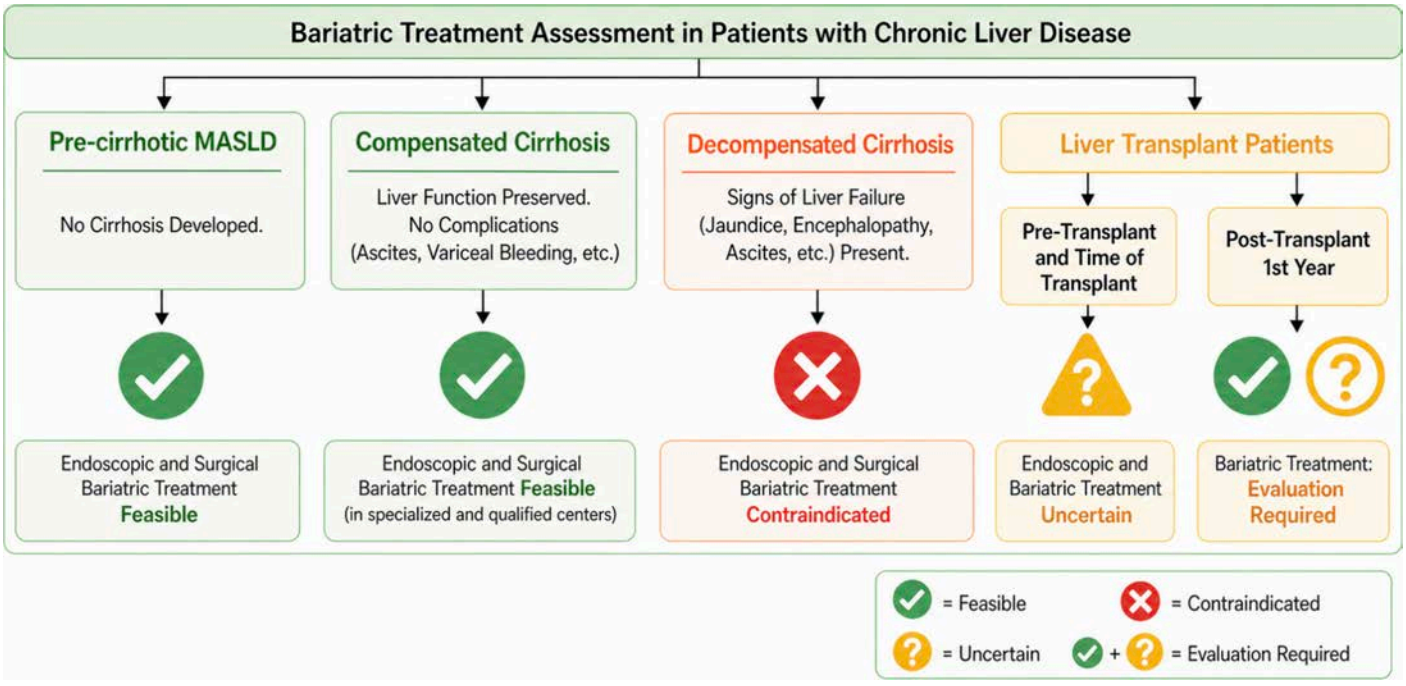


Figure 7. Bariatric treatment algorithm in patients with MASLD.

Bariatric Treatments in Special Populations

MASH Cirrhosis

Bariatric surgery may be preferred in patients with compensated advanced chronic liver disease (cACLD) or compensated cirrhosis (CC) secondary to MASH. However, the presence of clinically significant portal hypertension, indications, and type of surgery must be evaluated by an experienced multidisciplinary team in this specific patient population. In such cases, SG is preferred because of its lower complication rate and sustained long-term weight loss benefits.[151]

Although the perioperative risk is higher in patients with cACLD/CC than in those with pre-cirrhosis, beneficial long-term outcomes have been reported. A study matching 2,107 cirrhotic patients with non-bariatric cirrhotic patients showed that bariatric treatment led to a 37% reduction in all-cause mortality, a 76% reduction in liver-related mortality, a 47% reduction in the risk of decompensation, and a 60% reduction in the risk of transplantation. In the SPECCIAL study, conducted on a biopsy-proven patient group, the bariatric treatment group showed 50% less decompensation and 55% fewer Major Adverse Liver Outcomes (MALO) over a 15-year follow-up than the non-bariatric group.[151–153] Bariatric treatment is considered contraindicated in patients with decompensated cirrhosis unless performed in conjunction with liver transplantation.

Liver Transplant Patients

Bariatric treatment may be applied with careful evaluation in patients on the liver transplant waiting list with cACLD/CC.[154] Sleeve gastrectomy is the preferred approach and may be performed in combination with liver transplantation in selected cases in specialized centers.[151,154,155]

The recommendations are summarized in Figure 7.

Recommendations

1. Bariatric procedures are not a substitute for lifestyle interventions and should only be used as an adjunct when clinically indicated. Lifestyle modifications should be actively encouraged in all patients undergoing bariatric procedures. [LoE: Moderate; SoR: Strong]
2. Bariatric interventions should be performed in accordance with established obesity guideline indications. [LoE: Moderate; SoR: Strong]
3. Bariatric treatments are contraindicated in patients with decompensated cirrhosis. [LoE: Moderate; SoR: Strong]
4. Bariatric treatments are not recommended before or simultaneously with liver transplantation. It is advisable to wait until post-transplantation graft stabilization is achieved (>1 year). In selected cases, sleeve gastrectomy may be an option. [LoE: Low; SoR: Conditional]

Management of Metabolic Comorbidities and Cardiovascular Risk

MASLD is a multisystem disease rather than a condition limited solely to the liver.[156] Indeed, cardiovascular disease (CVD) represents the leading cause of mortality in individuals with MASLD, followed by extrahepatic malignancies. Overall, patients with MASLD have an approximately two-fold higher risk of fatal and non-fatal

Table 8. Checklist for baseline and longitudinal assessment of metabolic comorbidities and cardiovascular risk in MASLD

Time point	Assessment	Comments
At baseline	BMI and waist circumference	Record obesity and central adiposity
	Blood pressure	Measure systolic and diastolic blood pressure
	Fasting lipid profile	Total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides
	Lipoprotein(a)	Once-in-a-lifetime measurement
	Fasting plasma glucose and/or HbA1c	Consider OGTT if results are borderline or discordant
	Serum creatinine and eGFR	Preferably calculated using the CKD-EPI equation
	Urine albumin-to-creatinine ratio (UACR/ACR)	Baseline renal risk assessment
	Formal ASCVD risk estimation	Use a validated tool (e.g. SCORE2/SCORE2-OP in European/Turkish settings)
	Alcohol intake and tobacco use	Document and address at baseline
At every visit	BMI and waist circumference	Monitor change over time
	Blood pressure	Reassess and optimize control
	Alcohol intake and tobacco use	Reassess and reinforce counselling
Every 6–12 months	Fasting plasma glucose and/or HbA1c	Frequency according to baseline risk and diabetes status
	Fasting lipid profile	According to cardiovascular risk and lipid-lowering therapy
	Serum creatinine and eGFR	More frequent if diabetes, CKD, or higher renal risk
	ALT, AST, platelet count	Routine biochemical and fibrosis-related monitoring
Annually or risk-based	Urine albumin-to-creatinine ratio (UACR/ACR)	Especially in diabetes, hypertension, CKD risk, or advanced fibrosis
	ASCVD risk reassessment	Repeat if major risk factors change or at clinically appropriate intervals
	OSA screening	Use a validated questionnaire (e.g. Epworth Sleepiness Scale) in obesity and/or snoring
	Evaluation for PMOS/PCOS	In women with menstrual irregularities and/or hyperandrogenic features
	Sarcopenia screening	Consider SARC-F questionnaire, particularly in patients at higher clinical risk including cirrhosis and obesity treatments

ACR: Albumin-to-creatinine ratio; ALT: Alanine aminotransferase; ASCVD: Atherosclerotic cardiovascular disease; AST: Aspartate aminotransferase; BMI: Body mass index; CKD: Chronic kidney disease; CKD-EPI: Chronic kidney disease epidemiology collaboration; eGFR: Estimated glomerular filtration rate; HbA1c: Glycated hemoglobin; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; OGTT: Oral glucose tolerance test; OSA: Obstructive sleep apnea; PMOS: Polyendocrine metabolic ovarian syndrome; PCOS: Polycystic ovary syndrome; SARC-F: Strength, assistance with walking, rise from a chair, climb stairs, and falls; SCORE2: Systematic coronary risk evaluation 2; UACR: Urine albumin-to-creatinine ratio.

cardiovascular events compared with the general population. Liver-related mortality becomes the dominant cause of death only in those who have progressed to advanced fibrosis or cirrhosis.[157] The MASLD nomenclature places metabolic dysfunction at the center of the diagnostic framework and extends beyond a liver-specific condition, reflecting a broader systemic metabolic disorder. Importantly, accumulating evidence demonstrates that the risk of severe liver outcomes increases in a stepwise manner with each additional metabolic trait, rather than being determined by the presence or absence of any single syndrome definition.[158] In the treatment of MASLD, not only the liver disease itself but also associated comorbidities should be considered and managed through a multidisciplinary approach to reduce both liver-related and overall morbidity and mortality. The baseline and follow-up comorbid parameters in MASLD management are summarized in Table 8. In this section, the management of MASLD is discussed in the context of concomitant comorbidities.

