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Guideline

Guidelines for Diagnosis and Management of Metabolic Dysfunction-associated Fatty Liver Disease in Primary Care (2025)

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Abstract

Metabolic dysfunction-associated fatty liver disease (MAFLD) has become one of the leading causes of chronic liver diseases in China, imposing a substantial and growing burden on the healthcare system. Considering the large number of individuals affected by MAFLD and the gap in disease management capacity at the primary care level, standardized guidance tailored to primary healthcare settings is urgently needed. In response, the Chronic Disease Management Branch of the China Medical Biotechnology Association convened a multidisciplinary working group incorporating hepatologists, general practitioners, and other specialists to initiate the first China national Guidelines for Diagnosis and Management of Metabolic Dysfunction-associated Fatty Liver Disease in Primary Care (2025). These guidelines provide recommendations and suggestions covering screening, risk assessment, diagnosis, treatment, referral pathways, and follow-up tailored for primary care institutions, thereby improving the long-term outcomes for the population with MAFLD and comprehensively strengthening the role of primary healthcare in chronic liver disease management.

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Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD), previously referred to as non-alcoholic fatty liver disease, is the most prevalent chronic liver disease worldwide, affecting nearly one-third of adults.[1–3] The disease spectrum includes simple steatosis, metabolic dysfunction-associated steatohepatitis (MASH), liver fibrosis, cirrhosis, and even hepatocellular carcinoma (HCC).[4] MAFLD is closely associated with a high burden of comorbidities such as metabolic syndrome (MetS), type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD), cardiovascular disease (CVD), and extrahepatic malignancies, posing a substantial public health concern in China. Given its largely asymptomatic onset and insidious progression, MAFLD is frequently under-recognized and under-treated in routine clinical practice.[5]

In recent years, ongoing reform of the tiered healthcare delivery system has shifted the management of chronic noncommunicable diseases (NCDs) increasingly toward primary healthcare institutions. Primary care therefore plays a pivotal role in the early identification, risk stratification, long-term management, and coordination of care for patients with MAFLD. To optimize standardized, context-appropriate diagnostic and therapeutic pathways and to enhance lifelong NCD management at the primary care level, the Chronic Disease Management Branch of the China Medical Biotechnology Association convened a multidisciplinary expert panel comprising specialists in gastroenterology, hepatology, cardiology, endocrinology, and general practice to formulate the Guidelines for Diagnosis and Management of Metabolic Dysfunction-associated Fatty Liver Disease in Primary Care (2025). These guidelines aim to provide evidence-based recommendations for comprehensive management of MAFLD in primary healthcare settings. Additional details can refer to the China

Table 1. GRADE levels of evidence quality and recommendation strength[6]

Category	Description
Levels of evidence quality	
High (A)	Further research is very unlikely to change our confidence in the estimate of effect
Moderate (B)	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low (C)	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low (D)	Any estimate of effect is very uncertain
Levels of recommendation strength	
Strong (1)	Clear evidence that the benefits of the intervention outweigh the harms, or harms outweigh the benefits
Weak (2)	It is uncertain about the balance of benefit and harm, or the evidence suggests comparable benefit and harm regardless of quality

GRADE, Grading of Recommendations Assessment, Development and Evaluation.

Guideline for the Prevention and Treatment of Metabolic Dysfunction-Associated Fatty Liver Disease (Version 2024).[3]

The guidelines adopt the Grading of Recommendations Assessment, Development, and Evaluation system to rate the strength and quality of evidence.[6] The quality of evidence is categorized as A (high), B (moderate), C (low), or D (very low), and recommendations are classified as strong (1) or weak (2) (Table 1).[6] Based on evidence quality, patient values, preferences, and cost-effectiveness, the guidelines include 13 strong recommendations and 2 suggestions.

Overview

Recommendation

The prognosis of MAFLD is strongly associated with T2DM, CVD, extrahepatic malignancies, and CKD. Advanced liver fibrosis markedly increases the risk of liver-related events, including hepatic decompensation, HCC, liver transplantation, and liver-related mortality. (1A)

MAFLD is a common chronic liver condition induced by sustained metabolic stress and characterized by substantial clinical and biological heterogeneity. The development of MAFLD reflects the interplay of metabolic risk factors, genetic predisposition, epigenetic modifications, dietary patterns, and lifestyle factors.[3] Its clinical subtypes are summarized in Table 2.

The prevalence of MAFLD varies across populations, regions, and diagnostic criteria. A recent meta-analysis estimated a global prevalence of 32.4% in the general population.[7] Among Asian adults, the prevalence is 29.6% and continues to rise, increasing from 25.3% during 1999–2005 to 33.9% during 2012–2017.[8] In China, the pooled prevalence is 29.7%, with an incidence of 56.4 per 1,000 person-years. The prevalence of MAFLD increases with age and is higher in men than in women. However, rates rise more rapidly after menopause and may eventually exceed those observed in men.

The risk of MAFLD and its progressive forms is strongly associated with common cardiometabolic conditions, including overweight/obesity, T2DM, dyslipidemia, hypertension, and MetS. These factors not only drive MAFLD onset but also substantially increase the risk of progressing to MASH and liver fibrosis. Among overweight or obese individuals, the prevalence of MAFLD and MASH is approximately 51.6% and 25–30%, respectively.[7,9] In patients with T2DM, the prevalence of MAFLD, MASH, significant fibrosis, and advanced fibrosis is 65.04%, 31.55%, 35.54%, and 14.95%, respectively.[10] Hypertension increases the risk of MAFLD by 1.677-fold.[11] Among patients with dyslipidemia, the prevalence of MAFLD ranges from 27% to 92%, whereas 69.2% of individuals with MAFLD have dyslipidemia.[12] Moreover, MAFLD is increasingly recognized in individuals with coexisting chronic liver diseases, such as chronic hepatitis B infection and/or alcoholic liver disease (ALD)[13], underscoring the need for comprehensive risk assessment