Type 2 Diabetes Mellitus

T2DM is one of the most important comorbidities in MASLD, given both its high prevalence and its significant impact on prognosis. In individuals with T2DM, MASLD is associated with an increased risk of MASH, cirrhosis, HCC, and liver-related mortality, as well as atherosclerotic cardiovascular disease and extrahepatic malignan-

cies. Conversely, individuals with MASLD have a two- to five-fold higher risk of developing incident T2DM compared with the general population.[159] Therefore, all individuals with MASLD should undergo baseline assessment for dysglycemia using HbA1c and/or fasting plasma glucose and vice versa. Moreover, patients with T2DM should be prioritized for risk stratification and further diagnostic evaluation. In case of discordant or borderline results, or when clinical suspicion persists, an Oral Glucose Tolerance Test (OGTT) should be performed. Subsequent monitoring should be risk-stratified according to baseline findings and overall cardiometabolic risk. Individuals with normal baseline results should undergo reassessment at least every three years, whereas those with prediabetes should be monitored annually. Management of T2DM in MASLD should aim to optimize glycemic control while mitigating the risk of progressive liver disease. Lifestyle intervention remains the cornerstone of therapy and should be universally implemented. This includes dietary modification, regular physical activity, and behavioral support, all of which improve glycemic control and reduce hepatic steatosis. Pharmacological treatment should be individualized, balancing glycemic efficacy, safety, and weight effects. Management should follow established diabetes care principles while also accounting for liver-related outcomes as noted previously.[160]

Obesity

Although reported associations between obesity and MASLD vary due to differences in definitions and populations, obesity remains a principal driver of disease. Prevalence increases markedly with rising BMI, reaching approximately 60–90% in obesity, 75–90% in severe obesity, and up to 95% in individuals with BMI >40 kg/m^2. Overall, overweight and obesity predominate in MASLD, affecting approximately 85–90% of patients, whereas the lean phenotype is relatively uncommon, accounting for around 10–15% of cases.[161,162] Visceral adiposity is particularly important in driving progression to MASH, advanced fibrosis, and HCC. Obesity is an independent determinant of morbidity and premature mortality, largely mediated through cardiovascular disease, but also contributing to T2DM, chronic kidney disease, and malignancy.[163]

All adults with MASLD and overweight or obesity should receive structured lifestyle intervention. The presence of MASH and/or clinically significant fibrosis (≥F2) should be regarded as a high-risk feature that justifies earlier escalation to effective weight-loss strategies. Weight loss targets in MASLD are closely linked to histological improvement. A reduction of at least 3–5% of body weight is associated with improvement in hepatic steatosis. Greater weight loss of 7–10% is typically required for resolution of steatohepatitis, while a reduction of 10% or more is associated with improvement or regression of liver fibrosis.

Hypertension

Hypertension is defined as a systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg, or current use of antihypertensive medication. It is a frequent and clinically relevant comorbidity in MASLD, and several studies report on a bidirectional association. The incidence of hypertension increases with advancing liver disease, rising from approximately 6.5 per 100 person-years in early MASLD to over 14 per 100 person-years in patients with cirrhosis, reflecting progressive cardiometabolic and vascular dysfunction.[164]

Hypertension is independently associated with fibrosis progression and adverse liver outcomes. The risk of severe liver events increases in a stepwise manner with the accumulation of metabolic traits. Patients with both hypertension and dyslipidemia have an approximately 1.8-fold higher risk of progression to cirrhosis or hepatocellular carcinoma, underscoring the synergistic effect of cardiometabolic risk factors on liver disease severity.[165]

Blood pressure assessment should be an integral part of MASLD care, and monitored regularly during follow-up, with treatment targets aligned to contemporary hypertension guidelines.

Treatment target for optimal blood pressure control is <140/90 mmHg. Pharmacological treatment of hypertension in MASLD should follow standard hypertension management principles, with attention to agents that may offer additional metabolic or hepatic benefits. Renin–angiotensin–aldosterone system (RAAS) blockers, including angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARBs), are preferred first-line agents in the absence of contraindications. Beyond effective blood pressure control, RAAS blockade may attenuate hepatic fibrogenesis through anti-inflammatory and anti-fibrotic mechanisms. Among ARBs, telmisartan may be particularly attractive in selected patients because of its partial PPAR-γ agonistic activity, which has been associated with improvements in insulin sensitivity and reductions in hepatic fat content compared with other agents in this class.[166] Antihypertensive therapy should always be individualized based on blood pressure control, comorbidities, renal function, and tolerability. Furthermore, lifestyle modifications should complement pharmacotherapy for effective blood pressure management. In adults with hypertension, adopting a healthy dietary pattern, such as the Dietary Approaches to Stop Hypertension diet, and limiting daily sodium intake to less than 2,400 mg may help achieve target blood pressure levels.[167]

Dyslipidemia

Dyslipidemia is an important component of the metabolic dysfunction underlying MASLD and is incorporated into its diagnostic framework as a cardiometabolic risk factor. In adults with MASLD, dyslipidemia is defined by the presence of fasting plasma triglycerides ≥150 mg/dL, low HDL-cholesterol (<40 mg/dL in men or <50 mg/dL in women), or current use of lipid-lowering therapy. In addition, lipoprotein(a) represents an independent, genetically determined risk factor for atherosclerotic cardiovascular disease (ASCVD) and is increasingly recognized as relevant in this population.[168]

At the time of MASLD diagnosis and during regular follow-up, patients should undergo laboratory assessment of fasting plasma

triglycerides, total cholesterol, LDL-cholesterol, and HDL-cholesterol. A once-in-a-lifetime measurement of lipoprotein(a) is recommended, as elevated levels confer an independent and causal risk for Atherosclerotic Cardiovascular Disease (ASCVD) and may influence long-term cardiovascular risk stratification. The presence of dyslipidemia has been independently associated with progression to moderate-to-advanced liver fibrosis, particularly when combined with other metabolic risk factors.[169] Importantly, as MASLD advances to cirrhosis, serum lipid and lipoprotein levels may appear to "normalize" due to impaired hepatic synthesis. This apparent normalization should not be misinterpreted as risk reduction, as these patients often remain at high risk of coronary artery disease and adverse cardiovascular outcomes.

MASLD is not a contraindication to lipid-lowering therapy. Statins are safe across the entire spectrum of MASLD, including in patients with MASH and compensated cirrhosis, and do not increase the risk of hepatotoxicity when used appropriately. Statin use is associated with a lower risk of MASLD progression, MASH, liver fibrosis, and, in patients with cirrhosis, a reduced risk of hepatic decompensation and hepatocellular carcinoma.[170]

LDL-cholesterol treatment targets should be determined according to the patient's overall cardiovascular risk, in line with contemporary cardiovascular prevention guidelines. Routine discontinuation or dose adjustment of statins is not required in MASLD, and treatment should only be interrupted if transaminase levels exceed three times the upper limit of normal in the absence of alternative explanations. In patients with severe hypertriglyceridemia (≥500 mg/dL), treatment with fibrates should be considered to reduce the risk of pancreatitis, alongside dietary fat restriction and optimization of glycemic control.

Chronic Kidney Disease

Chronic kidney disease (CKD) is a common and clinically important extrahepatic comorbidity in MASLD. MASLD and CKD share multiple cardiometabolic risk factors, and accumulating evidence indicates that liver disease severity is directly linked to adverse renal outcomes. Individuals with MASLD have an approximately 1.4–1.5-fold higher risk of incident CKD (stage ≥3) compared with those without MASLD, independent of demographic factors and traditional CKD risk factors. MASLD is associated with an approximately two-fold higher risk of developing CKD over time.[171,172]

Clinicians should assess renal function using serum creatinine and estimated glomerular filtration rate, preferably calculated using the Chronic Kidney Disease Epidemiology Collaboration equation at diagnosis and follow-up. Albuminuria should be tested by spot urine albumin-to-creatinine ratio or, where appropriate, protein-to-creatinine ratio. Albuminuria provides important prognostic information and may precede detectable reductions in eGFR. Periodic monitoring of renal function should be intensified in patients with advanced liver fibrosis, given their higher risk of CKD progression. Individuals with type 2 diabetes or prediabetes warrant particular attention, as abnormal glucose metabolism markedly increases the risk of CKD through microvascular mechanisms and frequently coexists with progressive MASLD.

ACE inhibitors or ARBs are recommended in patients with albuminuria, as they provide renoprotective effects in addition to blood pressure control and may favorably influence fibrogenic pathways.[173] SGLT2 inhibitors are strongly recommended in patients with coexisting MASLD and type 2 diabetes, given their well-established renal protective effects and evidence for slowing CKD progression, alongside their metabolic benefits. Overall, early identification and proactive management of CKD are essential components of comprehensive MASLD care, as renal impairment substantially contributes to long-term morbidity and mortality in this population.

Atherosclerotic Cardiovascular Risk

CVD is the leading cause of death in individuals with MASLD, exceeding liver-related mortality in patients without advanced fibrosis. MASLD is strongly associated with ASCVD, as well as heart failure and cardiac arrhythmias, particularly atrial fibrillation. Overall, patients with MASLD have an approximately two-fold higher risk of fatal or non-fatal cardiovascular events compared with the general population, independent of traditional risk factors.[174]

The shift to MASLD places metabolic dysfunction at the core of disease pathophysiology and reinforces the need for proactive cardiovascular risk assessment and prevention. Traditional risk factors frequently cluster in MASLD, and reliance on liver-focused outcomes alone underestimates long-term prognosis. Cardiovascular risk assessment should therefore be integrated into routine MASLD care.

Cardiovascular Risk Assessment

All adults with MASLD should undergo formal cardiovascular risk assessment, irrespective of age, given the high background burden of cardiometabolic risk and the elevated lifetime risk of ASCVD in this population. Risk should be reassessed periodically, particularly when new metabolic risk factors develop.

For the Turkish population, cardiovascular risk assessment should be performed using the SCORE2 (Systematic COronary Risk Evaluation 2) risk estimation system developed by the European Society of Cardiology (ESC). SCORE2 estimates the 10-year risk of first fatal and non-fatal ASCVD events, specifically myocardial infarction and stroke, and is calibrated according to background regional cardiovascular risk. Türkiye is classified as a high-risk region within the ESC framework, and the corresponding SCORE2 charts should therefore be applied. SCORE2 is validated for adults aged 40 to 69 years, while SCORE2-OP (Older Persons) is designed for individuals aged 70 years and older. It is important to note that SCORE2 focuses on atherosclerotic outcomes and does not estimate the risk of heart failure, atrial fibrillation, or renal outcomes, nor does it incorporate albuminuria or non-traditional biomarkers.

American Heart Association Predicting Risk of Cardiovascular Disease Events (PREVENT) ASCVD risk calculator may be used in

selected settings. PREVENT can be applied from 30 years of age, provides both 10-year and 30-year risk estimates, and includes a broader range of cardiovascular outcomes, including heart failure.[175] PREVENT is derived from U.S. populations and is not regionally calibrated for Europe, therefore SCORE2 remains the preferred tool for routine cardiovascular risk assessment in Türkiye, in alignment with European prevention guidelines.[176]

Based on the estimated 10-year risk of ASCVD, patients are broadly classified as:

- Low to moderate risk: <5% (age-adjusted thresholds apply in younger individuals)
- High risk: ≥5% to <10% (includes many individuals with diabetes, CKD stage 3, or multiple metabolic risk factors)
- Very high risk ≥10% (includes patients with established ASCVD, diabetes with target-organ damage, severe CKD, or very high calculated risk)

In primary prevention, patients at moderate cardiovascular risk should generally aim for an LDL-cholesterol level below 100 mg/dL, while those at high risk should target LDL-cholesterol below 70 mg/dL with at least a 50% reduction from baseline. Individuals at very high risk, including those with established atherosclerotic cardiovascular disease, diabetes with target-organ damage, severe chronic kidney disease, or very high calculated risk, should aim for LDL-cholesterol below 55 mg/dL and a ≥50% reduction from baseline.

Obstructive Sleep Apnea (OSA)

OSA is a frequent extrahepatic comorbidity in MASLD, particularly among individuals with overweight or obesity. Compared with the general population, patients with MASLD have an approximately 2.2-fold higher risk of OSA, reflecting shared mechanisms such as insulin resistance, visceral adiposity, and intermittent hypoxia. OSA-related hypoxia has been associated with worsening metabolic dysfunction and more severe liver disease, including increased risk of steatohepatitis.[177]

Clinicians should maintain a high index of suspicion for OSA in patients with MASLD and should perform systematic clinical screening using targeted history and validated questionnaires, such as the Epworth Sleepiness Scale (and other recognized tools), focusing on symptoms of excessive daytime sleepiness, snoring, witnessed apneas, and nocturnal choking. Patients identified as being at high clinical risk should be referred for further diagnostic evaluation and management according to standard sleep-medicine practice.

Polyendocrine Metabolic Ovarian Syndrome (PMOS)

Polyendocrine metabolic ovarian syndrome (PMOS), previously known as polycystic ovary syndrome (PCOS), is a common multisystem endocrine and metabolic disorder affecting approximately one in eight women worldwide.[178] PMOS is characterized by hyperandrogenism, insulin resistance, and metabolic dysfunction, all of which promote hepatic fat accumulation and help explain its close association with MASLD. Women with PMOS have a markedly higher prevalence of MASLD and a more than twofold increased risk of developing type 2 diabetes. MASLD prevalence in PMOS ranges from about 34% to 70%, with a pooled estimate of around 43% in a large meta-analysis.[179] Emerging evidence suggests an association between PMOS and increased severity of steatohepatitis, although its impact on long-term fibrosis progression remains under investigation.[180] In women with MASLD, particularly those with features of hyperandrogenism or menstrual irregularities, PMOS should be considered and assessed as part of the broader metabolic evaluation.

Sarcopenia and Sarcopenic Obesity

Sarcopenia, defined by reduced skeletal muscle mass, strength, and function, and sarcopenic obesity, the coexistence of muscle loss with excess adiposity, are common in advanced MASLD, especially in cirrhosis. Compared with the general population, MASLD is associated with an approximately two-fold higher risk of sarcopenia.[181] Sarcopenia affects about 23.5% of patients with MASLD overall and increases markedly with cirrhosis, reaching approximately 41% and increasing further in advanced stages.[182] The majority of these patients have sarcopenic obesity.[183] Sarcopenia is associated with increased risk of fibrosis, hepatic decompensation, reduced physical function, and higher mortality.[184] In patients with MASH-related cirrhosis, nutritional and lifestyle interventions described under Role of Lifestyle Modifications should be adapted to preserve muscle mass.

Smoking and Alcohol

In addition to metabolic risk factors, alcohol consumption and tobacco use are important modifiers of disease course and cardiovascular risk in MASLD and should be routinely assessed. Notably, there is no established safe threshold for alcohol consumption in individuals with MASLD, and adverse liver and cardiometabolic effects may occur even at low or moderate levels of intake; the absence of criteria fulfilling overlap phenotypes such as MetALD does not imply safety. Tobacco smoking is independently associated with increased risks of cardiovascular disease, malignancy and all-cause mortality, and may further exacerbate both liver-related and extrahepatic outcomes.[185,186] Given their high prevalence in Türkiye and clinically significant impact,[187,188] alcohol use and smoking should be actively identified, counselled, and discouraged in all patients with MASLD as an integral component of comprehensive disease management. The ultimate goal should be complete smoking cessation and total abstinence from alcohol.