Table 2. The clinical classification of MAFLD

Type	Basic concept
MAFL	Early stage of MAFLD. Imaging evidence or liver biopsy showing more than 5% of macrovesicular or predominantly macrovesicular steatosis, with or without nonspecific hepatocellular ballooning or lobular inflammation. Within the fields of hematoxylin-eosin staining under light microscopy, hepatic steatosis can be graded as mild (S1), moderate (S2), or severe (S3) based on the proportion of steatotic hepatocytes (5–33%, 34–66%, ≥67%)
MASH	Liver biopsy in MAFLD patients showing more than 5% of steatosis accompanied by lobular inflammation and ballooned hepatocytes. The severity is categorized as early MASH (F0-F1), fibrotic MASH (F2-F3), and MASH-related cirrhosis (F4)
MAFLD-associated fibrosis	Liver biopsy showing liver fibrosis (F1-F3) or non-invasive tests indicating progressive fibrosis (≥F3) in MAFLD patients, with or without elevated serum transaminase and histologic features of MASH
MAFLD-associated cirrhosis	Cirrhosis indicated by non-invasive tests or liver biopsy in MAFLD patients, with or without histologic features of MASH

MAFLD, metabolic dysfunction-associated fatty liver disease; MAFL, metabolic dysfunction-associated fatty liver; MASH, metabolic dysfunction-associated steatohepatitis.

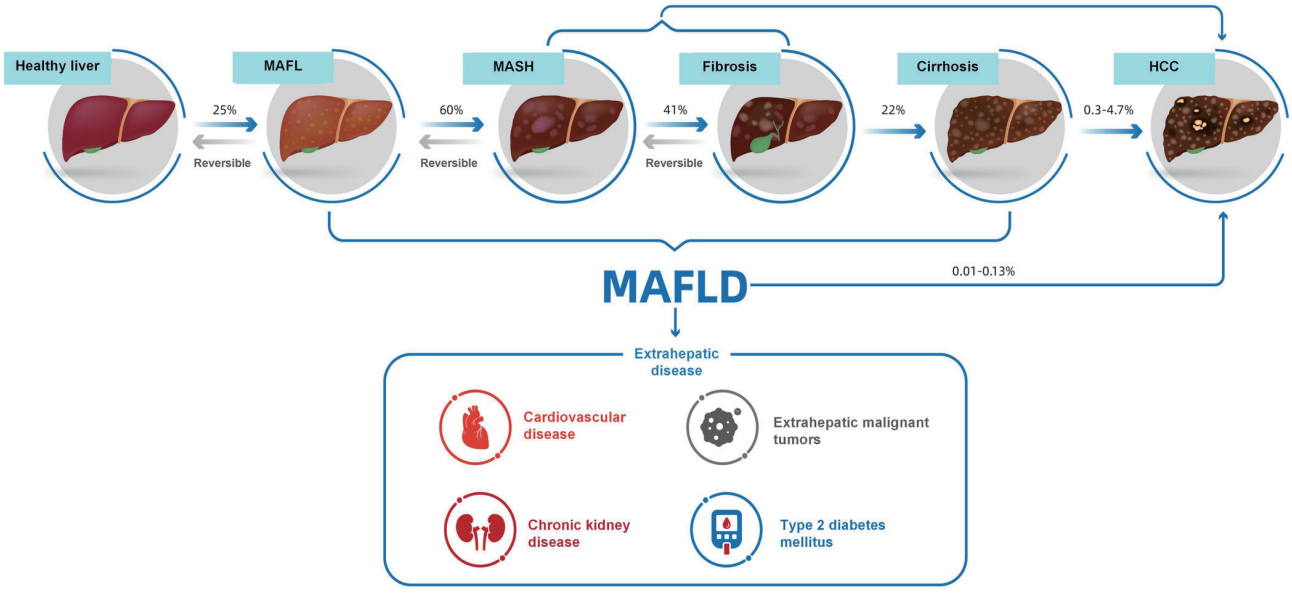

Fig. 1. The natural history of MAFLD. MAFLD, metabolic dysfunction-associated fatty liver disease. MAFL, metabolic dysfunction-associated fatty liver; MASH, metabolic dysfunction-associated steatohepatitis; HCC, Hepatocellular Carcinoma.

rather than exclusion-based diagnostic approaches.

Question 1: What are the natural history and outcomes of MAFLD?

MAFLD is a multi-system metabolic disorder that predisposes individuals to end-stage liver diseases, including decompensated cirrhosis and HCC, and substantially increases the risk of major cardiometabolic conditions such as T2DM, CVD, CKD, as well as extrahepatic malignancies.[14] Among patients with MAFLD, the leading causes of death are CVD and extrahepatic cancers (including endometrial, breast, prostate, colorectal, and lung cancers), followed by liver-related complications.[15,16] The incidence of MAFLD-associated HCC is approximately 1.25 per 1,000 person-years, rising to 14.46 per 1,000 person-years among individuals with advanced fibrosis or cirrhosis.[17] The natural history of MAFLD is illustrated in Figure 1.

Screening, diagnosis, and evaluation of MAFLD

Recommendations

Individuals with at least one MetS component and/or persistently elevated serum transaminases should undergo routine abdominal ultrasonography to screen for MAFLD. (1A)

Diagnosis of MAFLD requires confirmation of hepatic steatosis by imaging or histology, the presence of at least one MetS component, and exclusion of excessive alcohol intake (≥210 g per week for men, ≥140 g per week for women) and other causes of steatosis. (1A)

Patients with MAFLD should undergo regular surveillance to evaluate the risk and severity of liver fibrosis, hepatic decompensation, HCC, and extrahepatic comorbidities, including T2DM, CVD, malignancies, and CKD. (1A)

In primary healthcare settings, non-invasive tests (NITs) for liver fibrosis such as the fibrosis-4 index (FIB-4) should be used as a first-line tool for assessing the risk of advanced fibrosis. Patients with FIB-4 ≥1.3 (or ≥2.0 for those older than 65 years) should undergo transient elastography to assess liver stiffness measurement for further evaluation. (1A)

CVD risk in patients with MAFLD should be assessed using the China atherosclerotic CVD (ASCVD) risk chart, supplemented by additional testing such as 24-h electrocardiogram, heart rate variability, and carotid plaque assessment when indicated. (1A)

Question 2: Who should be screened for MAFLD?