Recommendations

1. Body mass index (BMI) and waist circumference should be recorded at baseline and reassessed at each follow-up visit. [LoE: Moderate; SoR: Strong]
2. Systolic and diastolic blood pressure should be measured at baseline and monitored at every follow-up visit. [LoE: High; SoR: Strong]
3. A fasting lipid profile, including total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides, should be obtained at baseline and repeated at intervals determined by the patient's cardiovascular risk category and lipid-lowering treatment status. [LoE: High; SoR: Strong]
4. Lipoprotein(a) should be measured once in a lifetime to refine long-term ASCVD risk assessment. [LoE: Moderate; SoR: Strong]
5. Fasting plasma glucose and/or HbA1c should be measured at baseline and monitored periodically thereafter, with frequency tailored to baseline results and the individual risk profile. An OGTT should be considered when results are borderline or discordant, or when clinical suspicion persists. [LoE: High; SoR: Strong]
6. Assessment of insulin resistance using the homeostasis model assessment of insulin resistance (HOMA-IR) or OGTT-derived indices may be considered in patients without established diabetes or dysglycemia when clarification of metabolic dysfunction is clinically relevant. [LoE: Low; SoR: Conditional]
7. Renal risk should be assessed at baseline using serum creatinine with estimated glomerular filtration rate and urine albumin-to-creatinine ratio, and monitored thereafter at intervals guided by fibrosis stage, diabetes status, baseline renal function, and albuminuria. [LoE: Moderate; SoR: Strong]
8. Formal ASCVD risk estimation should be performed using an appropriate validated risk tool (for example, SCORE2/SCORE2-OP in European/Turkish settings), and updated when major risk factors change or at clinically appropriate intervals. [LoE: Moderate; SoR: Strong]
9. Smoking and alcohol intake should be routinely assessed and actively addressed as part of comprehensive risk management at baseline and during follow-up. Complete abstinence from both smoking and alcohol should be the goal. [LoE: Moderate; SoR: Strong]
10. In patients with obesity and/or symptoms suggestive of OSA (e.g., snoring), screening with a validated questionnaire such as the Epworth Sleepiness Scale should be considered, with referral for diagnostic evaluation when clinical risk is high. [LoE: Moderate; SoR: Conditional]
11. All women with menstrual irregularities may be referred for evaluation for PMOS, particularly when accompanied by features of hyperandrogenism or insulin resistance. [LoE: Low; SoR: Conditional]
12. Patients with cirrhosis should be screened for sarcopenia using a brief validated tool such as the SARC-F questionnaire, with further assessment and nutritional/physical intervention where indicated. [LoE: Moderate; SoR: Strong]

Cirrhosis, HCC Surveillance and Liver Transplantation in Patients with MASLD

MASH has increasingly become an indication for liver transplantation in Türkiye, in parallel with the rising prevalence of MASH-related cirrhosis.[189,190] Therefore, the management of MASH should be optimized. In this section, MASH-cirrhosis–related complications, HCC surveillance, and liver transplantation are discussed.

Diagnosis of Clinically Significant Portal Hypertension in MASLD-Related Cirrhosis

The risk of complications in patients with MASLD is determined by the presence, severity, and development of esophageal varices. Non-selective beta-blockers (NSBBs) can reduce variceal hemorrhage and prevent decompensation in individuals with clinically significant portal hypertension (CSPH), defined as a hepatic venous pressure gradient (HVPG) ≥10 mmHg. CSPH is the main driver of decompensation in patients with cACLD, and non-invasive markers can help predict this risk.[191] According to the Baveno VII criteria, CSPH may be ruled out when LSM is <15 kPa and the platelet count is ≥150×10^9/L. In adults with LSM ≥20 kPa and/or platelet count <150×10^9/L, upper gastrointestinal endoscopy should be performed to screen for varices. CSPH can be ruled in when the LSM ≥25 kPa; however, only in non-obese (BMI <30 kg/m^2) adults.[192] The ANTICIPATE-NASH model (based on the combination of LSM, PLT, and BMI) may help to predict CSPH in individuals with compensated MASH-related cirrhosis.[193,194]

Spleen stiffness measurement (SSM) using a 100 Hz specific transient elastography probe is an emerging non-invasive tool for assessing CSPH. In patients with Compensated Advanced Chronic Liver Disease (cACLD), SSM may improve risk stratification for CSPH and high-risk varices, particularly in individuals who fall into the indeterminate ("grey zone") category of the Baveno VII classification (LSM ≥20 kPa or platelet count ≤150×10^9/L). This limitation is especially relevant in patients with MASLD and obesity, in whom the diagnostic performance of liver stiffness–based rule-in thresholds is reduced.[192] In patients who are not candidates for NSBBs (propranolol or carvedilol) and who would otherwise require endoscopic screening according to the Baveno VI criteria, an SSM ≤40 kPa may identify individuals with a low probability of high-risk varices in whom screening endoscopy can be safely avoided. The newly implemented SSM by VCTE at 100 Hz, when combined with LSM, PLT, and BMI in a composite model known as 'non-invasive CSPH estimated risk' (NICER), demonstrated a greater ability to discriminate for identifying patients with CSPH compared to the ANTICIPATE-NASH model.[195] A recent multicenter cohort study, predominantly including patients with MASLD, suggested that although SSM is associated with CSPH, its ability to predict hepatic decompensation is limited when LSM and serum albumin levels are considered.[196]

Recommendations

1. LSM by VCTE ≤15 kPa together with a platelet count ≥150×10^9/L effectively rules out CSPH in patients with MASLD and may help avoid unnecessary endoscopic screening for varices. [LoE: High; SoR: Strong]
2. In patients with cACLD and an LSM ≥20 kPa and/or a platelet count ≤150×10^9/L, screening endoscopy for varices is recommended. In experienced centers, spleen stiffness measurement (SSM) ≤40 kPa may be used as an adjunctive tool to refine endoscopy decisions in these patients. [LoE: High (endoscopy)/Moderate (SSM); SoR: Strong, SSM adjunct: Conditional]
3. If CSPH is present, NSBBs should be considered unless contraindicated or not tolerated. [LoE: High; SoR: Strong]

Hepatocellular Carcinoma Surveillance in MASLD

The recommendation for HCC surveillance in patients with cirrhosis is supported by a strong clinical rationale as well as evidence from a landmark randomized controlled trial.[197] Approximately 80–90% of HCC cases arise in individuals with cirrhosis, and surveillance aims to detect HCC at an early stage when potentially curative treatments are more likely to be feasible and improve survival. There is a consensus among all international societies that patients with MASLD-cirrhosis should undergo HCC screening, as they appear to have an average HCC risk of 1–1.5% year.

The prevalence of MASLD-related cirrhosis and HCC is increasing in Türkiye. In a recent multicenter study from Türkiye with 4953 cirrhotic patients, the etiology of cirrhosis before and after 2010 was compared, and the proportion of MASLD-related cirrhosis increased significantly after 2010, rising from 12% to 25%. In addition, another recent multicenter study from Türkiye reported that the proportion of MASLD-related HCC increased from 6.6% to 13.4% after 2016, reflecting the growing contribution of MASLD to the HCC burden.[190,198,199]

A substantial proportion of MASLD-related HCC cases arise in the absence of cirrhosis. Nevertheless, the overall risk of HCC among patients with non-cirrhotic MASLD remains low and does not generally justify routine surveillance. Therefore, the main challenge is to accurately identify individuals with sufficiently elevated HCC risk among patients with MASLD who do not have cirrhosis. Population-based studies indicate that the incidence of HCC in non-cirrhotic MASLD is low, ranging from approximately 0.08 to 0.63 per 1,000 person-years.[34] In a meta-analysis of 18 studies including 470,404 patients with MASLD without cirrhosis, the incidence rate of HCC was 0.03 per 100 person-years.[200] Another systematic review and meta-analysis of 61 studies reported that nearly 40% of MASLD-related HCC cases occurred in patients without cirrhosis, compared with approximately 15% of HCC cases related to other etiologies. However, only 33% of patients with NAFLD-related HCC underwent surveillance prior to diagnosis.[201] In a cohort study of 1,773 adults with NAFLD, the incidence rate of HCC among patients with advanced fibrosis (F3) was 0.34 per 100 person-years, indicating an intermediate risk that is lower than that observed in cirrhosis but not negligible.[202] However, there is currently no consensus regarding the benefits of routine HCC surveillance in non-cirrhotic MASLD or MASH. Furthermore, staging advanced fibrosis (F3) using non-invasive methods can be challenging, which complicates risk stratification and makes surveillance decisions less favorable from a cost-effectiveness perspective. Therefore, screening for HCC is strongly recommended in patients with MASH-related cirrhosis. Routine HCC surveillance is not recommended in noncirrhotic patients with MASLD/MASH because of insufficient evidence and the low overall incidence of HCC. However, selected patients at higher estimated risk—including those with advanced fibrosis (F3), a family history of HCC, multiple cardiometabolic risk factors (particularly T2DM), or ongoing alcohol consumption—may be considered for individualized HCC surveillance after careful clinical risk assessment until more robust evidence becomes available.[203]

Current international society guidelines recommend ultrasound-based surveillance every 6 months, with or without alpha-fetoprotein measurement, in individuals with cirrhosis, regardless of the etiology. Evidence supporting HCC surveillance with ultrasound and alpha-fetoprotein (AFP) originates from a randomized controlled trial conducted in China.[197] Ultrasound LI-RADS was subsequently introduced to standardize ultrasound interpretation; however, studies including patients with cirrhosis and MASLD have reported high rates of visualization score C (severe limitations), indicating substantial technical limitations and highlighting the operator-dependent nature of ultrasound.[204] Therefore, alternative imaging modalities such as MRI have been explored. Prospective and observational studies have shown that full MRI provides higher sensitivity and positive predictive value for detecting early HCC and is associated with fewer false-positive results than ultrasound. However, the routine use of full MRI for surveillance is limited by its high cost, long examination time, and need for specialized expertise. Abbreviated MRI protocols have been proposed as potential alternatives; however, current evidence remains limited, as most studies are retrospective simulations or include populations that do not fully represent surveillance cohorts. Therefore, further prospective studies and ongoing clinical trials are needed to clarify the role of abbreviated MRI in HCC surveillance.[205]

AFP is currently the only biomarker with sufficient evidence to support its clinical use in HCC surveillance when combined with ultrasound. Two meta-analyses have shown that adding AFP to ultrasound increases the sensitivity for detecting early-stage HCC compared to ultrasound alone, although this improvement is accompanied by a decrease in specificity.[206,207]

Additional risk stratification approaches combining clinical variables, biomarkers, or fibrosis-based non-invasive tests have been explored, but these models remain insufficiently validated for routine clinical implementation. Biomarkers commonly used to improve the performance of AFP include des-gamma carboxyprothrombin (DCP) and lectin-bound AFP (AFP-L3). Several models combine demographic and clinical variables and serum biomarkers, such as the HCC risk

Table 9. Management of comorbidities in patients with MASLD before liver transplantation. Modified from [151, 224]

Condition	Recommendations
Diabetes mellitus	• Screen for impaired fasting glucose (IFG) or glucose tolerance (IGT) and/or T2DM (OGTT, HbA1c) • Achieve good glycemic control before LT • Weight-lowering (e.g., SGLT2 inhibitors or GLP-1 receptor agonists) or weight-neutral agents (e.g., metformin) should be preferred when liver and renal functions allow, with careful assessment of liver disease severity to guide the optimal therapeutic approach.
Nutritional status	• Assess nutritional status before LT • Assess alcohol consumption • Healthy diet, physical exercise and lifestyle modification (including weight reduction in individuals with obesity)
Cardiovascular disease	• Pre-liver transplantation cardiovascular risk stratification is mandatory in such cases. • A structured, multidisciplinary, diagnostic, cardiac workup should be performed. • LT candidates with cardiovascular risk should be managed with goal-directed medical management (e.g. statins, anti-platelet agents, beta blockers, RAAS blockers), based on the stage of cirrhosis and renal function
Kidney dysfunction	• Kidney function should be adequately monitored before LT • Comedications need to be adjusted dependent on kidney function
Malignancies	• Screening for pre-liver transplantation malignancies should follow the same protocols as those applied to patients without MASLD-related cirrhosis.

OGTT: Oral glucose tolerance test; HbA1c: Glycated hemoglobin; SGLT2: Sodium-glucose cotransporter-2; GLP1RA: Glucagon-like peptide-1 receptor agonist; LT: Liver transplantation; RAAS: Renin-angiotensin-aldosterone system; MASLD: Metabolic dysfunction-associated steatotic liver disease.

score, aMAP, and GALAD.[204,205,208,209] The GALAD score, which incorporates AFP, AFP-L3, DCP, age, and sex, is one of the most widely studied biomarker-based models for HCC detection. In a recent study from Türkiye, the GALAD score had sensitivities for any-stage (75.8%) and early-stage (57.8%) HCC, with 93.5% specificity, and demonstrated the best performance in non-viral hepatocellular carcinomas (AUC 0.872).[210] In a meta-analysis of more than 19,000 patients, GALAD demonstrated good diagnostic performance for early HCC. In patients with nonviral liver disease etiologies, the score showed a pooled sensitivity of 0.87 (95% CI 0.81–0.91), specificity of 0.91 (95% CI 0.85–0.95), and an AUC of 0.94 (95% CI 0.92–0.96). However, most of the included studies were retrospective case–control studies with potential selection bias, which may have overestimated the diagnostic performance of the GALAD score.[211,212]

Recommendations

1. HCC surveillance should be performed in all individuals with MASLD-related cirrhosis. [LoE: Moderate; SoR: Strong]
2. Routine HCC surveillance is not recommended in noncirrhotic adult patients with MASLD due to insufficient evidence and the low overall incidence of HCC in this population. [LoE: Moderate; SoR: Strong] However, selected cases such as patients with high metabolic risk, specifically patients with T2DM, may be considered for HCC screening even in the absence of clinical cirrhosis signs. [LoE: Low; SoR: Conditional]
3. Abdominal ultrasonography combined with serum AFP measurement every 6 months is recommended as the primary method for HCC surveillance. [LoE: Moderate; SoR: Strong] However, when feasible, additional laboratory- and imaging-based tools, such as the GALAD score and MRI, may be considered because of their higher diagnostic accuracy. [LoE: Moderate; SoR: Conditional]

Liver Transplantation in MASLD-Related Cirrhosis

MASLD-related cirrhosis has become one of the primary reasons for liver transplantation (LT) in two major transplant registries in the U.S. Scientific Registry of Transplant Recipients (SRTR) and the European Liver Transplant Registry (ELTR).[213] In Türkiye, the proportion of LTs for MASLD-related liver disease increased nearly eightfold from 2010–2014 to 2015–2020.[189]

Patients undergoing liver transplantation for MASLD are often older and have multiple cardiometabolic comorbidities that increase the risk of perioperative complications and long-term risks. Despite the higher burden of cardiometabolic comorbidities, post-transplant survival among patients with MASH appears comparable to other etiologies,[214] as shown in a recent study including a large cohort of LT recipients from both the United States and Europe.[213]

Patients with MASLD, particularly those with T2DM, have an increased risk of cardiovascular and renal complications after liver transplantation, with cardiovascular events occurring most frequently during the early post-transplant period.[215,216] However, recent large registry analyses from the SRTR and ELTR suggest that post-transplant mortality is mainly associated with recipient and donor characteristics (recipient age, MELD score, severe hepatic encephalopathy, donor age, and transplant center volume) rather than the underlying liver disease etiology.[213]

Pretransplant Management of Comorbidities in Patients with MASLD-Related Cirrhosis

In Türkiye, where the prevalence of obesity, T2DM, and MASLD-related cirrhosis is increasing, careful cardiovascular assessment of LT candidates is essential. Current evidence does not support a fundamentally different CVD screening algorithm for MASLD; rather, a stepwise, risk-adjusted, and multidisciplinary approach should be adopted, integrating clinical cardiovascular risk factors, age, functional status, and local cardiology expertise.[151,217,218] Risk stratification tools such as the cardiovascu-

lar risk in orthotopic liver transplantation (CAR-OLT) and coronary artery disease in liver transplantation (CAD-LT) scores may assist in identifying candidates at a higher risk of cardiovascular complications and guide further diagnostic evaluation.[219,220] Because stress-based testing may have limited diagnostic accuracy in advanced cirrhosis, coronary computed tomography angiography (CCTA) may be considered in selected high-risk candidates, while invasive coronary angiography should be reserved for those with positive signals on stress tests or CCTA or strong clinical suspicion of clinically significant CVD. If indicated, revascularization should be performed. Until locally validated data become available, transplant centers in Türkiye should implement standardized evaluation protocols based on international guidelines, available resources, and multidisciplinary expertise.[154]

Management of patients with MASLD prior to liver transplantation requires a comprehensive multidisciplinary approach targeting metabolic comorbidities, nutritional status, cardiovascular risk, renal function, and malignancy screening. Glycemic control should be carefully optimized, with insulin considered the safest option in Child-Pugh class C cirrhosis, while oral agents may be used in patients with Child-Pugh class A and B. Cardiometabolic risk factors, including diabetes, hypertension, and dyslipidemia, should be systematically assessed and treated, given their impact on peri- and post-transplant outcomes. Nutritional assessment and tailored lifestyle interventions are essential, as both obesity and sarcopenia adversely affect the outcomes of transplantation. In addition, renal function should be closely monitored and preserved, and appropriate screening for malignancy should be performed according to international guidelines. A summary of these recommendations is presented in Table 9.