Obesity, T2DM, and MetS substantially increase the risk of MAFLD and its more advanced manifestations, including MASH, liver fibrosis, cirrhosis, and HCC.[18] The prevalence of MASH among overweight or obese individuals is 25–30%.[9] In patients with T2DM, the prevalence of MAFLD and MASH, as well as significant and advanced fibrosis, is markedly higher than in individuals without diabetes.[10] Other cardiometabolic conditions, particularly hypertension and dyslipidemia, also increase the likelihood of MAFLD, with more than half of MAFLD patients having at least one condition.[11,19] Furthermore, individuals with persistently elevated serum transaminases in the absence of an alternative identifiable etiology are at increased risk of MAFLD and fibrosis progression.[20] Therefore, routine abdominal ultrasonography should be performed to screen for MAFLD in individuals with at least one MetS component and/or asymptomatic hypertransaminasemia.

Question 3: How is MAFLD diagnosed?

Fatty liver disease is clinically heterogeneous. A diagnosis of MAFLD requires evidence of hepatic steatosis confirmed by imaging or histology, the presence of at least one MetS component, and exclusion of significant alcohol consumption (≥210 g per week for men, ≥140 g per week for women) and alternative etiologies of steatosis.[3] MetS components include: (1) BMI ≥ 24 kg/m^2, or waist circumference ≥ 90 cm

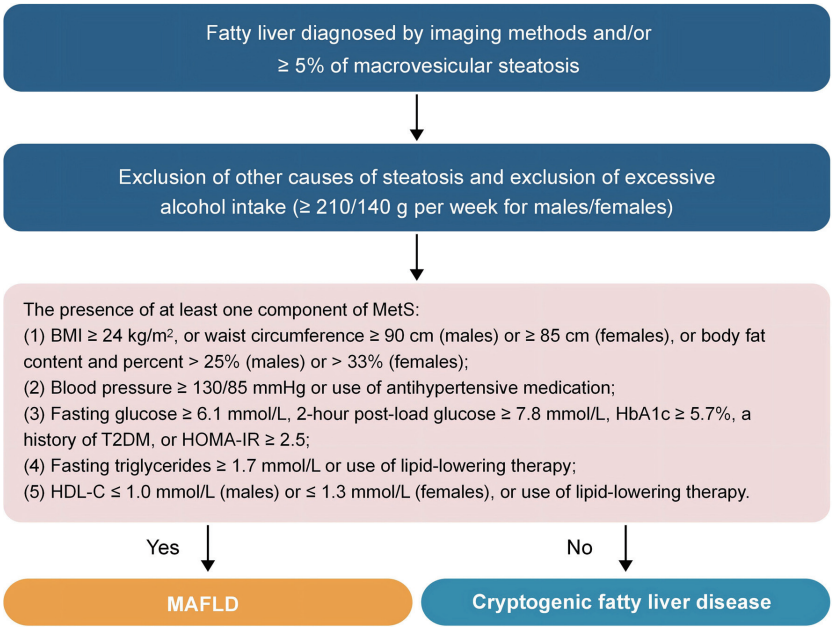

Fig. 2. The diagnostic flow chart of MAFLD. MAFLD, metabolic dysfunction-associated fatty liver disease; BMI, body mass index; HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment–insulin resistance; T2DM, type 2 diabetes mellitus; HDL-C, high-density lipoprotein–cholesterol; MetS, metabolic syndrome.

(males) or ≥85 cm (females), or body fat percentage >25% (males) or >33% (females); (2) Blood pressure ≥ 130/85 mmHg or use of antihypertensive medication; (3) Fasting plasma glucose ≥ 6.1 mmol/L, or 2-h post-load glucose ≥ 7.8 mmol/L, glycated hemoglobin ≥ 5.7%, a history of T2DM, or homeostasis model assessment-insulin resistance ≥ 2.5; (4) Fasting plasma triglycerides ≥ 1.7 mmol/L or use of lipid-lowering therapy; (5) Fasting plasma high-density lipoprotein cholesterol ≤ 1.0 mmol/L (males) or ≤1.3 mmol/L (females), or use of lipid-lowering therapy.

In addition to ALD, hepatic steatosis may occur secondary to malnutrition, exposure to medications or toxins, Wilson's disease, or hypobetalipoproteinemia. MAFLD also frequently coexists with chronic viral hepatitis or ALD. Clinicians should therefore carefully evaluate for alternative and/or concurrent causes of liver disease when MAFLD is suspected. The diagnostic flowchart is shown in Figure 2, and additional details on etiologic evaluation are provided in the 2024 China Guideline.[3]

Question 4: Which conditions should MAFLD patients be screened and monitored for?

MAFLD typically follows an indolent course. However, once advanced fibrosis or cirrhosis develops, the risks of liver failure, liver transplantation, liver-related mortality, and all-cause mortality increase sharply.[21] Progression to advanced fibrosis is a pivotal step in the natural history of MAFLD from MASH to cirrhosis and represents a key predictor of liver-related outcomes. Liver-specific and all-cause mortality increase in parallel with fibrosis severity, underscoring the central role of fibrosis assessment in long-term risk stratification. The incidence of MAFLD-related HCC also escalates with fibrosis progression. Among individuals with MAFLD-related cirrhosis, the incidence of HCC is comparable to that observed in cirrhosis due to other etiologies.[16] Among MAFLD patients with T2DM, the five-year risks of hepatic decompensation and HCC were 13.85% and 3.68%, respectively, markedly higher than among those without diabetes (3.95% and 0.44%, respectively).[9] Accordingly, HCC surveillance should be intensified in MAFLD patients with cirrhosis who coexist with diabetes.