Recommendations

1. Candidates with MASLD-related cirrhosis should undergo multidisciplinary pretransplant evaluation. [LoE: Moderate; SoR: Strong]
2. Pretransplant assessment should include systematic evaluation and optimization of cardiometabolic comorbidities, particularly coronary artery disease, type 2 diabetes, hypertension, dyslipidemia, obesity, sarcopenia, and chronic kidney disease. [LoE: Moderate; SoR: Strong]
3. CVD assessment in candidates with MASLD should follow a stepwise, risk-adjusted, multidisciplinary approach rather than a separate disease-specific algorithm. Risk scores such as CAR-OLT and CAD-LT may help identify candidates who warrant further cardiac investigation. [LoE: Moderate; SoR: Strong]
4. Because stress-based testing may have limited diagnostic performance in advanced cirrhosis, coronary computed tomography angiography may be considered in selected high-risk candidates, while invasive coronary angiography should be reserved for those with abnormal non-invasive findings or strong clinical suspicion of clinically significant coronary artery disease. [LoE: Moderate; SoR: Conditional]
5. Renal function should be closely monitored and preserved before transplantation, and simultaneous liver–kidney transplantation should be considered according to accepted criteria in eligible candidates. [LoE: Moderate; SoR: Strong]

Pretransplant Obesity and Management in Patients with MASLD-Related Cirrhosis

The impact of BMI on post-transplant outcomes remains controversial, and current evidence does not support specific BMI thresholds as contraindications to liver transplantation.[154,221–223] BMI alone inadequately reflects patient risk, as body composition—particularly sarcopenia and sarcopenic obesity—and overall nutritional status are more relevant determinants of outcomes.[224] Therefore, pretransplant management should focus on comprehensive nutritional assessment and optimization of modifiable risk factors. Pharmacological weight loss therapies, including GLP-1 receptor agonists, have not been sufficiently studied in transplant candidates and cannot currently be recommended. Endoscopic bariatric procedures are contraindicated in the presence of clinically significant portal hypertension, whereas bariatric surgery may be considered in carefully selected patients with compensated cirrhosis after failure of conservative measures, preferably in high-volume centers and with prior assessment of portal hypertension. Sleeve gastrectomy is the preferred approach and may be performed in combination with liver transplantation in selected cases.[154] In the setting of living donor liver transplantation, obesity alone does not appear to adversely affect graft or patient survival, although adequate graft-to-recipient weight ratio must be ensured, and sarcopenic obesity has been associated with impaired liver regeneration and worse outcomes.[223]

Recommendations

1. Body mass index alone should not be considered as a contraindication for liver transplantation. Risk stratification should incorporate body composition, sarcopenia or sarcopenic obesity, nutritional status, and overall frailty. [LoE: Moderate; SoR: Strong]
2. All candidates with MASLD-related cirrhosis should undergo formal nutritional and functional assessment, and tailored lifestyle and nutritional measures should be implemented whenever feasible. [LoE: Moderate; SoR: Strong]
3. Pharmacological weight-loss therapy cannot yet be routinely recommended in decompensated transplant candidates with MASLD-related cirrhosis because safety and efficacy data remain limited. [LoE: Low; SoR: Conditional]
4. Bariatric surgery may be considered only in carefully selected candidates with compensated cirrhosis, preferably in high-volume centers and after assessment for clinically significant portal hypertension; sleeve gastrectomy is the preferred approach. Endoscopic bariatric procedures should be avoided in clinically significant portal hypertension. [LoE: Low–Moderate; SoR: Conditional (for surgery)/Strong (against endoscopy in CSPH)]

Management of Cardiometabolic Risk Factors and Recurrence of MASLD After Liver Transplantation

In patients with LT due to MASLD who have a functioning graft, the primary causes of mortality are complications from cardiovascular disease and cancer. Management after LT in recipients with

Table 10. Management of cardiometabolic risk factors and recurrence of MASLD after liver transplantation. Modified from [224, 225]

Condition	Recommendations
Weight gain/obesity	• Dietary and lifestyle counselling should be implemented after LT, as rapid weight gain is common. • Obesity and related comorbidities should be actively treated because they contribute to cardiovascular risk, MASLD recurrence, and reduced long-term survival. • GLP-1 receptor agonists may be considered for weight control and obesity-related comorbidities, although transplant-specific data are limited. • Bariatric surgery may be considered in carefully selected recipients when other measures fail; sleeve gastrectomy is generally the preferred procedure.
Diabetes mellitus	• Good glycemic control should be pursued after LT to reduce cardiovascular and renal complications and possibly lower the risk of recurrent MASLD. • Long-term corticosteroid use should be avoided when possible, particularly beyond 3–6 months in recipients transplanted for MASH/MASLD. • Reduction of CNI exposure may be considered in selected recipients transplanted for MASH/MASLD, with or without adjunctive mycophenolate mofetil. • The choice of antihyperglycemic therapy should follow general clinical guidelines and account for renal function and drug interactions.
Hypertension	• Blood pressure should be regularly monitored and treated according to general clinical guidelines. • Optimal blood pressure control is strongly encouraged because it is associated with lower all-cause mortality and fewer cardiovascular events after LT. • Calcium channel blockers (Amlodipine or felodipine) are the first-line antihypertensive therapy. • In the presence of concurrent CAD, HF, CKD or stroke RAS blockers are the initial options. • Modulation of immunosuppressive therapy with the minimization of CNIs may be required.
Dyslipidemia	• Lipid disorders should be screened and treated according to general clinical guidelines. • Statins can be used after LT, including high-intensity statins when indicated, with careful titration and regular follow-up visits. • Attention should be paid to drug–drug interactions and adverse effects, although significant interactions with common immunosuppressive regimens appear to be limited.
Cardiovascular risk	• LT recipients for MASH/MASLD should be recognized as being at an increased long-term risk of cardiovascular events. • Management should focus on control of obesity, hypertension, T2DM, dyslipidemia, and other modifiable cardiovascular risk factors. • Routine follow-up should be individualized according to the overall cardiovascular risk rather than a fixed echocardiographic schedule for all recipients.
Kidney dysfunction	• Kidney function should be monitored longitudinally after LT. • Management should include optimization of T2DM and blood pressure control and consideration of immunosuppression minimization strategies when appropriate.

LT: Liver transplantation; MASLD: Metabolic dysfunction-associated steatotic liver disease; GLP-1: Glucagon-like peptide-1; MASH: Metabolic dysfunction-associated steatohepatitis; CNI: Calcineurin inhibitors; CAD: Coronary artery disease; HF: Heart failure; CKD: Chronic kidney disease; RAS: Renin-angiotensin system.

MASLD should focus on aggressive control of cardiometabolic risk factors, as rapid post-transplant weight gain, diabetes, hypertension, dyslipidemia, chronic kidney disease, and cardiovascular disease are common and substantially influence long-term outcomes.[224,225] Accordingly, post-transplant management should prioritize dietary and lifestyle measures, strict control of diabetes, hypertension, and dyslipidemia, careful monitoring of kidney and cardiovascular risk, and reduction of the metabolic burden of immunosuppression, particularly avoidance of prolonged corticosteroid exposure, and consideration of calcineurin inhibitor minimization where appropriate (Table 10).