Beyond liver-related outcomes, MAFLD is strongly associated with adverse CVD outcomes. Compared with individuals without MAFLD, those with MAFLD have significantly higher incidences of CVD events and CVD-related mortality. Importantly, MAFLD is associated with excess CVD risk independent of traditional cardiovascular risk factors, and this risk increases progressively with fibrosis severity.[10] Therefore, CVD risk should be systematically assessed as part of routine care among the population with MAFLD.

Patients with MAFLD also face an increasing risk of extrahepatic malignancies. The incidence and mortality of extrahepatic malignancies attributable to MAFLD are 10.58 per 1,000 person-years and 9.3 per 1,000 person-years, respectively.[11] These clinical findings reinforce the need for adherence to recommended screening for extrahepatic malignancies within this population.

In addition, MAFLD is closely associated with CKD. Individuals with MAFLD have a higher prevalence of proteinuria and renal dysfunction compared with the general population,[19] with risk further increased among those with MASH or advanced fibrosis.[20] Therefore, renal function should be assessed longitudinally, particularly in patients with MAFLD and progressive liver fibrosis.

Question 5: How can liver fibrosis in MAFLD be assessed by non-invasive methods?

Conventional abdominal ultrasonography has limited value for liver fibrosis assessment.[22] Liver biopsy remains the gold standard for diagnosing MASH and staging fibrosis. However, it is invasive and generally impractical for primary care settings.[23] Current guidelines recommend NITs to evaluate fibrosis severity and monitor longitudinal progression, among which the FIB-4 has been extensively validated for dynamic monitoring. The FIB-4 formula is:

$$\text{FIB-4} = \frac{\text{Age} \times \text{aspartate aminotransferase}}{\text{Platelet count} \times \sqrt{\text{alanine aminotransferase}}}.$$

Recommended thresholds categorize the risk of advanced fibrosis as follows: low risk, FIB-4 < 1.3 (or <2.0 for individuals aged ≥65 years); intermediate risk, 1.3–2.67 (or 2.0–2.67 for ≥65 years); and high risk, FIB-4 > 2.67.[1–3,24] Patients with intermediate or high risk should undergo transient elastography (FibroScan or FibroTouch) to measure liver stiffness. Where unavailable, primary healthcare facilities should refer patients to tertiary hospitals for further evaluation.

Question 6: How should CVD risk be evaluated in MAFLD?

CVD risk assessment in individuals with MAFLD should consider age, smoking and alcohol consumption, family history of ASCVD, and other metabolic risk factors, and should be integrated with the China ASCVD risk chart for stratification. Further detailed assessments are provided in the corresponding guidelines.[25–27]

Treatment of MAFLD

Recommendations

Lifestyle modification is the foundation of MAFLD management, including dietary, exercise, and behavioral interventions. Patients should reduce daily caloric intake and improve overall diet quality. Exercise prescriptions should align with individual preferences and capacity, with a recommendation of at least 150 min per week of moderate-intensity aerobic activity or at least 75 min per week of vigorous-intensity activity. (1A)

For overweight or obese patients with MAFLD, a weight reduction of at least 5% is recommended. If individuals with BMI > 28 kg/m^2 do not achieve this target after three months of lifestyle intervention, pharmacologic therapy may be considered. Bariatric and metabolic surgery may be considered for non-cirrhotic patients with MAFLD who meet established criteria. (1A)

For patients with MAFLD and T2DM, glucose-lowering agents with potential hepatic benefits, such as glucagon-like peptide-1 (GLP-1) receptor agonists, sodium-glucose cotransporter 2 inhibitors, or pioglitazone, should be prioritized. (1A)

For patients with MAFLD and hypertension, long-acting antihypertensive agents should be selected for initial or combination therapy based on blood pressure level, CVD risk, and medication safety. (1A)

Statins should serve as the cornerstone of lipid-lowering therapy, with low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and triglyceride targets set according to CVD risk stratification. (1A)

Hepatic inflammation and fibrosis severity should be assessed comprehensively using biochemical parameters, elastography, and clinical history to guide hepatoprotective therapy. If no improvement is observed within six months, treatment adjustment or combination therapy should be considered. (1A)

Traditional Chinese medicine (TCM) and/or external TCM therapies may be selectively used as adjunctive options in primary care. (1B)

Question 7: How should lifestyle modification be implemented for MAFLD patients?

Dietary management: Lifestyle modification represents the cornerstone of MAFLD management in primary care, offering clinically meaningful benefits across the spectrum of MAFLD, irrespective of pharmacotherapy. Caloric restriction is fundamental for patients with MAFLD who are overweight or obese. It is recommended that a reduction of approximately 500 to 1,000 kcal per day from baseline, with target daily intakes of 1,200–1,400 kcal per day for men and 1,000–1,200 kcal per day for women (1 kcal = 4.184 kJ), be implemented while maintaining adequate protein intake (≥1.2 g per kilogram per day) to prevent sarcopenia or minimize loss of muscle mass during caloric restriction.

Dietary composition should also be optimized. Evidence supports several structured dietary approaches, including low-carbohydrate, low-fat, intermittent fasting, Mediterranean, and Jiangnan-style dietary patterns, for weight reduction and improvement in cardiometabolic and hepatic outcomes.[2,28] A diet rich in vegetables, fiber, whole grains, legumes, fruits, and nuts is recommended. Consumption of saturated and trans fats, ultra-processed foods, processed meats, and foods high in added sugars or fructose should be minimized. Dietary prescriptions should be individualized according to patient preferences, cultural practices, and socioeconomic conditions to enhance long-term adherence. Dietary recommendations are summarized in Figure 3.