Recurrent and *de novo* MASLD are frequent after LT, particularly in recipients with multiple metabolic risk factors. Recent data suggest that recurrent steatosis may occur in up to 80% of recipients by 5 years after LT, while recurrent MASH has been reported in 28–60% of cases; in a multicenter cohort of recipients transplanted for MASLD-related cirrhosis, 5-year recurrence rates of metabolic syndrome, steatosis, steatohepatitis, and advanced fibrosis were 86%, 80%, 60%, and 20%, respectively. In a recent study from Türkiye, post-transplant MASLD prevalence was 34%. *De novo* MASLD and *de novo* MASH also occur commonly after transplantation, although published studies remain limited by heterogeneous definitions, inconsistent adjudication of pre-transplant MASLD, and variable histologic follow-up. Despite the high recurrence rate, the impact of recurrent MASLD on graft survival appears modest, whereas the accompanying burden of cardiovascular and metabolic complications may be more clinically consequential. At present, no validated surveillance strategy exists for recurrent MASLD after liver transplantation; however, ultrasound and transient elastography with controlled attenuation parameter may be reasonable for follow-up, with liver biopsy reserved for uncertain cases or when alternative graft pathology is suspected.[225,226]

Recommendations

1. Recipients transplanted for MASLD should undergo systematic post-transplant assessment and management of cardiometabolic risk factors, including obesity, diabetes, hypertension, dyslipidemia, chronic kidney disease, and cardiovascular disease. [LoE: Moderate; SoR: Strong]
2. Dietary counselling, physical activity, weight control, and optimization of diabetes, blood pressure, and lipid management should form the cornerstone of post-transplant care in MASLD recipients. [LoE: Moderate; SoR: Strong]
3. Immunosuppressive regimens should be adjusted, when feasible, to reduce metabolic burden, particularly through avoidance of prolonged corticosteroid exposure and consideration of calcineurin inhibitor minimization in selected recipients. [LoE: Moderate; SoR: Conditional]
4. Recurrent and *de novo* MASLD are frequent after LT, particularly in recipients with multiple metabolic risk factors. In the absence of a validated surveillance strategy, screening for recurrent MASLD or *de novo* MASLD may include ultrasound and transient elastography with controlled attenuation parameter, while liver biopsy should be reserved for uncertain cases or when alternative graft pathology is suspected. [LoE: Low; SoR: Conditional]
5. Long-term follow-up should also include monitoring for cardiovascular disease, chronic kidney disease, and extrahepatic malignancy, which substantially influence post-transplant outcomes in this population. [LoE: Moderate; SoR: Strong]

Research Gaps, Evidence Limitations, and Future Recommendations

Although the evidence base for MASLD has expanded substantially in recent years, several important gaps remain. First, robust population-based epidemiological data from Türkiye, particularly in children, adolescents, and older adults, remain limited. Second, further validation of screening strategies, non-invasive diagnostic tools and algorithms for treatment selection in Turkish cohorts is required, especially in patients with obesity and type 2 diabetes mellitus. Third, long-term real-world outcome data for newly approved liver-directed therapies, as well as antidiabetic and anti-obesity pharmacotherapies in MASLD, remain insufficient. This is particularly relevant with respect to fibrosis regression, hepatic decompensation, hepatocellular carcinoma development, and overall survival.

Additional uncertainties persist regarding optimal risk stratification for hepatocellular carcinoma in non-cirrhotic MASLD, the management of recurrent disease after liver transplantation, and the cost-effectiveness of screening and treatment strategies within local healthcare systems.

Future studies should prioritize prospective multicenter cohorts in Türkiye to generate robust real-world data on MASLD and MASH. Key areas of focus should include implementation research, optimization of screening and risk stratification strategies, and long-term comparative effectiveness analyses of lifestyle, pharmacological, endoscopic, and surgical interventions.

TASL Practice Guidance for the Diagnosis and Management of MASLD

Consolidated Recommendations (1–52)

1. SLD should be used as a comprehensive umbrella term for all hepatic fat accumulation etiologies. Within this framework, MASLD (formerly NAFLD) represents the largest metabolic subgroup. Due to the high concordance rate (up to 99%) between NAFLD and MASLD, which ensures the continuity of existing scientific data while providing an affirmative and non-stigmatizing diagnosis, the updated nomenclature is preferred in clinical practice. *[LoE: High; SoR: Strong]*
2. Considering its high prevalence and disease burden in Türkiye, MASLD should be recognized as a major public health concern. Efforts should be made to increase both public and professional awareness, ensuring that MASLD is routinely considered in clinical practice by healthcare providers. *[LoE: Moderate; SoR: Strong]*
3. The presence of at least one cardiometabolic risk factor, such as obesity, T2DM, or hypertension, is the primary driver for MASLD diagnosis and serves as the most important critical predictor of disease progression. Consequently, all patients should undergo regular and systematic evaluations for all cardiometabolic risk factors. *[LoE: High; SoR: Strong]*
4. Patients with T2DM, obesity + ≥1 cardiometabolic risk factor, or signs of hepatic steatosis should be screened for advanced liver disease. *[LoE: Moderate; SoR: Strong]*
5. Children with obesity, elevated transaminase levels, or conditions associated with a high metabolic burden should be screened for the presence of MASLD. These individuals should undergo regular long-term follow-up to monitor disease progression and liver-related outcomes. *[LoE: Low; SoR: Strong]*
6. The FIB-4 index should be utilized as the first-line tool for risk stratification in patients with MASLD. *[LoE: High; SoR: Strong]*
7. Patients who are not classified as low risk in the initial step should undergo further evaluation, preferably with VCTE, or MRE if available. *[LoE: High; SoR: Strong]*
    a. Patients at higher clinical risk, including but not limited to those with type 2 diabetes mellitus, should be prioritized for second-line assessment using VCTE. *[LoE: Moderate; SoR: Strong]*
    b. Where available, VCTE may also be considered as a first-line risk assessment tool in high-risk populations. *[LoE: Moderate; SoR: Conditional]*
8. Liver biopsy is not routinely required in the diagnosis of MASLD and should be reserved for selected cases where clinically indicated. *[LoE: Moderate; SoR: Strong]*
9. Lifestyle modifications aiming for a weight loss of at least 5% of body weight should be recommended for all patients with MASLD, with an optimal target of ≥10%. For lean individuals, a weight loss target of 3–5% of body weight should be aimed. *[LoE: High; SoR: Strong]*
10. The Mediterranean diet should be the preferred dietary approach. Consumption of ultra-processed foods and sugar-sweetened beverages should be minimized or avoided. *[LoE: Moderate; SoR: Strong]*
11. Coffee intake may be encouraged for patients without contraindications, provided that it is well tolerated. *[LoE: Moderate; SoR: Conditional]*
12. Physical activity combining aerobic exercise and resistance training should be encouraged and tailored to the patient's individual lifestyle and functional capacity. *[LoE: High; SoR: Strong]*
13. A high-protein diet and resistance training can be encouraged, particularly in elderly patients and those with MASH-related cirrhosis, to preserve skeletal muscle mass and prevent the development of sarcopenia. *[LoE: Moderate; SoR: Strong]*
14. Pharmacological therapy is not a substitute for lifestyle interventions and should only be used as an adjunct when clinically indicated. Lifestyle modifications should be actively encouraged in all patients receiving pharmacotherapy. *[LoE: High; SoR: Strong]*
15. Pharmacological therapy with a MASH indication should be targeted at patients with clinically significant fibrosis and should exclude patients with cirrhosis. Treatment eligibility should be based primarily on non-invasive assessment, with VCTE as the preferred modality where available. *[LoE: High; SoR: Strong]*
    a. Patients with VCTE liver stiffness values in the 10–15 kPa range may be considered a priority group for consideration of pharmacological therapy. *[LoE: Moderate; SoR: Conditional]*
    b. In patients with VCTE liver stiffness values in the 15–20 kPa range, pharmacological therapy may be considered only if cirrhosis has been confidently excluded through clinical assessment, laboratory parameters, and imaging findings. In cases of diagnostic uncertainty, liver biopsy should be considered. *[LoE: Moderate; SoR: Conditional]*

16. Patients with MASLD and T2DM should be considered for antidiabetic pharmacotherapies with potential hepatic benefits.