Exercise guidance: Physical activity provides independent benefits in MAFLD management by supporting weight control and reducing hepatic fat content.[29] Exercise prescriptions should be tailored based on baseline fitness, comorbidities, and patient goals, ideally following structured risk assessment and professional guidance (Fig. 3). Gradual progression is recommended for individuals with limited cardiopulmonary capacity, while higher-intensity and/or shorter-duration regimens may be appropriate for individuals with higher fitness. Long-term adherence is critical to provide sustained metabolic and hepatic benefits. Primary care providers can support the adherence by facilitating access to structured exercise programs and community-based resources.

Other lifestyle modifications: Behavioral interventions should address sedentary lifestyles, sleep hygiene, and substance use. Prolonged sitting is associated with an increased MAFLD risk and should be minimized. Smoking cessation and avoidance of excessive alcohol intake are recommended. Strict abstinence from alcohol is required for individuals with advanced fibrosis.

Question 8: How can MAFLD patients effectively achieve weight reduction?

Sustained weight reduction is a primary therapeutic target in MAFLD management, with recommended strategies outlined in Figure 3. If adequate weight reduction is not achieved with lifestyle modification alone, pharmacotherapy may be considered. In China, approved anti-obesity medications include GLP-1 receptor agonists (liraglutide and semaglutide) and orlistat. GLP-1 receptor agonists have demonstrated benefits in weight reduction, improvement of hepatic histology and metabolic parameters, and CVD risk reduction.[30–32] By contrast, orlistat may reduce serum transaminases but has limited effects on hepatic steatosis, steatohepatitis, or fibrosis, and is therefore not recommended as first-line therapy for MAFLD in China. For patients with obesity and MAFLD without cirrhosis who remain refractory to lifestyle and pharmacological therapies, metabolic and bariatric surgery may be considered in accordance with national guidelines.[33–35]

Question 9: How should glucose-lowering agents be selected for MAFLD patients with T2DM?

In patients with MAFLD and T2DM, antidiabetic therapy should

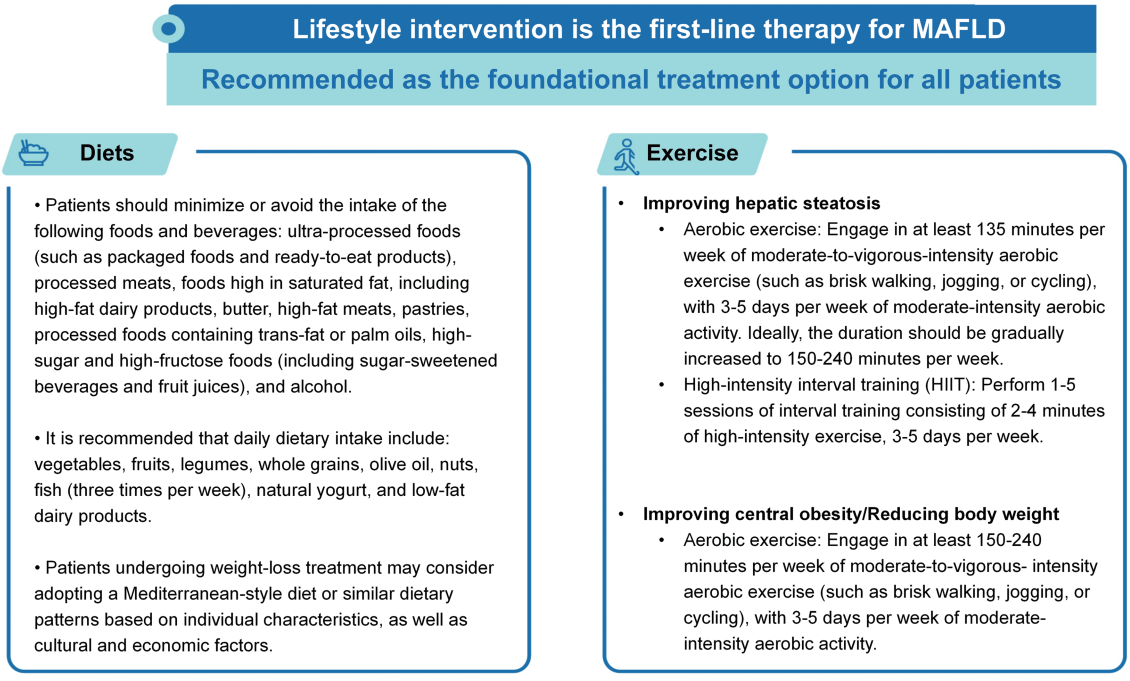

Fig. 3. Recommendations on diet and exercise for patients with MAFLD. MAFLD, metabolic dysfunction-associated fatty liver disease.

prioritize agents that provide metabolic, hepatic, cardiovascular, and renal benefits. GLP-1 receptor agonists such as semaglutide have been shown to improve hepatic histology by reducing steatosis, steatohepatitis severity, and fibrosis, and improve metabolic dysfunction.[36] Liraglutide alleviates steatohepatitis without worsening fibrosis and substantially improves glycemic control.[37] Treatment selection should be individualized based on the severity of MAFLD and comorbidities, with monitoring for gastrointestinal adverse effects and related complications. Sodium-glucose cotransporter 2 inhibitors such as dapagliflozin lower serum transaminases and hepatic fat content, improve body weight and insulin resistance, and provide cardiovascular and renal protection.[38] Pioglitazone improves MASH histology and insulin sensitivity but carries risks including weight gain, edema, heart failure, and bone loss.[39] Metformin has minimal effects on hepatic histology but may reduce MAFLD-related HCC risk. Insulin, acarbose, and dipeptidyl peptidase-4 inhibitors have not demonstrated histological benefit for MASH and should generally be reserved for glycemic control when needed. For MAFLD patients with decompensated cirrhosis and T2DM, insulin remains the preferred therapy, with close monitoring to prevent hypoglycemia.[40]

Question 10: How should antihypertensive agents be selected for MAFLD patients with hypertension?

Hypertension commonly coexists with MAFLD and contributes substantially to CVD risk; therefore, long-acting antihypertensive medications should be selected for initial monotherapy or combination therapy based on blood pressure levels, comorbid CVD and renal benefits, and avoidance of medications with potential hepatotoxic or nephrotoxic effects. Angiotensin receptor–neprilysin inhibitors should be used cautiously in individuals with estimated glomerular filtration rate <30 mL·min^{-1}·(1.73 m^2)$^{-1}$, renal artery stenosis, or moderate hepatic dysfunction. Evidence suggests that renin-angiotensin system inhibitors, including angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, are preferred options. Angiotensin II receptor blockers not only lower blood pressure but may also improve hepatic histology and serum fibrosis markers, and angiotensin-converting enzyme inhibitors may reduce liver-related adverse events in patients with MAFLD.[41,42] Blood pressure control, treatment tolerability, and antihypertensive agent–related adverse events should be monitored regularly.[43]

Question 11: How should lipid-lowering therapy be chosen for MAFLD patients with dyslipidemia?

Lipid management should be integrated within comprehensive MAFLD management. Lipid targets should adhere to existing clinical guidelines for the relevant risk category while also considering hepatic safety and fibrosis severity. Statins are first-line therapy for reducing ASCVD risk.[26–28] Evidence indicates that statins have a favorable hepatic safety profile and may delay hepatic fibrosis progression, reduce portal vein pressure, improve survival in compensated cirrhosis, and yield greater cardiovascular benefits in MAFLD patients with dyslipidemia.[44] Nevertheless, statins should be used with caution in individuals with decompensated cirrhosis or hepatic failure, and liver function should be monitored closely during treatment. Statins should not be withheld solely because of MAFLD or mild transaminase elevations. If transaminase levels increase to at least three times the upper limit of normal and/or total bilirubin levels rise, dose reduction or discontinuation should be considered. For mild elevations ($<3\times$upper limit of normal) of serum transaminases, it may be appropriate to maintain the current dose with close observation, dose adjustment, or switching to another type of statin metabolized via an alternative pathway.[45] For patients who are intolerant to statins or do not achieve lipid targets on statins alone, ezetimibe, proprotein convertase subtilisin/kexin type 9 inhibitors, probucol, or other lipid-lowering combination therapies may be considered. When serum triglyceride levels exceed 5.6 mmol/L, fibrates may be used to reduce the risk of

Table 3. Referral recommendations for patients with metabolic dysfunction–associated fatty liver disease in primary healthcare settings

Examination method	Findings	Referral recommendation
Abdominal ultrasound	Mild to moderate steatosis	Manage and follow up in primary healthcare settings
	Severe steatosis	Manage and follow up in primary healthcare settings
	Liver cirrhosis	Refer to a higher-level specialist hospital
	Space-occupying hepatic lesions	Refer to a higher-level specialist hospital
FIB-4	FIB-4 < 1.3 (or < 2.0 for individuals aged ≥ 65 years): low risk of advanced fibrosis	Manage and follow up in primary healthcare settings
	FIB-4 indicated as 1.3–2.67 (or 2.0–2.67 for individuals aged ≥ 65 years): intermediate risk of advanced fibrosis	Consider further transient elastography assessment. If such equipment is unavailable in primary healthcare settings, refer to a higher-level specialist hospital
	FIB-4 > 2.67: high risk of advanced fibrosis	Refer to a higher-level specialist hospital
Transient elastography (FibroScan or FibroTouch)	LSM < 8 kPa: advanced fibrosis unlikely	Manage and follow up in primary healthcare settings
	LSM 8–12 kPa: significant fibrosis	Refer to a higher-level specialist hospital
	LSM > 12 kPa: advanced fibrosis	Refer to a higher-level specialist hospital
	LSM > 20 kPa: cirrhosis	Refer to a higher-level specialist hospital
Liver biochemical tests	Persistent elevation of transaminases (ALT, AST) and/or elevated total bilirubin, GGT, ALP, or other related indicators	Refer to a higher-level specialist hospital
ASCVD risk assessment	Low ASCVD risk	Manage and follow-up in primary healthcare settings
	High ASCVD risk	Refer to a higher-level specialist hospital

FIB-4, fibrosis-4 index; ASCVD, atherosclerotic cardiovascular disease; LSM, liver stiffness measurement; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase.

acute pancreatitis, although cardiovascular benefits have not been clearly demonstrated. Omega-3 fatty acids and niacin may be used as adjunctive treatments for dyslipidemia.

Question 12: When should hepatoprotective drugs be used in MAFLD patients?

Primary care physicians should integrate serum biochemical results, hepatic imaging and/or histology, and medical history to determine the presence and severity of hepatic injury. Use of hepatoprotective therapy should be considered in individuals with active liver injury or an increased risk of progression, particularly those with at-risk MASH or advanced fibrosis with persistently elevated liver transaminases. A multi-center randomized controlled trial conducted in China demonstrated that vitamin E (α-tocopherol, 300 mg per day) significantly improved histological injury and lowered liver transaminase levels in patients with MASH.[46] Other hepatoprotective agents frequently used in China include silymarin, polyene phosphatidylcholine, bicyclol, glycyrrhizin preparations, reduced glutathione, S-adenosylmethionine, ursodeoxycholic acid, and other agents. These medications may be considered in patients with MAFLD who meet one or more of the following criteria: (1) Biopsy-confirmed MASH or significant fibrosis; (2) Persistently elevated liver transaminases or high-risk fibrosis indicators assessed by NITs; (3) Coexisting liver injury induced by medications, autoimmune diseases, or other causes.[3]

Question 13: How should TCM and external TCM therapies be used for MAFLD?