- **a.** Pioglitazone may be encouraged in patients with type 2 diabetes mellitus and coexisting MASLD, where clinically appropriate and as a combination therapy. *[LoE: Moderate; SoR: Conditional]*
- **b.** SGLT2 inhibitors should be considered in patients with MASLD and type 2 diabetes mellitus, particularly in the presence of established or high-risk cardiovascular and/or renal disease. *[LoE: High; SoR: Strong]*
- **c.** GLP-1 receptor agonists should be considered in patients with MASLD and type 2 diabetes mellitus, particularly in patients with coexisting obesity and/or in whom weight reduction is the key therapeutic target. *[LoE: High; SoR: Strong]*

17. Bariatric procedures are not a substitute for lifestyle interventions and should only be used as an adjunct when clinically indicated. Lifestyle modifications should be actively encouraged in all patients undergoing bariatric procedures. *[LoE: Moderate; SoR: Strong]*

18. Bariatric interventions should be performed in accordance with established obesity guideline indications. *[LoE: Moderate; SoR: Strong]*

19. Bariatric treatments are contraindicated in patients with decompensated cirrhosis. *[LoE: Moderate; SoR: Strong]*

20. Bariatric treatments are not recommended before or simultaneously with liver transplantation. It is advisable to wait until post-transplantation graft stabilization is achieved (>1 year). In selected cases, sleeve gastrectomy may be an option. *[LoE: Low; SoR: Conditional]*

21. Body mass index (BMI) and waist circumference should be recorded at baseline and reassessed at each follow-up visit. *[LoE: Moderate; SoR: Strong]*

22. Systolic and diastolic blood pressure should be measured at baseline and monitored at every follow-up visit. *[LoE: High; SoR: Strong]*

23. A fasting lipid profile, including total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides, should be obtained at baseline and repeated at intervals determined by the patient's cardiovascular risk category and lipid-lowering treatment status. *[LoE: High; SoR: Strong]*

24. Lipoprotein(a) should be measured once in a lifetime to refine long-term ASCVD risk assessment. *[LoE: Moderate; SoR: Strong]*

25. Fasting plasma glucose and/or HbA1c should be measured at baseline and monitored periodically thereafter, with frequency tailored to baseline results and the individual risk profile. An OGTT should be considered when results are borderline or discordant, or when clinical suspicion persists. *[LoE: High; SoR: Strong]*

26. Assessment of insulin resistance using the homeostasis model assessment of insulin resistance (HOMA-IR) or OGTT-derived indices may be considered in patients without established diabetes or dysglycemia when clarification of metabolic dysfunction is clinically relevant. *[LoE: Low; SoR: Conditional]*

27. Renal risk should be assessed at baseline using serum creatinine with estimated glomerular filtration rate and urine albumin-to-creatinine ratio, and monitored thereafter at intervals guided by fibrosis stage, diabetes status, baseline renal function, and albuminuria. *[LoE: Moderate; SoR: Strong]*

28. Formal ASCVD risk estimation should be performed using an appropriate validated risk tool (for example, SCORE2/SCORE2-OP in European/Turkish settings), and updated when major risk factors change or at clinically appropriate intervals. *[LoE: Moderate; SoR: Strong]*

29. Smoking and alcohol intake should be routinely assessed and actively addressed as part of comprehensive risk management at baseline and during follow-up. Complete abstinence from both smoking and alcohol should be the goal. *[LoE: Moderate; SoR: Strong]*

30. In patients with obesity and/or symptoms suggestive of OSA (e.g., snoring), screening with a validated questionnaire such as the Epworth Sleepiness Scale should be considered, with referral for diagnostic evaluation when clinical risk is high. *[LoE: Moderate; SoR: Conditional]*

31. All women with menstrual irregularities may be referred for evaluation for PMOS, particularly when accompanied by features of hyperandrogenism or insulin resistance. *[LoE: Low; SoR: Conditional]*

32. Patients with cirrhosis should be screened for sarcopenia using a brief validated tool such as the SARC-F questionnaire, with further assessment and nutritional/physical intervention where indicated. *[LoE: Moderate; SoR: Strong]*

33. LSM by VCTE ≤15 kPa together with a platelet count ≥150×10^9/L effectively rules out CSPH in patients with MASLD and may help avoid unnecessary endoscopic screening for varices. *[LoE: High; SoR: Strong]*

34. In patients with cACLD and an LSM ≥20 kPa and/or a platelet count ≤150×10^9/L, screening endoscopy for varices is recommended. In experienced centers, spleen stiffness measurement (SSM) ≤40 kPa may be used as an adjunctive tool to refine endoscopy decisions in these patients. *[LoE: High (endoscopy)/Moderate (SSM); SoR: Strong (endoscopy); Conditional (SSM adjunct)]*

35. If CSPH is present, NSBBs should be considered unless contraindicated or not tolerated. *[LoE: High; SoR: Strong]*

36. HCC surveillance should be performed in all individuals with MASLD-related cirrhosis. *[LoE: Moderate; SoR: Strong]*

37. Routine HCC surveillance is not recommended in noncirrhotic adult patients with MASLD due to insufficient evidence and the low overall incidence of HCC in this population. *[LoE: Moderate; SoR: Strong]* However, selected cases such as patients with high metabolic risk, specifically patients with T2DM, may be considered for HCC screening even in the absence of clinical cirrhosis signs. *[LoE: Low; SoR: Conditional]*

38. Abdominal ultrasonography combined with serum AFP measurement every 6 months is recommended as the primary method for HCC surveillance. *[LoE: Moderate; SoR: Strong]* However, when feasible, additional laboratory- and imaging-based tools, such as the GALAD score and MRI, may be considered because of their higher diagnostic accuracy. *[LoE: Moderate; SoR: Conditional]*

39. Candidates with MASLD-related cirrhosis should undergo multidisciplinary pretransplant evaluation. *[LoE: Moderate; SoR: Strong]*

40. Pretransplant assessment should include systematic evaluation and optimization of cardiometabolic comorbidities, particularly coronary artery disease, type 2 diabetes, hypertension, dyslipidemia, obesity, sarcopenia, and chronic kidney disease. *[LoE: Moderate; SoR: Strong]*

41. CVD assessment in candidates with MASLD should follow a stepwise, risk-adjusted, multidisciplinary approach rather than a separate disease-specific algorithm. Risk scores such as CAR-OLT and CAD-LT may help identify candidates who warrant further cardiac investigation. *[LoE: Moderate; SoR: Strong]*

42. Because stress-based testing may have limited diagnostic performance in advanced cirrhosis, coronary computed tomography angiography may be considered in selected high-risk candidates, while invasive coronary angiography should be reserved for those with abnormal non-invasive findings or strong clinical suspicion of clinically significant coronary artery disease. *[LoE: Moderate; SoR: Conditional]*

43. Renal function should be closely monitored and preserved before transplantation, and simultaneous liver–kidney transplantation should be considered according to accepted criteria in eligible candidates. *[LoE: Moderate; SoR: Strong]*

44. Body mass index alone should not be considered as a contraindication for liver transplantation. Risk stratification should incorporate body composition, sarcopenia or sarcopenic obesity, nutritional status, and overall frailty. *[LoE: Moderate; SoR: Strong]*

45. All candidates with MASLD-related cirrhosis should undergo formal nutritional and functional assessment, and tailored lifestyle and nutritional measures should be implemented whenever feasible. *[LoE: Moderate; SoR: Strong]*

46. Pharmacological weight-loss therapy cannot yet be routinely recommended in decompensated transplant candidates with MASLD-related cirrhosis because safety and efficacy data remain limited. *[LoE: Low; SoR: Conditional]*

47. Bariatric surgery may be considered only in carefully selected candidates with compensated cirrhosis, preferably in high-volume centers and after assessment for clinically significant portal hypertension; sleeve gastrectomy is the preferred approach. Endoscopic bariatric procedures should be avoided in clinically significant portal hypertension. *[LoE: Low–Moderate; SoR: Conditional (for surgery)/Strong (against endoscopy in CSPH)]*

48. Recipients transplanted for MASLD should undergo systematic post-transplant assessment and management of cardiometabolic risk factors, including obesity, diabetes, hypertension, dyslipidemia, chronic kidney disease, and cardiovascular disease. *[LoE: Moderate; SoR: Strong]*

49. Dietary counselling, physical activity, weight control, and optimization of diabetes, blood pressure, and lipid management should form the cornerstone of post-transplant care in MASLD recipients. *[LoE: Moderate; SoR: Strong]*

50. Immunosuppressive regimens should be adjusted, when feasible, to reduce metabolic burden, particularly through avoidance of prolonged corticosteroid exposure and consideration of calcineurin inhibitor minimization in selected recipients. *[LoE: Moderate; SoR: Conditional]*

51. Recurrent and de novo MASLD are frequent after LT, particularly in recipients with multiple metabolic risk factors. In the absence of a validated surveillance strategy, screening for recurrent MASLD or de novo MASLD may include ultrasound and transient elastography with controlled attenuation parameter, while liver biopsy should be reserved for uncertain cases or when alternative graft pathology is suspected. *[LoE: Low; SoR: Conditional]*

52. Long-term follow-up should also include monitoring for cardiovascular disease, chronic kidney disease, and extrahepatic malignancy, which substantially influence post-transplant outcomes in this population. *[LoE: Moderate; SoR: Strong]*

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