Guided by syndrome differentiation, TCM provides a structured framework for MAFLD management. Herbal prescriptions based on syndrome classification, Chinese patent medicines, and external therapies such as acupuncture and acupoint embedding have demonstrated beneficial effects on MAFLD. Primary healthcare institutions may adopt TCM as an adjunctive therapy to standard care, tailored to local institutional capacity, patient preferences, and clinical status, with reference to the corresponding guidelines.[47,48]

Referral and follow-up of MAFLD

Recommendation

Patients with ultrasonography-confirmed hepatic steatosis, low risk of advanced fibrosis by NITs, and low-to-moderate ASCVD risk may be managed and followed in primary care with risk factor control. Patients with suspected cirrhosis or hepatic lesions by abdominal ultrasound, intermediate-to-high risk of advanced fibrosis based on NITs, high or very high ASCVD risk, persistently elevated serum transaminases, or hepatic complications should be referred promptly to tertiary hospitals. (1A)

Question 14: Who should be referred in a timely manner?

Referral decisions in primary healthcare settings should be based on an integrated assessment of hepatic imaging findings, non-invasive fibrosis risk evaluations, biochemical re-

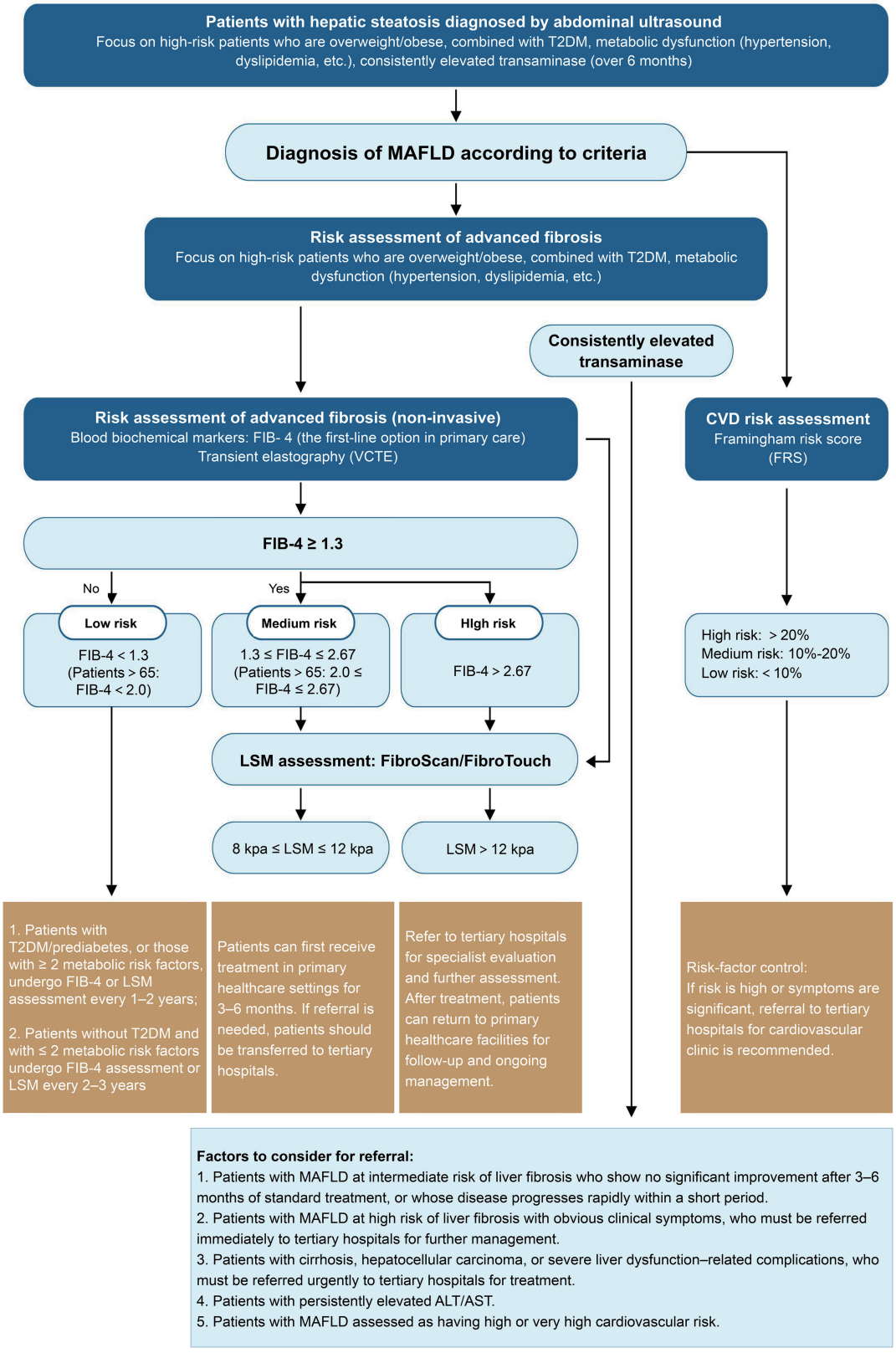

Fig. 4. Risk assessment and referral of patients with MAFLD. MAFLD, metabolic dysfunction-associated fatty liver disease; FIB-4, fibrosis-4 index; LSM, liver stiffness measurement; T2DM, type 2 diabetes mellitus; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 4. Follow-up recommendations for patients with metabolic dysfunction–associated fatty liver disease

Patients group	Follow-up interval	Assessment
All patients with MAFLD	Long-term	Regular evaluation of body weight, waist circumference, blood pressure, and lifestyle factors such as diet, exercise, smoking, alcohol consumption, and medication adherence
All patients with MAFLD	Every 3 to 6 months	Liver and renal function tests, fasting glucose, blood lipids
All patients with MAFLD	Every 6 to 12 months	Routine blood test, abdominal ultrasound, and carotid ultrasound
All patients with MAFLD	Annually	Evaluation of FIB-4 or transient elastography
MAFLD patients with normal BMI	Annually	Body composition analysis (body fat percentage, skeletal muscle mass, etc.)
Patients without abnormal glucose metabolism	Annually	Monitoring HOMA-IR
Patients with advanced liver fibrosis	Annually	Measurement of serum AFP
Patients with cirrhosis	Every 6 to 12 months	Measurement of serum AFP, gastroscope to assess esophageal varices, and monitoring for liver-related decompensation

BMI, body mass index; FIB-4, fibrosis-4 index; HOMA-IR, homeostasis model assessment of insulin resistance; AFP, alpha-fetoprotein.

sults, and ASCVD risk stratification (Table 3, Fig. 4).

Primary management of MAFLD

Recommendation

Primary healthcare institutions should optimize care pathways for MAFLD management and follow-up and develop dedicated fatty liver clinics according to local needs and resources. (1C)

Question 15: What health management measures are required for patients with MAFLD?

MAFLD is a chronic progressive condition that requires continuous, multidisciplinary management. Key goals are to reduce the risks of cardio-renal-metabolic disease, malignancies, and liver-related events, while improving patient-reported outcomes and overall quality of life. Effective health management relies on long-term patient engagement and active self-management supported by primary healthcare teams.[49] Key components include:

Raising disease awareness among the public, patients, and their families: Limited recognition of MAFLD is a major barrier to effective care. Primary healthcare institutions should leverage their expertise in NCD management to provide structured health education on disease mechanisms and associated risks. Education should promote lifestyle modification, adherence to standardized care, and prevention of disease progression and cardiovascular events. Delivery formats may include in-person education, community activities, and digital tools such as online platforms or social media. Integrating MAFLD education with diabetes, hypertension, and broader NCD management programs may improve overall health benefits.

Severity assessment and medication counseling: Primary care physicians should assess disease severity and stratify risk by MAFLD phenotype and stage routinely. Patients with intermediate-to-high risk of advanced fibrosis or cirrhosis should be referred to tertiary hospitals in a timely manner. During treatment and follow-up, patients should receive counseling on therapeutic goals, medication use, anticipated benefits, and potential adverse effects.

Therapeutic follow-up: Patients at intermediate or high risk of advanced fibrosis, cirrhosis, or those at high ASCVD risk require regular follow-up, including periodic evaluation of hepatic and renal biochemistry and fibrosis assessment using non-invasive modalities.

Lifestyle guidance and psychological support: Individualized dietary and physical activity interventions should be reinforced throughout management, especially for patients with obesity or T2DM. For patients with psychological distress, low motivation, or reduced self-efficacy that limits adherence, timely psychological support and behavioral counseling should be offered to promote sustained behavioral change and long-term engagement in self-management.

Question 16: How should primary healthcare institutions establish a dedicated fatty liver disease clinic?

Primary healthcare institutions should leverage their strengths in NCD management to establish standardized fatty liver disease clinics for MAFLD diagnosis, treatment, and follow-up. Such clinics should support a tiered care model with timely referral to specialist hospitals when appropriate.

1. Infrastructure: (1) Clinic facilities: A designated consultation area and regular outpatient service hours should be established. Basic equipment for physical assessment should include stethoscopes, measuring tapes, sphygmomanometers, height and weight scales, and patient educational materials. Clear and efficient referral pathways to secondary or tertiary liver care centers should be defined.

(2) Hospital facilities: Such clinics should be equipped with abdominal ultrasonography. Where feasible, additional devices such as body composition analyzers and liver transient elastography instruments are recommended to support further risk stratification and longitudinal monitoring.

(3) Medication availability: Essential medications aligned with national guidelines should be available, including agents for cardiometabolic risk management and hepatoprotective medications where indicated.

(4) Patient education environment: Where resources permit, dedicated education areas such as education centers or resource rooms may be established to support structured health education and self-management.

2. Personnel: (1) Core clinical team: Clinics should be staffed by at least one general practitioner or internal medicine physician trained in MAFLD assessment and management.

(2) Extended care team: Nurses, health managers, dietitians, and qualified TCM practitioners may contribute to individualized patient support, lifestyle counseling, and NCD co-management.

(3) Multidisciplinary coordination: A multidisciplinary MAFLD management team should be formed, including hepatologists, metabolic specialists, general practitioners, nurses, TCM practitioners, and public health workers. The team should coordinate screening, standardized management, health education, and follow-up across service areas. Follow-up recommendations are summarized in Table 4.

Conclusions

These guidelines provide a structured framework for primary healthcare professionals to strengthen screening, diagnosis, assessment, comprehensive management, and follow-up of patients with MAFLD. Primary healthcare institutions are encouraged to utilize their strengths in NCD management to improve patient education, promote understanding of MAFLD among patients and families, and reinforce long-term self-management capacity. Patients should be guided toward healthy lifestyles and early, standardized care to slow disease progression and reduce risks of hepatic and extrahepatic complications. Integration of MAFLD management with programs targeting obesity, diabetes, dyslipidemia, and hypertension will help establish a comprehensive multi-morbidity management model. Close collaboration with hepatologists and specialists at higher-level hospitals is essential to build an effective two-way referral mechanism within a tiered healthcare network. These guidelines were developed through multidisciplinary collaboration. Recommendations were formulated through rigorous review and discussion and reflect expert consensus. After extensive discussion, consensus was reached for the final version. Given regional variation in economic conditions and healthcare capacity across China, some unresolved issues were not addressed in these guidelines. As primary care experience accumulates and new evidence emerges, updates are anticipated to support ongoing refinement.

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Conflict of interest

JGF has been an Associate Editor of *Journal of Clinical and Translational Hepatology* since 2013. JL has been an Editorial Board Member of *Journal of Clinical and Translational Hepatology* since 2025. The other authors have no conflicts of interest related to this publication.

Author contributions

The first draft (WN, JS, JGF, JL), and the supervision of the manuscript (JS, JGF, JL). All authors contributed to the study conception and design, commented on previous versions of the manuscript. All authors have read and approved the final version and publication of the manuscript.

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